Scottish Hospitals Inquiry

Witness Statement of

Louise Slorance

WITNESS DETAILS

1. My name is Louise Slorance. My date of birth is [redacted] 1976. I am [redacted] years old. I am a policy and public affairs officer.

2. I am the wife of Andrew Slorance. [redacted] 1971. Andrew passed away on 5 December 2020 from what was reported as COVID-19.

3. I live with my children in Edinburgh.

OVERVIEW

4. My husband was first diagnosed with Mantle Cell Lymphoma (MCL) in 2015. In January 2019 he suffered a relapse of his MCL. It was agreed that a wait and see approach would be adopted due to staging showing a very low prevalence of MCL. Following the enlargement of a pelvic lymph node in November 2019 however, Andrew started treatment on Ibrutinib as a bridge to Allogenic Stem Cell Transplant (SCT) in 12-18 months' time. At this point a referral to NHS Greater Glasgow and Clyde (GGC) for the transplant was made (Donor allogenic SCTs are only carried out in Glasgow which acts as a national service).

5. Andrew was admitted to the Queen Elizabeth University Hospital (QEUH), Ward 4B on 26 October 2020 to undergo the allogenic SCT. Andrew developed COVID and aspergillus while he was an inpatient. Despite

interventions he passed away on, 5 December 2020. I will discuss this further below.

6. Due to COVID restrictions at the time of Andrew's admission to the QEUH in 2020, visiting was only allowed in special circumstances. I therefore was only allowed to visit for ventilation in November, and, in December 2020 shortly before Andrew's death. As a result, I am unable to comment on the conditions of the hospital during his admission, however Andrew and I were in constant communication through phone calls and text so I am able to speak to the experience that Andrew had at the hospital and the experience his family had in terms of communication outside the hospital.

7. There are some specific details I would like to mention in this statement. Prior to admission at the QEUH, Andrew and I attended 2 pre-admission meetings, the first on, 21 January 2020 and the second on, 13 October 2020.

8. Andrew was prescribed anti-fungal prophylaxis as part of the standard treatment for a patient receiving an allogeneic stem cell transplant. I have identified three occasions during his admission where his prophylaxis medication was not given. The incubation period where he could have potentially been developing aspergillus due to this presents a large period of time. Andrew was diagnosed with asymptomatic COVID-19 on the 8th day of his admission and medical notes have recorded 1 negative aspergillus test in November 2020 and 3 positive and 1 negative test for aspergillus in December 2020.

9. After Andrew's death I will discuss the decision not to conduct a post mortem on the advice of an ICU doctor. I will further discuss my experience of requesting all of Andrew's medical records from NHS GGC and what they have and have not revealed. I will finally discuss the difficulties I have had with requesting records in relation to whole genome sequencing for Andrew. These test results would allow us to calculate the probable routes and potential sources of infections however to date NHSGGC have not provided me with this information with no clear reason as to why.

10. I have prepared a timeline which sets out the dates of key events that occurred while Andrew was in hospital and key events that occurred after his death. The timeline is attached to this statement at **(LS/01-appendix 1)**.

Family Background

11. Andrew and I were married on [redacted] 2007. We have 3 children together: [redacted], 16; [redacted], 13 and [redacted], 11. I also have two stepsons: [redacted], 25 and [redacted] 22. Andrew was a faithful and trustworthy civil servant of over 20 years, dedicated to his work and loyal to each and every government he served.

SEQUENCE OF EVENTS: THE FAMILY'S EXPERIENCE AT QEUH

<u>Key events and pre-admission meetings between January 2019 – October 2020</u>

12. My husband, Andrew, was first diagnosed with Mantle Cell Lymphoma (MCL) in 2015. In January 2019 he suffered a sudden bleeding event which led to the discovery that he had relapsed from his MCL. Following his diagnosis at the Western General Hospital, Edinburgh an initial referral was made to NHS GGC to investigate the possibility of sibling donors for an allogenic stem cell transplant, while staging tests were carried out. Staging showed that there was a very low prevalence of MCL and therefore a watch and wait approach was agreed.

13. Following the enlargement of a pelvic lymph node, Andrew started treatment on Ibrutinib in November 2019 as a bridge to Allogenic SCT, to take place in 12-18 months' time. At this point a referral to NHS GGC for the transplant was made. No other option was given.

14. The first of two pre-admission meetings with the transplant team was held face to face in Glasgow on 21 January 2020 with Andrew and I, and Dr Grant

McQuaker who was one of the haematologists at Bone Marrow Transplant (BMT) Ward (4B). At this meeting we were told they had a match and wished to perform the transplant in March 2020. We were advised that the transplant would be taking place at the Queen Elizabeth University Hospital (QEUH) and not at the Beatson Cancer Centre as we had been previously informed. I asked Dr McQuaker when the transplant department had moved from the Beatson Cancer Centre and was told it had moved 18 months ago, in 2018. The shock at the quick timing was also discussed at the meeting and the transplant consultant having admitted to very little or recent experience with MCL, suggested we talk with Andrew's Edinburgh consultant, Dr Fiona Scott, in regard to the timing. At a further meeting later that week with Dr Scott we had this conversation and agreed to the transplant taking place at the end of April 2020. This timing was picked to allow us more time, keep the potential donor and have half term with the children before admission.

15. I have subsequently discovered that Ward 4B was closed in August 2015 and all patients were moved back to the Beatson Cancer Centre due to air quality issues. The QEUH Independent Review published in June 2020, identifies in 8.9.10 that, "there were particle readings indicating that the isolation rooms intended and occupied by adult haemato-oncology patients and including potential BMT patients on Ward 4B were unsatisfactory and showed evidence of potential risk for future patient infection by airborne route." Section 8.9.11 states that, "the finding prompted the urgent transfer of the patients to the Beatson West of Scotland Cancer Centre, Gartnavel Hospital where non transplant patients remained for several weeks and transplant patients remained for over two years before returning". Dr McQuaker failed to advise Andrew and I of this at the time of our meeting. Disclosure of this at the time would have allowed for the necessary conversations to be had about how we could mitigate risks or make an informed decision about how we would proceed. It has since come to light that NHS Scotland patients may be treated in BMT units in England.

16. Baseline tests needed to be carried out in advance of the transplant however these were not carried out. A colonoscopy appointment was never received,

then lockdown was introduced and shortly after, around the beginning of April the CT scan was cancelled. It is important to note that the lack of tests and communication was significant as a CT scan and colonoscopy was a vital step that should have taken place 3 months after his treatment [Ibrutinib] had commenced in November. This scan would have allowed the assessment of the effect of this treatment on the cancer. Following the CT cancellation Andrew phoned his Edinburgh consultant to confirm the transplant itself had been cancelled, which it had. NHS GGC documentation, received through a subject access request, shows that on 13 March 2020 the transplant was likely to be delayed and on 20 March it was marked as delayed. Neither of these updates were communicated to Andrew, or as far as I'm aware, NHS Lothian.

17. In May NHS Lothian Radiography telephoned Andrew directly to offer him a new CT appointment due to the previous cancellation due to COVID. As no scan had taken place since the start of treatment and despite no current plans for the transplant. Andrew accepted it and a CT scan took place in May. This scan showed that there had been a significant reduction in the level of lymphoma with lymph nodes having reduced in size.

18. At the end of July, Andrew received a phone call from Glasgow advising him that the transplant would be able to proceed in October. His Edinburgh Consultant then ordered the baseline CT scan and colonoscopy again.

19. It is worth noting that at this point and at the point when Andrew was admitted in October, he was in excellent health. He was cycling daily and was in a good physical condition to withstand such a dangerous procedure.

20. Another chest CT took place in September and the result was given verbally over the phone by Andrew's NHS Lothian Consultant, Dr Scott. Andrew remained stable as compared to the CT in July.

21. On 13 October 2020 Andrew attended the second pre-admission meeting in Glasgow. NHS GGC advised that I was unable to attend with Andrew due to

COVID restrictions. Andrew subsequently used his mobile phone on loudspeaker for me to participate in the meeting. This meeting was held with Dr Anne Latif. With a surge in COVID cases in Glasgow at this time, I asked about the risks to Andrew of contracting COVID during and after the transplant with the understanding that Andrew's immune system may take 1-2 years to recover. My questions were dismissed, and I was told that the transplant patients they had treated were asymptomatic and did fine. When I asked about the resumption of transplants and any new measures that had been introduced I was told they had continued throughout the pandemic. Shortly after this, Andrew was asked to sign the transplant consent form (which we had both received in January, had had time to digest and knew the contents well) and an 'additional' consent form due to the COVID pandemic, the Supplementary COVID Consent. Summarised by Dr Latif I was told this form said that Andrew understands that they may be short staffed, they may not have an available CCU bed and there was an increased risk of mortality from COVID. He signed it. The 2 pre-admission meetings defy GMC guidance *Decision making and consent*. This sets out that all patients have the right to be listened to, and to be given the information they need to make a decision and the time and support they need to understand it. All patients have the right to be involved in decisions about their treatment and care and be supported to make informed decisions if they are able. They also must be honest and open and act with integrity.

22. I did not see the second consent form for COVID until after Andrew died when it was included with his belongings. At no point does the form mention that Andrew could be moved out of the protected environment, necessary for transplant patients. Both Andrew and I believed that he would receive any critical care required within the protective environment of the transplant ward or ICU/critical care. Within the second paragraph of this consent form, it states that discussion would be had if there was a high risk and it weighed against the risk of delaying transplant. This highlights that for some it would be better to delay proceeding and for others it would be better to proceed. It is normal procedure for a multi-disciplinary team (MDT) meeting to take place in the

week leading up to admission due to nature of the treatment. The second consent form is attached to this statement at **(LS/02-appendix 2)**

23. There are two entries in Andrew's medical notes prior to admission on 20 October 2020. Andrew had undergone his CT scan at this point. Dr McQuaker reviewed the image and reports – "fatty liver, despite not overweight, minimal lymphadenopathy". The second comment was from Dr Anne Parker, "Severe fatty liver, minimal if any LN visible on CT scan" - the differences are notable. Neither Andrew nor I were aware of these comments, all we were told by his NHS Lothian consultant was the CT scan results were stable. There is an expectation that a full clinical decision making process would have been carried out at a MDT weighing the risks and benefits of proceeding. This does not appear to have happened, there is certainly no record of it.

24. NHS GGC were aware of the ongoing issues with 4B at this point linking the substandard ventilation and water systems and a rising risk of COVID 19 in the locality of the hospital.

25. Later in the second pre admission conversation it was established that GGC were not aware that Andrew had experienced reactions to platelets and required premedication and irradiated blood when receiving blood products. This was an example of poor communication or a lack of knowledge of Andrew's needs. The overall plan was not impacted but it required further organisation by NHSGGC. Irradiated blood only comes from Edinburgh so it should be prescribed at a point when it is predicted they are needed. The blood has to be 'biked' through and does go off after a period. It was unsettling that GGC were not aware of this. Andrew had a respiratory emergency in NHSL in 2016 as a result of this which left him with long lasting psychological effects. When he coughed, he quite often stopped breathing. This was a panic attack response which meant he would need to be talked down by myself to enable him to breathe again.

26. Due to my work I was aware of the paediatric infections that had happened at the QEUH, however Andrew asked that we didn't speak about this following

the knowledge that the transplant would be carried out at the hospital. Returning home after the meeting Andrew was visibly upset but said very little. I knew he was terrified about what was about to happen, we both were.

27. Andrew attended the Western General Hospital Edinburgh, for his colonoscopy on the 21 October. The written colonoscopy report, noted no signs of lymphoma and a normal presentation of the colon, awaiting biopsy results. This was received by NHS GGC the same day.

28. On 23 October a pre-admission COVID test was conducted by the Western General Hospital Edinburgh. The result was negative. On this day he was a day patient at the day oncology ward at the WGH to have his Hickman Line inserted. When I was phoned by nursing staff to say I could come and collect him, I was told to come to the day ward to pick him up. I refused due to the potential for COVID transmission and arranged an alternative pick up point. Both of us were acutely aware of the risk of COVID, Andrew had shielded from the outside world, and, his family all the way through lockdown to protect him as far as we could from COVID. The Chief Medical Officer (CMO) at Scottish Government at the time, Dr Catherine Calderwood, had advised Andrew to shield and work from home ahead of lockdown and schools closing. As a result of this advice and based on the associated risk, our children stopped attending school prior to the closure of schools. We were acutely aware of the very high risk to Andrew posed by COVID and took all possible precautions to mitigate risk no matter what the cost.

Admission to the QEUH; COVID diagnosis October 2020- December 2020

29. Andrew was admitted to Ward 4B at the QEUH on 26 October 2020. Due to COVID restrictions the nurse came to the doors of the ward and told us to say our goodbyes. I was not allowed to enter the ward and remained in the corridor outside.

30. On admission to the ward, a COVID swab was taken and was reported negative on 27 October.

31. On the afternoon of 26 October, Andrew text me that his isolation room was incredibly warm, and he would not require the sweaters and jogging bottoms he had packed. Over the next couple of days, the temperature in the room was unpleasant and the room thermostat was unable to control it so he reported the problem to the nurses. Subsequently, he was told that maintenance was unable to resolve this while a patient was housed in the room as the problem was located inside his isolation room.

32. On 27 October a doctor came to see him, prior to starting treatment, to say there was a bug in his Hickman Line and they would come back later to discuss. A nurse later responded to Andrew requesting a follow up stating that the doctor had gone into the wrong room, later that day the patient in the next-door room was moved.

33. On this day Andrew sent me a text that said, "*Just had a shower. It's as good if not better than ours! And room v warm so I'll be in shorts not trackie bottoms*". He also spoke about a conversation he had with the psychologist where he advised them that, "*You are the best judge of my mental health. He or colleague Kathleen are always happy to speak to you if you need it.".* I was the person to speak to about Andrew practically and emotionally.

34. On 28 October, Andrew started his conditioning treatment for the Stem Cell Transplant (day -7). Clinical notes state on this date: "gram +ve cocci in HL [Hickman line], micro will try to identify new HL inserted 23/10/20. P: continue as per protocol. Add vanc to broad spectrum Abx if pyrexial". There is no further information or follow up on this in any of the notes.

35. On 29 October (day -6) a second COVID PCR test, taken on 28 October and was reported as negative. Andrew text me this day saying, "*What a waste bringing my trackie bottoms. Far too warm for joggers!"*

36. On 1 November Andrew text me saying, " *I just want a bit of fresh air!!". "I will try to be positive but I really do miss just a bit of fresh air and a comfy seat".*

37. On 2 November (day -1) Andrew was administered with a particular conditioning medication for the first time and spiked a temperature, developed hives and suffered respiratory distress. He was treated rapidly for the medication side effects and these resolved within 2 hours. However the temperature spike demanded a repeat COVID test. He sent me a text saying he was trying to be brave in what must have been frightening situation. In the medical records it states that on this day Andrew was also started on a 3-day course of Tazocin however there is no explanation in the records as to the reason for this.

38. Overnight into the 3 November Andrew started on Dexamethosone and Ciclosporin as part of the conditioning regime and became tight chested. This resolved following a change in dosing. During the morning the same day, Andrew text me saying that he was being moved rooms within Ward 4B. He said it was something to do with COVID. *"Think they are creating a wing for any transplant patients that have COVID".* Late in the afternoon a consultant, Dr McQuaker, informed Andrew that he was COVID positive and they would shortly be doing a second test to confirm. It is important to note that the first room move took place before the test result had been established. He was also told it was too late to stop the transplant so the donor cells would be infused, as planned on 4 November. The list of negative and positive COVID PCR tests are attached to this statement at **(LS/03-appendix-3)**

39. Following the consultant's visit, Andrew rang me in tears to convey the news. In the evening, Andrew moved rooms again to be closer to the nursing station, the second move of the day. At this point I had never been contacted by the hospital.

40. In our conversation Andrew's mind was also on what the children knew. He asked me what I had told them. I told him that the children knew the truth that he was COVID positive but it could be a false positive so they were doing a second test. Our entire family were relying on Andrew communicating what

was happening while dealing with the most frightening news. He was sat in the hospital alone, his thoughts about his children and his will.

41. On 4 November the second COVID positive result confirmed the COVID diagnosis, however Andrew remained asymptomatic. Stem cells were infused (Day 0). I put in a call to Dr McQuaker that afternoon to discuss the implications of Andrew contracting COVID considering the conditioning treatment had been completed and his immune system would soon be non-existent. During this conversation I was informed that Andrew would be moved out of the Transplant ward, either to the infectious diseases ward or to the renal ward (Ward 4A). It was Dr McQuaker's preference for this to be renal as they were used to using a Hickman line. I was informed that whichever ward he was relocated to, Andrew would now be under the joint care of infectious diseases and transplant. During our call Dr McQuaker took another phone call with the news that there was a bed available on the renal ward. Dr McQuaker confirmed to me that Andrew would be moving to 4A in the next couple of hours.

42. In an email dated 18 Dec 2020 from a Nursing Staff Member she stated following a discussion with medics, "We moved AS to room 76 so he could get his Stem Cells with our Team (BMT) and then transferred to a COVID ward the following day." This communication is the first time I have seen Ward 4A being described as a COVID ward. This e-mail is attached to this statement at **(LS/04-appendix 4).** The email suggests that NHS GGC disguised the nature of the move toward 4A. The COVID consent form at no point states if Andrew contracted COVID he would be moved to a COVID ward which presents other, potentially fatal infection risks to immunocompromised patients. The supplementary COVID consent did not cover this action. NHS GGC were acting out with Andrew's consent.

43. Later that afternoon Andrew moved rooms for a third time within 24 hours to Ward 4A. Following the move to ward 4A, Andrew phoned me and told me that there was no access to bottled water on this ward (only, bottled water was drunk on Ward 4B) and this had made him very anxious.

44. According to the NHS GGC Patient Placement Standing Operating Procedures which list all rooms with specialist ventilation, ward 4A has no specialist ventilation and no HEPA filtration. For BMT rooms national guidance recommends an air change rate per hour (ACH) of 10 ACH. According to the Independent Review at sections 7.5.24 and 7.5.29 within 4B it is 6 changes and within 4A this is 2.5 ACH as opposed to 6 ACH for general rooms. The Review states at section 5.5.21, “therefore it would need to be upgraded to achieve 10 ACH, including major strip out and reinstatement of all associated plant.” And “available knowledge that show there is an inverse relationship between infection risk and air change rates; risk falls with progressively higher air change rates.”

45. That evening, 4 November, 10 days after admission it finally became clear why the hospital had not been providing me with updates. They had noted my telephone number incorrectly on admission. This would have been identified earlier had anyone attempted to contact me earlier in the admission. Up until this point there was an informal arrangement that Andrew would phone me into ward rounds. On this day a nurse, from ward 4A had realised the error when she had tried to ring me, obtained the correct telephone number from Andrew and subsequently updated me on the new ward.

46. Around this time I received a letter from the WGH confirming that the biopsies taken during the colonoscopy showed that no lymphoma was present. (I never told Andrew this).

47. On 5 November Andrew text me saying: *“I’m on the move again…. Room 9 in same ward”*. I asked him why he was moving again. His response to me was “*As I’m on IVs the staffing ratio is ‘better round the corner’. Move done already*”. This was the fourth move of a COVID positive patient within 48 hours. Andrew remained asymptomatic.

48. During a ward round on 5 November, Dr McQuaker stated that as Andrew could remain COVID positive long after the infectious period, he could be

discharged COVID positive once the transplant process was complete. Andrew and I spoke about this later on in the day, expressing our discomfort at the possibility of Andrew being discharged while COVID positive. The reasons encompassed both Andrew's safety and that of our family, with the potential of myself and the children contracting COVID. This was the last time I had any communication with Dr McQuaker and from medical records, it is apparent that Dr McQuaker was only consulted by phone for the remainder of Andrew's admission.

49. Following the move into the general specification room on 4A, the records support that Andrew became neutropenic on 7 November and pancytopenic on 9 November, which is when a patient has low red/white blood cells. He then had no immune system and was extremely vulnerable to infection, fatal risks are associated with even the most mild and common infections.

50. On 9 November Andrew started developing temperatures through the night. On 10 November - Andrew texted me to say nurses had told him his blood cultures had grown a bug. By 12 November his oxygen saturations were dropping in addition to the temperatures. The same day transplant team confirmed a bug in the Hickman line. I have subsequently learned from a test result taken on 9 November that there was a positive sample taken from his Hickman line for staphylococcus epidermidis, reported on 12 November which could have been the cause of the line infection. The positive test result is attached to this statement at **(LS/05-appendix 5)** It was recommended on 9 November, that he be started on teicoplanin and vancomycin. He was started on Teicoplannin on 10 November. The morbidity and mortality meeting (M&M) presentation I have received, states that on this day the patient was "not clinically septic" and then on 11 November "more septic". Teicoplannin was stopped on 11 November and started again on 14 November. He then remained on teicoplanin until his death, stopping briefly for a day on 4 December. He started on Vancomycin on 11 November and stopped on 14 November. No reasons for these medication changes are provided in the notes I have received, nor is there any record of decision making. I attach the

morbidity and mortality meeting presentation to this statement at (**LS/06-appendix 6)**.

51. In relation to the staphylococcus epidermidis, I am aware that on 12 November a further Hickman line test, sampled on 10 November, was negative for infection. So why did he remain on teicoplanin until death? I have never been told what his diagnosis was. Andrew had three Hickman lines. The results provided in his medical records for 12 November are only for one line and there is no identifier for which of the three lines this sample was taken from. If the line that had been found positive for S.Epi was negative within 24 hours, the most probable explanation is an environmental contaminate of the first sample. This in turn would mean that the medical records do not provide the cause of neutropenic sepsis. If the positive line remained positive, where is the test result?

52. On this day Andrew became quite quiet. He text me saying, *"I Think COVID is kicking in now. My oxygen level dropped in the middle of the night so I used a basic mask to recover them. I was given a chest Xray but no result. Temp was 39+ most nights so didn't get my platelets. No paracetamol to control temp as may be affecting my liver*."

53. Also on 12 November a pharmacist entry in the medical notes states: "note vancomycin dose missed last night and has now not received dose for >24hr (received loading dose @14:35). Note also deterioration in renal function." Further clinical entries shows that further errors occurred later this day in the administration of vancomycin. Nursing notes reveal, "error overnight and today x2 vancomycin doses missed due to miscommunication and myself not being familiar with what line on Hickman can be used". I had been told by Dr McQuaker prior to the move that renal staff were used to using Hickman lines and that was why the preference was for Andrew to be moved to 4A.

54. On 13 November Andrew's Hickman line was removed due to the possibility of a bacterial infection from the line. In conjunction with infectious diseases (ID) he was started on dexamethosone and Redesimir for COVID. The

registrar phoned me and I asked whether ID knew that he had been given Dexamethosone as part of his conditioning and early in his course of COVID as that has been found to be detrimental in the course of COVID. The registrar wasn't sure but said they would speak to ID. I was never updated further.

55. I received a text from Andrew early that afternoon saying that he would probably need to give stool sample soon regarding diarrhoea, transplant would be speaking to respiratory about his chest and that they may need to take sample of fluids from his lungs. The stool sample is requested by the haematology doctor treating Andrew that day and noted in the clinical records. I do not have test results for the stool sample. The Staph epidermidis was now negative and the CT scan report states the scan was more in keeping with atypical pneumonia, and less likely COVID 19. This information was removed from the GGC Case Review. In my opinion Andrew was left in a completely unprotected environment at his time of most need of protection. I have no records to investigate the cause of an atypical pneumonia.

56. Also on this day, nursing notes reveal that Andrew was given an overdose Gliclazide and required close monitoring overnight, a DATIX was completed. The DATIX reference is provided in the notes. I had no knowledge of this adverse event, prior to obtaining the BMT notes in February 2022.

57. On 14 November, Dr Clark writes in clinical notes "Maybe 2nd source infection."

58. On 15 November Andrew text me first thing saying his temperature was low, 35.2 and he was still on low flow oxygen. The ward round from transplant provided reassuring news that there had been no escalation in his condition and that oxygen was not being required. Dr Clark also told Andrew that the stem cells had engrafted and without COVID he would likely be discharged at the end of the week. This was upsetting for Andrew to hear. Late afternoon this changed and he was put on nasal probe oxygen again. I was updated by Andrew on this news.

59. Clinical notes from an ID ward round on 16 November suggest, “ideally need bronchoscopy, BAL to PCP PCR”. A letter sent from Dr Scott, NHS Lothian Consultant to Andrew’s GP about this period stated, “He was extremely unwell immediately post transplant with concerns about septic lung emboli.” This was not communicated to myself, or I presume Andrew, by NHS GGC.

60. It became harder and harder to talk to Andrew as he found it tough with the mask. On 16 November late in the evening, my husband text to say: “*Moving to HDU in next hour or two. Numbers aren’t getting any worse but wrap round expertise is much better if needed and any additional oxygen can only be given there*”. I was not made aware when he was moved. The NHS GGC review states Andrew was housed in room 78 on HDU. This room also had no specialist ventilation and therefore was delivering 2.5 air changes per hour according to the NHS GGC SOP on patient placement. The next morning on 17 November the ward round update explained that Andrew was now under the joint care of Critical Care and Transplant. Later that day Andrew was started on CPAP. I was led to believe that moving him to critical care was a precautionary measure however the medical notes show that this move was due to his increasing oxygen requirements.

61. The only way I could receive regular updates was when Andrew would call me during the ward rounds so I could hear what was being said, I was not phoned by medical staff. Due to his oxygen supplementation I was unable to hear what was being said.

62. On 18 November at the end of the ward round call I requested a Teams meeting between myself, transplant and CCU to fully understand the situation. I explained that there had been no direct contact with CCU doctors and that the noise coming from Andrew’s oxygen supplementation was limiting what I could hear during the round updates. I was told by Dr Andrew Clark that they did not have the time and, “there are other patients in the hospital”. I did not believe this was an unreasonable request and in fact it had been suggested to

me by a Lothian clinician who said that this was welcomed by consultants as a means to communicate with the family.

63. In the clinical records, Dr Clark notes transplant issues including, profound T cell dysfunction, secondary hypogammaglobulinemia and pancytopenia. This not only means Andrew was highly susceptible to infection but will have limited, if any immune response to infection. Dr Clark then lists general issues including “Sepsis - bacterial” and “Hypoxia - likely multifactorial”. Medical records do not indicate a clear diagnosis of a specific bacterial cause of sepsis or further attempts to identify the bacteria. An email sent by Dr Clark on this day states: “He has had septic complications post transplant...his lines were changed... he has pulmonary infiltrates / consolidation...we had hoped his hypoxia was bacterial (emboli from line) but it is worsening as his bacterial indices improve)”.

64. During the morning ward round Dr Clark spoke to Andrew regarding the possibility of convalescent plasma to treat the COVID. Dr Clark was hopeful that funding would be granted for this on compassionate grounds. Dr Clark records plan for convalescent plasma in his clinical notes. Andrew was not eligible for convalescent plasma due to his reactions to blood products. It appears from internal emails that Dr Clark was unaware of Andrew’s reactions at this time. Again on this day nursing notes state that Isavuconazole was not given “as none available”.

65. On 19 November Andrew wasn’t able to phone me anymore, he was struggling to speak. Andrew had picked up from nurses' conversations in his room that due to his O2 supplementation there were increasing thoughts of the requirement for ventilation. When he relayed this to me, I asked him if a consultant had spoken to him and his response was, “*No consultant. But I’m very nervous*”.

66. Late morning of 20 November, I received a call from Dr Appleton, an ICU consultant, who was with Andrew in his room. He told us that due to further deterioration Andrew needed to be ventilated today. I was advised that I

should come through as soon as possible. Dr Appleton advised us that Andrew had a one in twelve chance of survival. An ICU admission form states the reason for admission as “pneumonia - bacterial” and previous location as “not relevant”. A COVID 19 database form also records “CPAP pre ICU – N”, when Andrew was given CPAP in HDU.

67. I was driven through to Glasgow by my friend, [redacted], straight after. On arrival in CCU I was taken to the family room with Dr Andrew Clark and an ICU doctor. During this, I was told repeatedly by Dr Clark that the transplant had been a success. The ICU doctor talked through the chances of survival following ventilation and what potential recovery looked like. In response I asked the question of whether we should be putting Andrew through this level of intervention considering his MCL and recovery time from SCT of up to two years. I also spoke about the mental toll on Andrew from his first transplant. Dr Clark again repeated that the transplant had been a success and that it was curative. I do not accept that allogeneic SCT is a curative treatment for MCL, it offers the potential for long term control but there is not the evidence for cure. He went on to state, with the support of the ICU doctor, that they would not ventilate if they did not think there was a chance of success. Andrew was ventilated and moved to ICU early evening.

68. I would like to point out that at this point I recall clearly when I was on the video calls for the ward rounds when Andrew was in HDU, the room that had a lot of light and the door to enter was on the right-hand side of the bed as Andrew lay in it. When he was to be ventilated and I attended in person, the room was darker and the door was on the left-hand side of the bed as Andrew lay in it. They were very clearly different rooms. This illustrates that there is at least one further room move that is not recorded in the records. When did they move him and why is it not in the Patient Pathway?

69. Andrew was ventilated while I waited just outside the room with a male nurse. I was told that there were no other COVID patients in this area. Straight after ventilating Andrew, the doctor held open the door and updated me on how the procedure had gone. He said it had gone well and there were no problems so

I could go back into the room. I believed this to be against COVID guidance so asked if Andrew was fully sedated, as he was I saw no point in putting myself at further risk. As I left the ward, I observed an elderly male patient in the room next door to Andrew – he was fully dressed and eating his evening meal. These rooms have no positive pressure lobby and no specialist ventilation, nor was there HEPA filtration in Andrew's room, therefore the elderly patient was at risk of contracting COVID from Andrew. On returning home, I checked the relevant guidance in place for procedures such as ventilation. Doors should not be held open and the room should have been allowed to settle for a minimum of 15 minutes prior to individuals entering.

70. ICU clinical notes revealed that a second procedure took place late that evening. The records state, "Uncomplicated procedure. Difficulty aspirating distal lumen. CXR confirmed line position, however line 16cm in length, felt possibly not in central vein, thus discussed with Dr Wright. Plan resite a RIJ CVC and remove LIJ CVC". I was never informed about the misplacement of the line nor this second procedure, as Andrew's representative, I would suggest this was done in the absence of consent.

71. On Sunday 22 November I received 4 calls over the course of the day from NHS Contact tracing regarding a positive COVID test for Andrew. This was two sets of two calls – each set was a 'first contact call' followed by an update call confirming that contact tracing was not required. Contact tracers said they were contacting myself as the patients representative but did not know Andrew was ventilated and had been in the QEUH for 4 weeks. I tweeted the experience out of anger and frustration at having to explain my husband's situation twice on the same day and in front of my children. Scottish Government were alerted to my tweet. Following receiving an uninitiated call from the Director of Test and Protect at Scottish Government later that week, the explanation provided was that the hospital failed to a tick a box indicating that contact tracing was not required.

72. From 24 November I received daily calls from ICU to update me on Andrew's condition. He remained stable until 29 November. The nature of the updates I

received was quite variable to the doctor phoning and again what information I was given was dependant on who it was. I also had to phone the nurses to receive further information. It was only once suggested putting the phone to Andrew. There were issues about what personal information they had about Andrew, despite giving it on admission to ICU, they didn't record it until a few days later having asked me again.

73. On 29 November I was notified in the morning of a serious deterioration in Andrew's condition. I was told he was not yet at end of life and therefore hospital policy did not permit his 5 children and wife visiting. I raised the possibility of accessing ECMO and was simply told that Andrew was not eligible. I was not given a reason for his ineligibility. I also discussed with the doctor on the phone the possibility of writing up Andrew's case due to the limited studies of COVID in patients with mantle cell lymphoma. I was keen that something positive came about from Andrew's situation. The doctor said he would carry out a literature search and take this forward. I have not seen an article published that resembles Andrew's case to date. Andrew's condition remained static over the next few days.

74. On 30 November ICU notes state that "Left ankle very lax compared to right. internally rotated and plantar flxed". It is noted that a discussion was had with the consultant and a referral to orthotics, however neither investigation of causation is noted nor the potential of this being symptomatic of a stroke.

75. Also on this date, 30 November, Microbiology advice to check galactomannan twice weekly. The first galactomannan test was carried out the following day, 1 December.

76. Two galactomannan tests were carried out 1 December at 04:21 and 17:07 respectively. The results for both tests were reported at 15:07 on 3 December following authorisation by Dr Laura Cottom. The values were 1.870 and 3.820 for the first and second test respectively. A positive result is when the value exceeds 0.5.

77. Visiting specialities notes record a subsequent conversation on 3 December between Dr Anne Parker (Haematology) and ICU in respect of the result: “Contacted to discuss galactomannan result and advice micro re: ambisome. Dr Parker advised will have significant impact on renal function and K. Also likely very poor prognosis if true positive.” As the communication notes support, I was told nothing about the tests or the impact on prognosis. The communication record that references this is attached to this statement at (**LS/07-appendix 7**).

78. Medical records show that a Beta Glucan test was carried out early morning of 4 December and sent to the Public Health Mycology reference laboratory. There was subsequently a delay of over 72 hours between the sample being taken and it being received by GGC microbiology. The sample was the only received by the PHE lab on 8 December after Andrew’s death.

79. In the afternoon of 4 December I received a later than normal update call from ICU, around 4:30pm, to say that Andrew was less well. ICU communication notes state that I was told there was, “the potential for additional infection” - this is over 24 hours after they had received two positive galactomannan test results, this information was hidden from me. This communication record is attached to this statement at **(LS/08-appendix 8).** They were concerned and would try to arrange a compassionate visit for myself, only, over the weekend. At 10:30pm I received the final call to say Andrew may not make it through the night and to come in. Had I been informed on 3 December, with full transparency on what was known at that time, the way in which Andrew’s family had to say goodbye could have been very different.

80. Myself, my two stepsons and my friend, [redacted], arrived at CCU reception around 12:30am on 5 December. [redacted] stayed in the relatives room while myself and the boys sat with Andrew. When someone came to take myself and the two boys into the clinical area to see Andrew, I requested FFP3 masks that were available on the table. I was told by the woman that as we had not been fit tested for them we were not allowed and that a wrongly fitting FFP3 would fail to protect us as much as a surgical mask. We then each had

to complete a contact tracing form before reaching an area for donning and doffing PPE. A nurse then showed us the correct routine for donning and doffing PPE, including mask, gloves and aprons before taking us through to Andrew. I had not been shown the PPE process when I attended HDU for ventilation.

81. Having said their final goodbyes, Kyle and Glen left the hospital at around 4am. I spent the remainder of the night between the relatives room and Andrew's ICU room, using the ladies toilet in the relatives room area. Spending this time period around CCU, [redacted] and I made observations regarding cleaning. One example is on arrival there was a Biro on the toilet floor along with other rubbish. The cleaners attended around 7 am yet the Biro remained in the same location throughout our attendance.

82. Around 6.30am I went back into Andrew's room, medical staff were handling Andrew and I was told not to enter, I remember being shocked in respect of the angry tone with which this was said. When I returned, the day staff were in and asked if anyone was with me and they would come and speak to me in the relative's room soon.

83. Later Dr Pam Doherty and Andrew's nurse came to the relatives room, introduced themselves to [redacted] and relayed the news that Andrew was "actively dying" and they would be turning off ventilation shortly. It was explained that patients take a varying amount of time to die following this and I would be alone in the room. [redacted] accompanied myself and Andrew.

84. Andrew died at 11:36am on 5 December 2020. Dr Doherty and the nurse would come and speak to myself and [redacted] in the relatives room following Andrew's death.

85. Following Andrew's death, Dr Doherty informed me that I should expect the medical death certificate by 9am Monday 7 December and contact from the Registrar that same day. [redacted] and I left the hospital with all Andrew's

belongings at 1.30pm. [redacted] had never been asked to complete a contact tracing form.

86. Around 8pm on 7 December I was phoned by an ICU doctor regarding the delay in issuing the death certificate. I was told then that the delay was due to all COVID-19 deaths requiring to go to the Procurator Fiscal (PF) but as the PF had now signed off the death, I would receive emails for the death registration by 9am Tuesday.

87. As part of this conversation, I was asked whether I had any concerns or questions regarding Andrew's death. I explained that my main issue was to identify how Andrew had contracted COVID within the protective environment of Ward 4B and to ensure that the appropriate infection prevention and control measures were in place to ensure no other transplant patient succumbed to the same fate. In addition, I asked whether whole genome sequencing (WGS) had been carried out to identify the source of the COVID. The doctor did not know but said he would find out. I was now informed I would have the death certificate by 9am Tuesday 8 December. Having not received the death records the following morning, I was again surprised to receive a further call from the ICU doctor at 1:30pm on 8 December. It was then explained to me that due to the comments I had made in the previous conversation, they had delayed issuing the death certificate while they made further enquiries into infection prevention and control procedures in place on Ward 4B. It was at this time I was told of three clinical staff on Ward 4B being found to be positive for COVID-19 at the time Andrew was found to be COVID positive. The ICU doctor carried on by saying that he was happy with the infection control measures in place on the ward and saw no reason for an autopsy to be carried out as, "it wouldn't tell us anything we didn't already know". He asked whether I was in agreement with this. Prior to this there had been no suggestion that a post mortem would be required, certainly there was no clear context as to where this autopsy comment had come from. He made no reference to the WGS I had requested in the previous conversation.

88. I was offered to speak to transplant straight after Andrew's death, I declined at that time. On 7&8 December when ICU rang me transplant's offer to speak to me was repeated, I again declined. I was angry that transplant had said so many times that the transplant had been a success, as Andrew said in a text to me, "making the point they've done their bit to the letter!!", yet he contracted COVID while under their care and died. After Christmas 2020 I received a letter repeating the offer and saying sooner rather than later is better, I did not respond as I was waiting to see the medical records.

89. It was 8 December at 14:11 that I eventually received the death certificate. The death certificate form is attached to this statement at **(LS/09-appendix 9)** It listed the primary cause of death as COVID19. But it also listed the time interval between onset and death as 1 month and 9 days, which takes you back to the date of admission. It is evidenced in negative test results that Andrew did not have COVID-19 on admission. In addition, ICU clinical reports clearly report the length of illness prior to admission to ICU as well as the length of time the patient was there. In part 2a of the Death certificate it states that Mantle Cell Lymphoma was a cause of death with a time interval between onset and death of 4 years. Andrew was diagnosed in 2015 so this was also inaccurate. Part 2b listed stem cell transplant time between onset and death - one month. The question on the certificate that asked if the body was a public health hazard was initially ticked no, subsequently crossed out and then the yes box was ticked. Following a conversation with COVID Deaths Investigation Unit (CDIT), it emerged that the report to them in respect of Andrew's death, on 7 December 2020, stated that the family had no concerns around the circumstances of Andrews death. This resulted in the investigation being closed at the time. Since the call with CDIT I have received a copy of this form through SAR. I assume this is the copy that was sent at this time, however an internal email from Dr Andrew Mackay on 24 November 2021 states that he will complete the form to report to PF via SFIU. It is unclear when the only version I have was submitted. The form as stated was not true, I expressed concerns to them in response to NHS GGC posing the question. They made no attempt to correct the record.

90. In paragraph 84 I stated the reason I was given for the death referral to the PF; all COVID-19 deaths required reporting. The Mortality and Morbidity (M&M) presentation of January 2021 states, “been reported to the Procurator Fiscal as possible hospital acquired infection (HAI). Been reviewed by local infection control team who say indeterminate as was still in window to become positive after admission”. Internal NHS GGC emails state this was not HAI, long past January 2021. The UK wide definition for HAI COVID-19 was >7days probable hospital acquired. Furthermore, a COVID 1st stage mortality review has “IPCT discussion / assessment – No" and “MM Datix – NO".

Medical Records and Aspergillus test results

91. Shortly after Andrew’s funeral I still had substantial concerns around the decision to proceed with the transplant, in light of COVID and the negative biopsy results. As a result of this I requested all of Andrew’s medical records from both NHS Lothian and NHS GGC on 22 December 2020.

92. Shortly after, I received some medical notes from NHS GGC through the post. Having reviewed what had been sent, it was immediately obvious that this was not a complete set of records. I emailed NHS GGC on 18 January 2021, specifying the exclusion of scans, x-rays, cultures and the clinical notes from his time within the care of the Bone Marrow Transplant (BMT) team.

93. At the end of January 2021, I received a second tranche of notes through the post. The covering letter referred to lab results that would be emailed in due course. The email was received on 1 February 2021. Contained in the second tranche of notes were positive aspergillus tests results, including the 2 positive galactomannan tests carried out on 1 December 2020 which had both come back positive and the beta D Glucan test carried out by the Public Health England Mycology Reference Laboratory. At the point these tests had been conducted Andrew was already in ICU and was ventilated and paralysed. This was the first time I had ever heard of aspergillus. No one had advised me at the time and Andrew was not able to receive information like this. I also still did not have any clinical notes from the BMT team.

94. I conducted my own research online and found that this was a fungal infection that can prove fatal in immunosuppressed patients. This is why the protective environment of Ward 4B and the appropriate use of anti fungal prophylaxis are crucial in mitigating this risk.

95. I was aware of what medication Andrew should have been on as on Andrew's admission he received a copy of his treatment protocol which he'd sent me at the time. This lists all the medication that Andrew should be on with dates bar anything additionally required for emerging infections or other clinical need during the admission.

96. According to his protocol, Andrew should have started Posaconazole on day 0 which is the day of infusion of the stem cells, 4 November 2020. The protocol states that the levels should be checked on day 7, 11 November. However, when looking at the blood science spreadsheet, I could see that the level was not taken.

97. There was a gap in information and there were no notes regarding prophylaxis and any clinical decision making surrounding it. As I did not have BMT notes, I had no medication charts nor clinical notes which may have described the stoppage.

98. I would like to point out that when I had requested the records I had received the assistance from a medical colleague to assist in filling out the request for Andrew's notes to ensure I received all the notes. Despite this I was not provided with everything I requested.

99. I subsequently spoke to Linsay Allan from NHS GGC legal aspects team on the phone. Ms Allan told me that the BMT notes were <u>not</u> on the portal and that the service manager for haematology would need to be contacted and she provided me with the phone number.

100. In July 2021 I met with Anas Sarwar about my concerns about the QEUH. I was aware he had taken an interest around what had happened at the hospital and due to his knowledge I wanted to engage with him. Jackie Ballie also became involved at this stage lodging parliamentary questions for answer by the Scottish Government, namely the Cabinet Secretary for Health, Humza Yousaf. She also wrote letters to members of the Senior Management Board for the Greater Glasgow and Clyde Health Board. None of these referred directly to Andrew's case at this time. No substantial answers were received. Anas also raised the issue at First Ministers Questions (FMQs) on the 18/25 November and 2 December 2021.

101. I did not contact NHSGGC again until 23 September 2021, when I again raised the issue of missing medical records specifying the bone marrow transplant notes. I had emailed Linsay Allan directly, as the person I had been in contact with to date, however, I later became aware that Linsay had left NHS GGC earlier in the year despite the email address still being active and there being no out of office reply. I therefore emailed the generic email address for patient access to medical records on 8 November 2021 raising the lack of any bone marrow transplant clinical records.

102. On 9 November 2021 I received a ZIP file by email containing all the ICU medical notes. These notes were very detailed and contained minute by minute notes, including care, contact with myself and decisions. There was an entry in the ICU communication notes that mentioned that Dr Pam Docherty had told me on the 4 December that there was, "potential for an additional infection," as well as noting the two positive galactomannan tests in the clinical notes. The two positive results are received and referred to in notes of the previous day, 3 December.

103. Again, no BMT notes though. On this day I also received an apology from a supervisor in the team for anything that had previously been missed and that this had now been processed for me.

104. Following interviews between myself, the Daily Record and BBC Scotland, the story of my husband's death was run on 18 November, along with Anas Sarwar asking FMQs in the Parliament on the same day. A letter dated the same day was sent to me from Dr Margaret McGuire, the Director of Nursing at NHS GGC. In her letter Dr McGuire wrote that following the media coverage she would like to offer to meet with me, with senior clinicians and nurses. However, an email from Dr Andrew Mackay to Scott Davidson on 24 November 2021 states, “I remain happy to meet Mrs Slorance, but understand that we are likely well past the point where that would have been of assistance to either party.”

105. Dr McGuire went on to assure me that they will be open and honest and they do not wish me to have doubts or unresolved concerns. Dr McGuire then stated that this would be better held face to face. As a family we were still limiting contacts and avoiding crowded places so the emphasis on face to face felt inappropriate and honestly, unacceptable in the circumstances. In my response to Dr Margaret McGuire’s letter of 18 November 2021, I again requested GGC provide the acute notes from transplant along with other missing records. I also made a subject access request for both myself and Andrew.

106. On 25 November 202, I received a voicemail from the First Minister’s Private Secretary stating that the First Minister (FM) had emailed me a letter that morning regarding Andrew’s case. I attach a copy of this letter to the statement as (**LS/10-appendix 10**). The letter outlined the initial actions that the Scottish Government would take. An external review would be carried out by NHS Lothian, commissioned by the Chief Nursing Officer (CNO) Alex McMahon and Health Improvement Scotland (HIS) would carry out a general review of aspergillus in the QEUH. In earlier versions of this letter it was stated that the Cabinet Secretary for Health had instructed HIS to carry out the aspergillus review. I would be kept updated. I replied to the FM that day requesting actions to be taken immediately to ensure the safety of all haemo-oncology patients at the QEUH, both paediatrics and adults. This would not be replied to until April 2022 following further correspondence from myself.

This is despite a draft response from the FM being submitted to her private office on the same day. Government communication received through SAR, highlights that the FM failed to respond to the proposed draft and subsequently the letter was pulled due to a delay on the Lothian review.

107. On 6 December 2021, I was contacted by Stewart Whyte from NHS GGC Information Governance to advise that he would be taking forward the Subject Access request aspect of my letter to Dr McGuire.

108. On 22 January 2022 I received a reply from Dr McGuire. Dr McGuire stated in this that I had been provided with the BMT notes in the notes posted to me on 5 January 2021, i.e. the first batch of notes I was sent.

109. On 25 January 2022 I received the SAR response from Stewart Whyte. This contained a further four files of clinical records. There were still no acute records from BMT.

110. On 30 January 2022 I requested a review of the SAR, specifying among other things the retrieval of the missing BMT notes. In Stewart Whyte's response to this on 31 January, he highlighted that clinical notes would normally be provided by the legal aspects team. This is my reply to this: "*In regard to the BMT notes, yes they should be provided by legal aspects but have not been and this forms part of the reason for my subject access request, as I stated in my letter to Dr McGuire. An email from Jennifer Hayes on 061221 in Correspondence 4 may provide part of the answer to this issue – "Re inpatient stay, when I looked on Track Care, it looked like he spent all of it in ICU – is that incorrect or is there a bit behind the scene that I can't see?*"".

111. On 7 February 2022, Mr Whyte emailed again stating that, "the BMT records are kept in the clinical portal system, all of which were provided on 5 January 2021". Mr Whyte went on to explain why the CareView notes (ICU) had taken 3 follow ups by me to receive: *"CareView records were provided to you by email on 9 November 2021. CareView records cover ICU beds but this was overlooked as Andrew was in an ICU bed but our system had the bed marked*

as CCU therefore the records staff did not check for CareView records for the original response." This reason is not supported by an email from Dr Andrew Mackay to Scott Davidson saying: "T*he potential for additional infection is a direct quote from the patient's communication notes on Careview. This section is not routinely printed out via portal so I can only assume that a formal request for Careview notes was made*". In my response, I outlined that there was evidence that the BMT notes were not on the portal in January 2021 so I could not have received them.

112. On 11 February Mr Whyte emailed stating that he had reviewed the portal with the clinical service manager and both, "the nursing notes and some medical notes were uploaded to the system in December 2020". They should have been provided on 5 January but they would reprint and review before sending to me.

113. On 22 February 2022, I received another letter from Dr McGuire which states the following: "*When you advised us again on the 30th January 2022 that you still did not have the BMT records, a further investigation was undertaken and the team reviewed Clinical Portal to print all records which could be identified as relating to Bone Marrow Transplant. A clinical review of the records was undertaken to check for accuracy, which was completed on the 16th February 2022. On the 17th February a Clinical Portal audit was performed at which point it was confirmed that the records in question were not scanned until 12th January 2021 and therefore could not have been included in the original records sent on 5th January 2021. The records had been quarantined in the scanning folder for a period due to Covid measures. The Health Records Team had mistakenly assumed that the BMT records had been uploaded to the Clinical Portal when the notes were printed and sent to you on the 5th January 2021."*

114. By the end of February 2022, I finally received a paper-based copy of the BMT nursing and medical notes.

115. Despite the onerous journey I have been on to obtain the medical records I now have, I have no confidence that this is a complete set. Missing information has been outlined throughout this statement.

116. I would also like to point out that there are glaring errors in the records that remain without explanation. For example, the infection control form lists COVID 19 tests and sampling method differs from the information contained in the excel spreadsheet provided by Margaret McGuire. For example on 27 November 2020 the spreadsheet states they took a throat and nose swab. This couldn't have happened as Andrew was ventilated at this point. The infection control form however states that a nasopharyngeal swab was taken which makes sense with Andrew circumstances at this point. How can two sets of 'records' have different 'facts' about the method of sampling that occurred?

117. I am also aware that there are specific documents for the reporting of M&M meetings and for recording decision making, such as a preadmission multi-disciplinary meeting. I do not have these documents.

118. This year I have become aware, through a further subject access request, that there are full notes from microbiology, Infectious Diseases and respiratory that I have also not received. I submitted another request for this and any other forgotten records on 22 February 2023. I received a response on 22 March 2023 stating that, "*the board have complied with its obligations to provide you with all the information you are entitled to receive in response to the requests you have submitted"*. I requested all medical notes in December 2020. The response, and all previous documentation received, fails to provide documentation of the microbiology team's daily input into the decision making while Andrew was on ITU, which was referenced in an internal email from microbiology that I received through SAR.

119. To further illustrate the significant problems with how NHS GGC are maintaining their records. I wish the Inquiry to consider the following. As a result of one of the SAR requests, I have received extracts from BMT forward

planning lists. This document includes planning for Andrew's transplant however the dates on it are incorrect. They seem to be planning for the transplant to take place as early as July 2019 when Andrew was on "watch and wait". They record commencement of Ibrutinib six months earlier than this actually occurred. Had NHS GGC been working to the correct timelines and ensured accurate record keeping, then the transplant could have taken place up until May 2021. This would have allowed Andrew to have proceeded with the transplant when COVID did not present the high risk it did from October to December 2020.

Internal Case Review

120. I attach a copy of the NHS GGC Case Review on Andrew's case to this statement as **LS/11-appendix 11.** It must be noted first and foremost in respect of the NHS GGC case review that this was initiated in response to media coverage on 18 November 2021, not proactively by the health board following a patient death from an HAI, at the time of death, as should be the case. This is despite NHS GGC statements to the media:

BBC Scotland on 18 November: "After an initial clinical review, we are confident that the care and treatment provided was appropriate and we do not recognise the claims being made."

Daily Record on 18 November: "There has been a clinical review of this case and we would like to reassure the family we have been open and honest and there has been no attempt to conceal any information from them."

121. *Learning from adverse events through reporting and review* is the national framework developed by the Adverse Events Programme Board, for which Dr Margaret McGuire was the Co-chair. In Andrew's case, NHS GGC did not classify his death as an adverse event. In a letter from GGC's Director of Nursing, Dr Margaret McGuire, on 21 January 2022 she states: *"We do have robust systems and processes in place to investigate when there has been an*

adverse incident or event for a patient, and there are clear criteria for a situation like this. Whilst I do not wish to upset you any further, or be at all insensitive, we did not undertake one of those processes at the time of Andrew's death, as we did not believe there to have been any failures in Andrew's care."

122. During Andrew's admission he contracted two hospital acquired infections – these are clearly incidents or adverse events as defined by the national framework for adverse events.

123. Conversely, NHS GGC looked to reassure the public at the time of writing using the concurrent media attention and issued the following statement to the media.

124. NHS GGC said, "There has been a clinical review of this case and we would like to reassure the family that we have been open and honest and there has been no attempt to conceal information from them." The media were also sent background information including: "After being diagnosed with COVID, Mr Slorance was moved to a negative pressure room within the same ward." Ward 4B does not have a negative pressure room, placement in a negative pressure room would have been against NHS GGC's own BMT Policy and Patient Placement Policy and in fact, Andrew was never in a negative pressure room. There was an e-mail from Dr Christine Peters on 18 November 2021 to Professor Angela Wallace who was Director of Infection Prevention Control at Greater Glasgow. This states that a negative pressure room would be against patient placement policy. I attach a copy of this e-mail to this statement at **(LS/12 – appendix 12**).

125. Subject access information has confirmed that NHS GGC began the internal review of Andrew's case on 19 November 2021 and finished on 25 November 2021. The review gives the impression that Andrew was covered by anti fungal prophylaxis throughout however after reviewing the medical records and subject access information I have identified 3 occasions where the medication was not given, following initiation. I have created a chart which

sets out the medication he was given and when at **LS/13-appendix 13)**. Given that Andrew had 3 positive aspergillus tests results and clinical presentation suggestive of invasive aspergillosis I expected that the case review would cover this absence of anti fungal medication, particularly as Andrew was an immunosuppressed patient that was housed outside of the appropriate protective environment, in order to consider its significance in the death of a patient. The GGC Review chose not to cover this. I have created a chart based on the test results that demonstrates the gaps and the associated range for incubation of aspergillus. I attach this chart to the statement at **(LS/14 – appendix 14).**

126. During the construction of the review, the absence of anti-fungals was raised in an email from Dr Clark to Dr Mackay on 21 November, "the Posaconazole was only given for 2 days and there was a break of 4-5 days with no antifungal therapy. I do not think this made any difference and am relaxed about it but I think we should not have the statement you made about Posaconazole prophylaxis throughout the stay in BMT unit – he was not there from day 0, posa started on day +1 and finished after a dose on day +2". The chart reveals the extent of Andrew's vulnerability during his admission.

127. An internal report was submitted for the NHS GGC case review by Dr Andrew Clark. I attach a copy of this report to the statement as **(LS/15-appendix 15)**. This references that the period of pancytopenia was particularly stormy for Andrew and was almost certainly not related to COVID. He then references that this was most likely to be bacterial though other atypical infections can never be excluded 100%. The information is omitted from the GGC case review. Dr Clark also states in his report that it looks as if Andrew, "could have developed a co-infection with Aspergillus. Tests became positive despite being on ISA [Isavuconazole] which could mean resistance to Fungi Azoles [Isavuconazole is an azole]. The AG [galactomannan] test can be falsely positive but his levels were high as was his Beta, D Glucan." Again this specialist opinion is not reflected in the review. Through making a number of SAR requests I obtained an internal version of the NHSGGC Case Review

which differs from the version I received which I attach to this statement as **LS/16-appendix 16.**

128. The GGC review states that, “repeat aspergillus antigen serology”, was performed on 1/12/20. The meaning of this statement is unclear. ‘Repeat’ tests were done 18 days after, the initial (negative) test, however escalation of anti-fungal medication, with the initiation of Isavuconazole at the time of the initial test. The review does not provide adequate reasoning for the tests on this date, nor does it address the high and increasing value of the results of the 2 tests. With the review stating empirical treatment as the reason for the escalation of anti-fungal treatment in mid November, why were the repeat tests not conducted earlier?

129. The GGC Review states that the clinical picture was suggestive and not diagnostic of aspergillus. Diagnosis for this group of immunocompromised patients post-transplant is particularly difficult as they receive prophylaxis treatment, diagnosis should therefore be defined by the EORTC (European Organisation of Research and Treatment of Cancer) guidance. This is not referred to in the GGC Review.

130. Outlining relevant epidemiology within the hospital at the time, Dr Christine Peters, clinical lead of microbiology, stated the following in an internal email on 18 November 2021: *“I was involved in the microbiology advice for the patient that is being discussed in the press and recall the case very clearly. We were treating the patient for presumed Aspergillosis based on clinical findings and galactomannan (antigen) positive tests. This is not a definitive diagnosis, but was the most likely cause of infection at the time of demise and he was on full treatment with antifungal agents. The negative PCR that came back after death does not rule out the diagnosis. “Re aspergillus I am aware that in Nov 2020 there was a paediatric haemonc case who died of aspergillosis who had also been housed in 4B, and we highlighted fungal infections in the paeds group to the IPCT at the time. I think this may be relevant in any retrospective assessment of the fungal infection risk as well as*

the fact that he was not housed in a positive pressure room throughout his neutropenic stage." This was not included in the case review, nor did records show that further investigation occurred, and Dr McGuire's letter stating there was no need for further investigation.

131. On 2 December 2021, the First Minister, Nicola Sturgeon told the Scottish Parliament, *" I asked NHS Greater Glasgow and Clyde to do an internal review. It has advised me that, based on the work that it has done so far, there is no child who had Aspergillus noted on their death certificate as a direct or contributory cause of death".*

132. Not only was this key epidemiological information and opinion excluded from the review, as was Dr Peters clinical involvement, but the addendum on aspergillus in the review was authored by Dr Laura Cottam, Consultant Microbiologist at the Glasgow Royal Infirmary.

133. The Review also references the absence of BAL or tissue sampling making confirmation very difficult. BAL sampling was suggested on two occasions, it was not carried out on either. Andrew was aware of the first occasion as he text me to tell me. On the second occasion he was ventilated and not deemed stable enough for the procedure.

134. Tissue sampling is a key element of a post mortem and NHS GGC have suggested that this type of sampling is required for a confirmed diagnosis of aspergillus. Without there being a previous opportunity to obtain these necessary tissue samples, why was I advised by an ICU doctor that, "a post mortem would not tell us anything that we didn't already know?". According to the NHS GGC case review this is factually untrue, a post mortem would have confirmed, or otherwise, the diagnosis of aspergillus. At the time I agreed to not having a post mortem. I was completely unaware of any test or treatment for aspergillus, the only named infection I had been given was COVID 19. Had I been informed of the positive galactomannan results and the need for tissue samples for confirmation, I would have definitely requested the post mortem.

135. There was no post mortem to confirm diagnosis and no investigations took place on or around the time of Andrew's death. The NIPCM stated in 2020: "The Healthcare Infection Incident Assessment Tool (HIIAT) should be used by the IPCT or HPT to assess every healthcare infection incident i.e. all outbreaks and incidents including decontamination incidents or near misses in any healthcare setting (that is the NHS, independent contractors providing NHS Services and private providers of healthcare). NHSGGC failed to do this for both infections. In respect of aspergillus, GGC's failure to report single cases was highlighted by the latest Health Improvement Scotland inspection report for the QEUH. The HIS report also describes the Health Board's evidence that the IPC team would review potentially related aspergillus cases 30 days either side of the positive test. The IPC review would therefore be expected to cover both the patients highlighted by Dr Peters yet this, again, was never done.

136. Fundamental to the case review and more specifically incident management, is the rooms and wards Andrew was housed in and the dates of these. The timeline and ward movements outlined in the review is factually inaccurate. These inaccuracies include wrong dates and the complete omission of two rooms on Ward 4B and 4A respectively. The actual timeline is as follows:
    - Ward 4B: 26/10 - 3/11/20 Moving 4 hours before the positive COVID result.
    - Ward 4B: 03/11-3/11 AM-PM
    - Ward 4B: 3/11 - 4/11 To be closer to the nursing station due to COVID positive.
    - Ward 4A: 4/11 - 5/11 As referred to following my telephone call with Dr McQuaker.
    - Ward 4A: 5/11 - 17/11 Moved to room 9.
    - HDU: 17/11- 20/11
    - HDU: Moved rooms at a point unknown before I attended on 20 November, single room, no lobby
    - ICU: 20/11 - 5/12 Single side room with lobby.

I cannot confirm the majority of room numbers as Andrew only told me a room number in the case of room 9 on 4A and I do not recall seeing room numbers when accessing HDU or ICU.

137. The case review also fails to explicitly state the type of rooms and the protection they offer to different patient cohorts. However, it is clear from the NHSGGC SOP for patient placement, active at the time, that Ward 4A and HDU did not provide any specialist ventilation and were therefore of general room specification. In addition, the NHS GGC SOP does not state COVID 19 as a contraindication to placement within a BMT room. Key to the placement of a patient who was known to become pancytopenic within a couple of days is full risk assessment of potential options and communication with the patient and relatives to seek agreement and consent. I have no evidence that this risk assessment was carried out, nor that these issues were discussed with Andrew, they were not discussed with me. In my view, and in regard to the consent forms that Andrew signed, once he was placed outside of the protective environment, he was being treated without consent. Neither supplementary COVID consent nor the BMT consent covered this possibility.

138. There are other examples of inaccuracies and missing information from the case review that I have not detailed in this statement but would be happy to provide to the Inquiry if that would be of interest to them.

External Case Review (NHS Lothian)

139. The completed NHS Lothian review was received by Scottish Government on 20 December 2021 and emailed to me on 19 January 2022. I attach a copy of this Review to the statement at **(LS/17 – appendix 17).** .

140. The First Minister, Nicola Sturgeon stated in the Scottish Parliament on 25 November 2021, “Those actions include an independent external review of Andrew’s case notes.” The NHS Lothian report states on page 1, “No

reviewer had the opportunity to examine the records of care" and "The method used has limitations, most notably that case notes and actual records were not seen, which would be the normal way expert opinion is usually given." An internal Scottish Government email states "the primary focus of the review was one of communication" not the HAIs I was primarily concerned with.

141. All information and opinion provided in the external case review has been based on the limited and in some cases inaccurate information, contained in the case review carried out by NHS GGC. It is also clear from information received by SAR that a direct communication line between Lothian and GGC did not exist, all communications went through the Chief Medical Officer at Scottish Government, Professor Alex McMahon. This included extensive follow up questions from NHS Lothian for NHS GGC.

142. There are other examples of inaccuracies and information omitted from the case review that I have not detailed in this statement but would be happy to provide to the Inquiry if that would be of interest.

MEETINGS

143. At the point the Reviews were published I was invited by the CMO to attend a meeting with himself, NHS Lothian and NHS GGC about the case reviews. The first meeting was agreed to take place on the 28 February 2022, which was subsequently postponed due to me raising concerns about the lack of appropriate attendees. On 21 March 2022 I received a letter from Alex McMahon advising that no further meetings would be offered on the basis that I wished legal representatives to attend. Essentially that if I wished a meeting to go ahead, it would have to be without my solicitors, I agreed to this. A further meeting was agreed for 1 April 2022 but again this was withdrawn, this time due to the attendance of Jackie Baillie who had been noted as an attendee in the first proposed meeting. In the letter from Alex McMahon withdrawing the offer of the Scottish Government led meeting, I was directed

to Scott Davidson at NHS GGC, “who stands ready as your point of contact going forward to arrange a meeting.”

144. At this point, my main focus was the aspergillus and understanding the microbiology aspect of Andrew’s care. As a result, I contacted Dr Christine Peters directly as Andrew’s treating microbiologist. Dr Peter’s replied, commenting that she was always happy to meet families and would escalate my request. On Saturday, 30 April, I received an email from Gareth Bryson, Clinical Director for Laboratory Medicine, saying that Scott Davidson would be happy to arrange a meeting between Dr Mackay and Dr Clark. Several emails later it was clear I would not be allowed to meet with Dr Peters and was again contacted by Dr Davidson.

145. By mid May 2022, Dr Davidson had proposed GGC attendees as Dr Mackay, Dr Clark, Prof Leonard (infection control) and Dr Peters and requested my attendees. He mentions in this email that he has copied in Alex McMahon “for awareness”. I confirmed my attendees as Jackie Baillie and a friend. My attendees were rejected stating that this changed the intention of the meeting and I was informed I may bring “appropriate family / loved one”, the meeting was about my deceased husband. Regarding Ms Baillie an internal GGC email comments in June 2022, “I think we should say she wants to bring [redacted]...let folk see how political she is.” A further email from Scott Davidson in regard to attendees stated his duty of care to staff due to the media and political scrutiny. My initial request was a one to one meeting with Dr Peters. Further emails were exchanged until a final email from Prof Angela Wallace, Executive Nurse Director, in August 2022 referring me to the NHS GGC complaints service. Suffice to say there has been no meeting with either Scottish Government, NHS GGC or NHS Lothian to discuss Andrew’s care or the case reviews to date.

146. [redacted]

[redacted]

Political Intervention

147. As I have stated previously to the Procurator Fiscal, I have messages on both Andrew's phone and my own regarding the involvement of Ministers and senior Scottish Government Civil Servants, namely the CMO and National Clinical Director, during Andrew's admission.

148. Prior to his admission in October 2020, there was involvement of Scottish Government officials as far back as March 2019. Following offers of support and help from colleagues, Andrew emailed Shirley Rogers and Jason Leitch regarding several months of difficulties his clinical team were facing in their attempt to secure a urgent colonoscopy. This led to Andrew having to sign a consent document to allow Scottish Government to access his medical records. This was then sent to his government email address and subsequently to Shirley and Jason. Following the medical records consent, [redacted] reportedly led to a review of how colonoscopy referrals from haemo-oncology could be expedited where necessary.

149. In July 2020, Andrew was notified by NHS GGC that his stem cell transplant was being provisionally booked for October 2020 and baseline tests, in the form of a CT scan and colonoscopy, would be carried out prior to admission. The baseline tests inform the decision making to proceed with the transplant, as well as providing a baseline to measure the success of treatment.

150. In August / September 2020, prior to those baseline tests Andrew was in a face to face meeting with Jason Leitch, National Clinical Director. Andrew reported to me that night, that Mr Leitch was 'absolutely sure' that the transplant would go ahead in October. I would expect Mr Leitch, in his position of National Clinical Director, to be aware of NICE guidance in place at

the time - COVID-19 rapid guideline: haematopoietic stem cell transplantation (nice.org.uk) as well as the clinical decision making process required for treatment of this kind at any time. How could Jason Leitch be so sure? The rates of COVID were increasing, reported by the National Clinical Director at the time, and restrictions were put in place. Even without the risk posed by COVID, Mr Leitch was sure in the absence of baseline tests and associated clinical decision making.

151. Following receipt of the medical notes I have looked for documentation of the MDT meeting to discuss Andrew's case and achieve consensus, in line with NICE guidance, as to whether to proceed with the transplant. There is no record of an MDT or the clinical decision-making process. This constitutes medical negligence as care falls below standards.

152. On 5 November, following Andrew's COVID positive test, Jeane Freeman, the current Cabinet Secretary for Health at the time, sent Andrew the following message: "*I know Jason and others are in touch and on the case to make sure everything that needs to happen to wrap around and protect you does happen. But I'm your Cabinet Secretary my dear so anything you need, you tell me and don't footer around on it. You're a bit precious and you matter to very many of us*." It would appear that even the Cabinet Secretary for Health cannot protect patients from the effects of a substandard hospital.

153. Jason Leitch, National Clinical Director, also contacts Andrew directly the same day, with the messages offering a view different to the official classification HAI COVID. Having confirmed Andrew was tested pre-admission, he goes on to say: "*You could have been incubating. Stragglers incubate longer than 14 days. What are the staff saying? And what can I do?? Negative doesn't mean you weren't incubating. I know you know that."* Andrew's response, "Not dwelling on how I got it", must have been reassuring to Mr Leitch.

154. I had had a phone conversation with Jason Leitch earlier the same day. In that call, the message had been similar regarding incubation comparing Andrew to

an “elite sportsman” where incubation had apparently been seen to be longer, Andrew was no elite sportsman. I had also asked him about WGS of Andrew’s PCR due to the potential for the source to be either the Edinburgh Cancer Centre or the QEUH but was told this was a decision for the GGC Health Board. We continued to exchange text messages and WhatsApps between 5 November 2020 until 18 November 2020. I heard nothing more until 5 December 2020 at 15:33, just 4 hours after Andrews death, *“How are things?? Any change?”*.

155. Professor Sir Gregor Smith had also communicated his influence at Health Board level stating in a message to Andrew prior to admission, *“That’s what we are here for – to breathe fear of god into the teams looking after the people that matter.”*

156. Following the CNO’s final withdrawal of the offer of hosting a meeting with myself, Prof McMahon directed me to liaise solely with NHS GGC and specifically Scott Davidson. However, it soon emerged that this was not the end of Scottish Government’s involvement. In May 2022, an email from Dr Davidson stated “I have copied in Alex McMahon”, in June, “I have had the opportunity to discuss the current situation with Professor McMahon who is supportive of this proposal, and I hope that we will be able to move forward as proposed” and in July, “I have discussed the content and approach outlined within this letter with the CNO and he is in agreement with this course of action.”

157. Furthermore, subject access request information demonstrated co-ordinated working between Scottish Government and NHS GGC from November 2021 onwards. From this, it is apparent that Scottish Government were seeking sight of all external communications regarding Andrew’s death, including the case reviews, media statements and communication with myself. Scottish Government oversight remains to the present day. Scottish Government were also kept up to date by NHS GGC on offers of meetings, calls and their content. This information would form part of the 27 FMQ briefings I have

received. (I was not sent the briefings for 18, 25 November or 2, 9 December 2021.

158. Within Scottish Government, evidence shows that my activity is monitored; from my tweets, to my allocation as Core Participant on this Inquiry. As these are published, officials write submissions on the content with advice on a potential response. The lists of people in receipt of this information include the FM (Nicola Sturgeon), Cabinet Secretary for Health (Humza Yousaf), Special Advisors and the Director General for Health. All required to respond to a widow only seeking factual answers.

Overall impact

159. By the time Andrew died, our 3 children had not seen him for six weeks. They had said goodbye on the stairs at home at 7:30am on 26 October 2020. The wider family had not seen him since a garden visit in July 2020.

160. When the first phone call came in the night of 4 December to say he wouldn't survive the night, my 9, 10 and 13-year-old rushed to dress and pack a bag each, they wanted to say goodbye to their dad. Each one of them had packed a mask, hand sanitiser, a clean set of clothes and a bottle of water and were sitting on my bed when the second call came in. The children could not go into ICU. Ten minutes later, I left them, still sitting on my bed crying uncontrollably. This image will never leave me.

161. After his death, we mourned his COVID death. This was during a period where there were strict COVID restrictions. You could not have people in your home, meaning that throughout Andrew's time in the QEUH and following his death, the support from friends and family was incredibly limited. For myself, at home, I was a single parent, but the reality was I was also supporting my scared and now, ill husband remotely while trying to keep up to date about his medical situation and treatment without ever being in the hospital. Looking

back I have no idea how we managed to get through the admission in these circumstances.

162. His funeral was limited to 20 people but we didn't mind. Andrew had shielded from the outside world and within his home, from his family, since March 2020 - this was how you kept the vulnerable, safe. I know the whole family questioned the sacrifices we had made for many months to ensure Andrew's safety and yet the hospital had not managed to protect him at all, but not one of us said it out loud. It was a burden we took on individually from the youngest member, aged 9, to the oldest, aged 81. With the information divulged in the medical notes, this all changed.

163. With full lockdown in place from January – March 2021, I read the medical records when the children were in bed. As issues arose, all I could do was internet research to understand the implications in rare moments alone. (As NHS GGC have criticised the use of internet based research by families in a previous concluding statement, I wish to highlight that I have sought expert opinion since.) During this time, I was isolated and supporting my grieving children alone.

164. As restrictions lifted, the implications of the positive aspergillus tests became clearer, and the question of why I was never told, louder. Knowing ICU had been told of the likely outcome on 3 December, I thought a lot about how that would have changed the way Andrew's family got to say goodbye. The trauma of a late night call to say get here now is difficult to put into words, the logistics are, however, easier.

165. Only two, at a push three people were allowed into ICU. Having been told the younger 3 could not go, at 10:30pm that Friday night I had to choose who could see Andrew in his final hours – his parents, his sister or his two sons? I wouldn't ask my worst enemy to make this choice. My two stepsons, with enormous brevity, sat beside their dad and said their goodbyes. Andrew's parents and sister said their goodbyes via a mobile phone on loudspeaker. I

cannot imagine the pain you must feel saying your final goodbye to your child over the phone.

166. In the medical notes ICU are told of this potential outcome on 3 December, he died nearly 48 hours later on 5 December. Each and every member of the family could have had some time with Andrew to say goodbye in person, IF, this had been communicated to us.

167. Our grief has been suspended since finding out that Andrew had contracted a fungal disease. The expression of grief is partially reliant on understanding the circumstances and causes of the persons death. Once it was clear that details from Andrew's time in the QEUH had been hidden from us, we could no longer mourn a solely COVID death – were we a COVID bereaved family like so many others over the last three years or are we a bereaved family from an avoidable death? Where do we belong? Without answers to our questions, we will never know.

168. Trust was lost. We, confidently, placed trust in the hospital and the clinicians treating Andrew to deliver his life prolonging treatment. Every member of the family, from the youngest to the oldest, was aware of the risks of the treatment and we each prepared ourselves for the worst, while hoping for the best. Since the initial media coverage we have lost trust in information given to us by NHS GGC or Scottish Government. We have watched as false statements are given to the media, spoken in Parliament and communicated directed to us, the bereaved family. It would appear that the whole truth, cause and effect, is not an objective of any review into Andrew's case.

169. Since January 2021 there has been a huge psychological impact on myself specifically. Much of the communication I have received has been sent, around or after, close of business, or to put it another way, our family's teatime and sometimes after 7pm at night. Other communication has been sent on a Friday night, a well commented on strategy, that maximises the negative impacts whilst minimising any immediate action a receiver may take. A Scottish Government email states, "*Can you send the following three*

attachments to Mrs Slorance tonight from CNO, please?". This is referring to CNO's email containing the NHS GGC case review and NHS Lothian case review. The email was sent at 7.41pm.

170. Processing these communications needed to be as internal as possible to protect my children and left me, again, feeling very isolated. I am sure that my grieving children felt the stress I was enduring at times and my guilt over that will remain with me for the rest of my life. I did not give them my full attention and support during one of the worse times in their lives.

171. The sequence of events I experienced to receive the transplant notes involved many GGC emails questioning my ability to recognise the notes in question. I am not a health care professional and despite knowing I had not received them, the constant questioning makes you doubt you own judgement. This was the case, not just with the transplant notes, but with many other issues as well, particularly when inaccurate statements were made by others. You doubt everything you know to be true, you even doubt what you see despite it being in black and white in front of you. I cannot underestimate the effect on myself and my family, it is a truly devasting addition to grieving the loss of your father, husband and son.

172. Then there is the realisation that Andrew died from avoidable harm, the consequences of a substandard hospital. Some of Andrew's friends and colleagues had known for years about theses issues yet, waved him off with fanfare. Primary systems, ventilation and water, were way below acceptable standards but here they were encouraging him into this building to have his immune system actively destroyed, the risk could be no bigger. Patients had already died and they did nothing. That is manslaughter.

173. Much of what has happened since the first media story, only serves to compound the anger and strengthen this view. The Health Board continues to withhold information, give inaccurate public statements, withdraws meetings and constructs a case review that is limited on actual fact. All this with the full support and weight of Scottish Government behind them. One could be

forgiven for believing this is a cover up in the highest echelons of our most powerful establishments.

174. The information I have received through SAR's has reinforced just how many people, both at Scottish Government and NHS GGC are involved in monitoring what I say and controlling the information I receive, in private, in public and in the Scottish Parliament, in regard to Andrew's time and death at the QEUH.

175. Both organisations have called into question my character and intruded into my personal life. As an example, this is the content of an NHS GGC email chain:

Person 1: Can we please add Louise Slorance on to our list for social listening?

Person 2: Sure do you just want social? Also do you want mentions of her or her posts?

Person 1: [redacted]. Both please. Her Twitter handle is @Louise Slorance

Person 2: Ok no worries. I'm also going to include content around Andrew as he can get mentioned without her too. Will add to daily alerts.

There is not one aspect of my life that has been left unaffected.

176. All this grieving family asks for, and has ever wanted, is the whole truth and nothing but the truth. It would appear that, that is just too much to ask.

177. I believe that the facts stated in this witness statement are true. I understand that this statement may form part of the evidence before the Inquiry and be published on the Inquiry's website.

LIST OF EXHIBITS

LS/01 – appendix 01 : Louise Slorance timeline

LS/02 – appendix 02: COVID-19 consent form

LS/03 – appendix 03: list of COVID PCR tests

LS/04 – appendix 04 e-mail chain about COVID wing –

LS/05 – appendix 05 staphylococcus epidermidis test result

LS/06 – appendix 06 : morbidity & mortality presentation:

LS/07 – appendix 07 communication record: galactomannan test

LS/08 – appendix 08: communication record: additional infection

LS/09 – appendix 09 : Death certificate form

LS/10 – appendix 10 : Nicola Sturgeon letter

LS/11 – appendix 11: NHSGGC Case Review

LS/12 – appendix 12: Angela Wallace and Christine Peters e-mail

LS/13 – appendix 13 : Chart: Antimicrobial medications

LS/14 – appendix 14: Chart: incubation period aspergillus

LS/15 – appendix 15 Internal report: Dr Andrew Clark report

LS/16 – appendix 16 Internal version of NHSGGC Review

LS/17 – appendix 17 Lothian Peer Review

COVERING SHEET – Louise Slorance

LS/01 – appendix 01 : Louise Slorance timeline

Andrew and Louise Slorance Timeline **LS/01 – appendix 01**

2019

- In 2019 Andrew relapses with Mantle Cell Lymphoma (MCL) which he was originally diagnosed with in 2015. A "wait and see" approach is adopted due to the low prevalence of MCL. At this time a referral to NHS GGC was made for sibling donor testing for the transplant.
- Following an enlargement of a pelvic lymph node in November 2019, Andrew commences treatment on ibrutinib as a bridge to allogenic stem cell transplant (SCT). A referral to NHS GGC for the transplant was made in November.

2020

21st January:

- Andrew and Louise attend the first pre-admission meeting at the QEUH with the transplant team and Dr Grant McQuaker. A transplant date of March 2020 is proposed and Louise and Andrew were advised that the transplant would be taking place at the QEUH and not the Beatson Cancer Centre.
- A further meeting took place during this week and it was then agreed that the transplant would take place in April 2020.

20th March:

- Due to the country going into lockdown and the emerging COVID pandemic, NHS GGC record Andrew's transplant as delayed.

May

- First CT since commencing Ibrutinib

September – October

- Andrew undergoes a colonoscopy and CT scan in order to prepare him for transplant in November 2020.

October

13/10:

- Andrew attends the second pre-admission meeting at the QEUH with Dr Anne Latif. Louise attends by telephone. Louise raises concerns around the COVID-19 risks with cases being very high in Glasgow at this point. The concerns are dismissed.
- Andrew is presented with two consent forms; a transplant consent form (which he was already aware of) and a supplementary COVID consent form (which he was unaware of).

21/10:

- Two entries in Andrew's medical records confirm that the CT scan has been reviewed and that the two doctors reviewing it have differing views on Andrew's liver health. Protocol dictates that a clinical decision making process should have been conducted weighing out the risks and benefits of proceeding with a stem cell transplant. There are no records available supporting that this process occurred.
- Andrew attends the Western General Hospital, Edinburgh, for a colonoscopy. The results noted that there were no signs of lymphoma and there was a normal presentation of the colon. GGC received the results on the same day.

23/10:

- A pre- admission COVID test was conducted by the Western General Hospital, Edinburgh. The result is negative.
- Andrew's Hickman line is also inserted.

26/10:

- Andrew is admitted to the QEUH ward 4B to undergo the allogenic Stem Cell Transplant (SCT). Louise says goodbye to him at the ward door. Due to COVID restrictions she is not allowed to enter the ward.
- A COVID swab is taken.
- Andrew texts Louise telling her the room he is in is incredibly warm.

27/10:

- The COVID swab taken on 26/10 is negative.
- A doctor tells Andrew that there is a bug in his Hickman line. Later that day he is told that this is a mistake and that it was the patient next door that had a bug in his Hickman line. This patient was moved.

28/10:

- Andrew starts his conditioning treatment for the Stem Cell Transplant.
- A second COVID PCR test is taken

29/10:

- The COVID PCR test taken on the 28/10 is negative.

<u>November</u>

1/11:

- Andrew texts Louise saying "*I just want a bit of fresh air!!". "I will try to be positive but I really do miss just a bit of fresh air and a comfy seat".*

2/11:

- Andrew is administered with a conditioning medication and for the first time spikes a temperature, developed hives and suffered respiratory distress. The temperature spike demanded that a repeat COVID test was taken.
- The medical records show that Andrew was started on a 3-day course of Tazocin. No reason for this is given in the records.

3/11:

- Overnight into the 3rd Andrew is started on dexamethasone and ciclosporin as part of the conditioning regime.
- Andrew texts Louise that morning telling her he is being moved rooms within ward 4B telling her it was "something to do with COVID". He believed that the hospital was creating a wing for transplant patients with COVID.
- Late in the afternoon Andrew is informed that he is COVID positive. A second test is taken to confirm.

- The first room move occurs before the first test result is reported. Andrew is told it is too late to stop the transplant. Andrew moves rooms again in the evening to be closer to the nurses station. No one from the hospital phones Louise.

4/11

- The COVID test taken on 3/11 is confirmed as being positive.
- The transplant takes place and the stem cells are infused on this day.
- Louise speaks to Dr McQuaker in the afternoon to discuss the situation. She is informed that Andrew is being moved out of ward 4B into Ward 4A. There was no access to bottled water in 4A.
- It becomes apparent that the hospital had not been contacting Louise because they held the wrong telephone number for her.

5/11:

- Dr McQuaker suggests to Andrew during a ward round that there is a possibility that he could be discharged while COVID positive.
- Andrew is moved to room 9.

7/11:

- Andrew becomes neutropenic

9/11:

- As well as being neutropenic Andrew becomes pancytopenic. He remains in ward 4A which has no specialist ventilation and no HEPA filtration.
- Andrew is started on teicoplanin and vancomycin.

10/11:

- Andrew texts Louise advising her that the nurses have told him his blood cultures have grown a bug.

11/11:

- Teicoplanin is stopped. Vancomycin medication is started. No reason for the medication change is given in the records.

12/11:

- Andrew's oxygen saturation levels drop in addition to temperature spikes. The transplant team confirm that Andrew has a bug in his Hickman line.
- The medical records support that a positive sample taken on 9/11 grew staphylococcus epidermidis which was reported on 12/11. A further Hickman line test result (taken on 10/11) was negative for infection.
- Andrew tells Louise that he is feeling the effects of COVID now and becomes quiet.

13/11:

- Andrew's Hickman line is removed due to the possibility of a bacterial infection from the line.
- A CT scan report confirms that Andrew's presentation was more in keeping with atypical pneumonia and less likely COVID 19.This information has been removed from the GGC Case Review. There are no records to investigate the cause of atypical pneumonia.

14/11:

- Andrew starts on teicoplanin again and remains on this until his death apart from 1 day on the 4/12 when it was stopped briefly. Vancomycin is discontinued on 14/11. – No reasons for the medication change are given in the records.
- Dr Clark writes in the clinical notes: "*Maybe 2nd source infection*".

15/11:

- Andrew receives reassuring news that there has been no escalation in his condition however by the afternoon this changed and he is put on a nasal prong for oxygen requirements.

16/11:

- Andrew texts Louise advising her that he is being moved to the High Dependency Unit (HDU) shortly. Louise is not advised by the hospital when this move occurs.
- The NHS GGC Review states that Andrew was moved to HDU room 78. This room does not have specialist ventilation.

17/11:

- Andrew is started on Continuous Positive Airway Pressure (CPAP). Louise was under the impression that moving Andrew to HDU was precautionary however the records reflect that it was due to his oxygen requirements. This was a single room with no lobby and no specialist ventilation.

18/11:

- Louise requests for a Microsoft Teams meeting with the Transplant and CCU teams to fully understand the situation. Prior to this Andrew was dialling her into the ward rounds to listen to the discussion but Louise could not hear what was being said due to the machinery and background noise. The request for a meeting is denied by Dr Andrew Clark saying that the team did not have the time with the comment "there are other patients in the hospital".

19/11:

- Andrew isn't able to phone Louise anymore, he is now struggling to speak. He tells Louise via text that he could overhear the nurse conversations talking about him having an increased need for ventilation.

20/11:

- Louise receives a phone call from Dr Appleton in ICU advising her that Andrew needed to be ventilated that day. Andrew was given a 1 in 12 survival chance. Louise is advised to come through to the hospital as soon as possible.
- She immediately travels through and meets with Dr Andrew Clark and an ICU doctor to discuss the ventilation. He is ventilated while Louise waits outside the room. Medical notes showed that a line later had to be re-sited due to an error in positioning.
- As Louise leaves the ward she witnesses another patient in the room opposite Andrew. These rooms had no lobby and no specialist ventilation. This patient was at risk of contracting COVID from Andrew as a result.

22/11:

- Louise receives 4 phone calls from Track and Trace as a result of a positive test for Andrew carried out in the QEUH. In anger she tweets about the situation and the Scottish Government are alerted to her tweet.

24/11:

- From this day onwards Louise receives daily phone calls from ICU to update her on Andrew's condition. He remains stable until 29/11.

29/11:

- Louise is notified in the morning of a serious deterioration in Andrew's condition. She is advised that he is not yet at end of life and therefore hospital policy does not permit her and Andrew's 5 children a compassionate visit.

30/11:

- Microbiology advice is recorded as being to check Andrew's galactomannan twice weekly.

December

01/12:

- Two galactomannan tests are carried out on Andrew. These tests are used to detect invasive aspergillosis.

3/12:

- Galactomannan test results are reported this day as being positive. A conversation is noted in the records between Dr Parker (Haematology) and ICU to discuss. It is recorded that there would be a poor prognosis if this was a true positive. Louise was not advised of this at the time.

4/12:

- A Beta D glucan is carried out.
- Louise receives a phone call from ICU to say that Andrew was less well. A compassionate visit would be organised for Louise at the weekend, however at 10:30pm that night she receives a further call advising her to come through to Glasgow immediately. Only 2 of Andrew's children are permitted to attend as well forcing Louise to leave 3 of their children at home in deep distress.
- The medical records record that Dr Docherty tells Louise that there was "potential for an additional infection". The two positive aspergillus results are noted by Dr Doherty on this day. Nothing was communicated about aspergillus to Louise.

5/12-

- Louise and her two stepsons arrive at the QEUH at 12:30am. Andrew dies at 11:36am.
- Dr Doherty speaks to Louise about the death certificate. She is advised that she could expect it by 9am on 7/12.

7/12:

- No death certificate arrives. At 8pm that night she is phoned by an ICU doctor telling her that there has been a delay in releasing the certificate due to all COVID-19 deaths requiring to go

to the Procurator Fiscal (PF) but as the PF had signed off the death, she would receive emails for the death certification by 9am on 8/12

- During this conversation Louise raises that she wishes to identify how Andrew contracted COVID within the protective environment of Ward 4B and to ensure that the appropriate IPC measures are in place in future. She also asks whether whole genome sequencing has been carried out. The doctor did not know but would find out.

8/12:

- Louise receives a phone call at 1:30pm from the ICU doctor. It is explained that due to her comments there has been another delay in releasing the death certificate. Louise is then advised that 3 staff members had tested positive for COVID-19 at the same time Andrew tested positive. The doctor suggests that there is no need for a post mortem. Prior to this no suggestion of a post mortem had been raised.
- WGS is not mentioned.
- Andrew's death certificate is released to Louise at 14:11.

22/12:

- Louise requests all of Andrew's medical records from both NHS Lothian and NHS GGC.

2021

January

- Louise receives the first tranche of medical records in early January. She reviews these and it becomes immediately clear that the records are not complete.

18/1

- Louise e-mails NHS GGC notifying them that in the request for records they had failed to provide her with the scans, x-rays, cultures and clinical notes from his time within the BMT team.

End of January:

- Louise receives a second tranche of medical records via post, the covering letter advising that lab results would be e-mailed in due course. Contained within the clinical notes are two positive aspergillus test results.

July

- Louise meets with Anas Sarwar and raises her concerns about the QEUH. Jackie Ballie starts to lodge parliamentary questions to the Scottish Government. She writes letters to members of the Senior Management Board for NHSGGC. Replies were received from the board but the answers were not comprehensive, some of the Parliamentary Questions were answered.

September

23/9:

- Louise again raises the issue about the missing medical records contacting NHSGGC.

November

8/11:

- Louise becomes aware that the person she e-mailed on 23/9 no longer works for NHSGGC so she e-mails the generic e-mail address for patient access.

9/11:

- Louise receives a ZIP file with all the ICU medical notes.

18/11:

- Anas Sarwar raises the issues for the QEUH and Andrew's case at First Ministers Questions.
- A story on Andrew's death is run by the Daily Record and the BBC.
- Louise receives a letter sent by Dr Margaret McGuire, the Director of Nursing offering to meet Louise and senior clinicians. Louise responds again requesting for the missing medical records.
- Dr Peters states in an e-mail on this day that "*we were treating the patient for presumed aspergillosis based on clinical findings and galactomannan (antigen) positive tests"…"The negative PCR that came back after death does not rule out the diagnosis"*.

19/11:

- An internal review of Andrew's case begins.

21/11:

- During this review process an internal email from Dr Clark to Dr McKay notes that Posaconazole was only given for 2 days with a break of 4-5 days with no antifungal therapy. ***Please refer to the prepared antifungal chart.***

25/11

- The internal review of Andrew's case concludes.
- Louise receives a letter from the First Minister via e-mail. This letter outlines the initial actions that Scottish Government will be taking; an external review would be carried out by NHS Lothian and Health Improvement Scotland would carry out a general review of aspergillus in the QEUH.
- Anas Sarwar again raises the issues at First Ministers Questions.
- Louise responds to the FM's letter requesting actions to be taken to immediately ensure the safety of all haemo-oncology patients at the QEUH.

December.

2/12:

- Anas Sarwar again raises the issues at First Ministers Questions

20/12

- Scottish Government receives the completed NHS Lothian review

2022

January

22/1:

- Louise receives a letter from Dr McGuire stating that she had received all of Andrew's BMT notes on 5/1/21 and that Andrew's death is not an adverse event.

25/1:

- Louise receives a response to a SAR request she has made to NHSGGC. This contains four files of clinical records that she previously had not received.

February

22/2:

- As is described in the statement, there is an ongoing discussion about the medical records which leads to the discovery that the BMT notes were quarantined after Andrew's death and as such never provided to Louise. This is set out in a letter to Louise from Dr McGuire.
- Louise receives the BMT records by the end of this month. She remains unconvinced that these are the full records.

28/2

- After the Reviews are published, Louise is invited to a meeting to discuss them. The first meeting date was proposed on 28/2 which was then postponed due to Louise raising concerns about the attendees.

March

21/3:

- Louise is advised that no further meetings will be offered on the basis that there is a disagreement about who should attend the meeting. Louise is ultimately referred to Scott Davison at NHSGGC as a point of contact. To date no meeting has occurred.

2023

February

22/2:

- Louise has become aware through the subject access requests she has made, that there are full notes from microbiology, infectious diseases and respiratory departments that she has not received. A further request has been made on this day.

March

22/3:

- Louise receives a response from NHSGGC stating that the "*board have complied with its obligations to provide you wish all the information you are entitled to receive*".

COVERING SHEET – Louise Slorance

LS/02 – appendix 02 : COVID-19 consent form

NHS
Greater Glasgow
and Clyde

COVID19 Supplementary Consent form for Transplantation

Due to the current situation in relation to the SARS-CoV-2 (coronavirus) – COVID19 pandemic we have required to make significant changes to our transplant and cellular therapy service.

As a consequence of COVID19 and its effect on our healthcare system patients undergoing transplant at this time will be at much greater risk than would normally be the case. We need to discuss this extra risk and weigh it against the risk of delaying transplant at this time. For some patients it may be better to delay transplant until the virus situation is under control, for other patients, where there is a narrow window of opportunity to proceed with transplant and there is a high risk of relapse or progression it will still be possible to proceed if all parties agree. This document serves as a record of acknowledgement of the key risks involved in delaying or proceeding at this time.

KEY RISKS OF PROCEEDING

1. Transplantation will cause profound damage to your immune system. This damage will last for many months and during this time you will be susceptible to infection. Transplant patients are likely to be at the highest risk of both becoming infected with the pandemic COVID19 virus and from developing severe and potentially fatal COVID19 virus complications. This risk will be ongoing for many months post-transplant during which time patients will require be in protective self-isolation.
2. Our service is likely to be affected by staff shortages as a consequence of infection and requirement for isolation due to the COVID19 virus, as such there may be less doctors, nurses and other members of staff to look after you while you are in hospital.

3. The hospital is under sustained pressure due to the pandemic and as such it may be more difficult to arrange investigations, specialist consultations and tests than it would normally be, and these may take longer or be unable to be provided.

4. Most transplant patients will not require intensive care during their admission, however for a minority of patients who become very unwell it may be appropriate to consider transfer patients to critical care or intensive care. The reason for doing so is to provide intensive monitoring and organ support such as breathing support using a mechanical ventilator, medicines to improve blood pressure or dialysis to support kidney function for a short period of time while the underlying problem is treated.

   Critical care areas will be under intense pressure due to the number of patients with severe COVID19 virus infection – this means that it may not be possible for you to receive intensive care support or be transferred to intensive care if you become very unwell. If this is the case, then you will be supported on the transplant unit as far as is possible. However, this support will not include measures normally available in intensive care and therefore in these circumstances you are likely to have a significantly reduced chance of survival.

Additionally, due to the pandemic COVID19 virus situation

1. Patients will be tested for COVID19 virus twice on admission to the ward and will not proceed with the transplant if found to be COVID19 virus positive.
2. Due to the risk of COVID19 virus infection, visitors for adult patients on the BMT unit will not be permitted.
3. Transplant is a very complex therapeutic process, given the evolving situation, there may be last minute disruption that prevents the transplant proceeding as intended, it is therefore possible that your transplant may need to be cancelled at short notice.

NHS Greater Glasgow & Clyde **FORM No. BMT 103 119 01**

Haemopoietic Stem Cell Transplantation Services

COVID19 Supplementary Consent form for Transplantation

I acknowledge the statements above; I am happy that there has been enough time for discussion of these matters, am happy to proceed with the transplant as planned and I agree to abide by the directions of the transplant team.

Patient	
Name: X	[redacted]
Signature	[redacted]
Date: X	13/10/20

Clinician	
Name:	ANNE-LOUISE LATTA
Signature	[redacted]
Date:	13/10/20

COVERING SHEET – Louise Slorance

LS/03 – appendix 03 : List of COVID PCR tests

Date	SARS-CoV-2 PCR result	Pre-conditioning regimen	Day
23/10	Negative	-	-12
26/10	Negative	Hospital admission	-9
28/10	Negative	Fludarabine starts	-7
02/11	POSITIVE*	Alemtuzumab/MP	-2
03/11	POSITIVE	Alemtuzumab/Melphalan	-1
04/11	-	PBSC transplant	0
10/11	POSITIVE		+6
16/11	POSITIVE		+12
20/11	POSITIVE		+16
27/11	POSITIVE		+23
03/12	POSITIVE		+29
05/12	death		+31

* 8 days following admission

COVERING SHEET – Louise Slorance

LS/04 – appendix 04 : e-mail chain about COVID wing

[redacted]

From: [redacted]
Sent: 18 December 2020 11:03
To: Joannidis, Pamela
Cc: Halliday, Lisa; Clark, Andrew; Campbell, Myra
Subject: RE: 4B QEUH patient covid positive timeline

Hi Pamela,

Yes A.S. tested positive on the 2/11/2020 but was not reported till 3/11/2020 afternoon. He was swabbed that day due to being pyrexial with his chemotherapy as part of his sepsis screen.

[redacted]

From: Joannidis, Pamela
Sent: 18 December 2020 09:30
To: [redacted]
Cc: Halliday, Lisa <Lisa.Halliday[redacted]>; Clark, Andrew <Andrew.Clark[redacted]>; Campbell, Myra <Myra.Campbel[redacted]>
Subject: RE: 4B QEUH patient covid positive timeline

Thank you [redacted] good to speak to you yesterday.
This is very helpful. Pt was first +ve on 02.11.2020.

Pamela

From: [redacted]
Sent: 18 December 2020 09:02
To: Joannidis, Pamela <Pamela.Joannidis[redacted]
Cc: Halliday, Lisa <Lisa.Halliday[redacted]; Clark, Andrew <Andrew.Clark[redacted]; Campbell, Myra <Myra.Campbel[redacted]
Subject: 4B QEUH patient covid positive timeline

Hi Pamela,

I am just replying to your email following your telephone call yesterday (17/12/2020) regarding Patient A.S. CHI [redacted] whom tested COVID positive in ward 4B QEUH.

A.S. notes are not yet scanned on portal but looking at his BMT protocol I can give you the date that I was in his room. I went into his room to introduce myself to him on Tuesday 3/11/2020 and was standing inside his room near the door, that was closed with full PPE – Gloves, apron and mask, and he was sitting on his chair. I was then in his room a further twice that day. I put his chemotherapy on a flush (Melphalan) as his nurse was on her break. I then went in later that day with his nurse to check his second chemotherapy (Alemtuzamab). All times we had full PPE on. The ward was contacted on that day to say that he tested positive for COVID. Following discussions with the medics we moved A.S. to room 76 so that he could get his stem cells by our team then transfer to a covid ward after his cells the following day. We ensured that the same nurse looked after him and minimised the other staff members contact with him following the positive result. I tested positive on my weekly asymptomatic staff test on the 9.11.2020 I was tested every Monday and my last test prior to this result was on the 2.11.2020 and was negative.

The other member of staff that tested positive was [redacted] She had face to face contact with A.S. on 28.10.2020 and tested positive herself on 5.11.2020. She was picked up via our weekly asymptomatic staff testing programme.

Hope this information helps. If you need anything else please let myself [redacted] know.

Kind Regards,

[redacted]

COVERING SHEET – Louise Slorance

LS/05 – appendix 05 : Staphylococcus epidermidis test result

B.cult-Hickman line

Time Collected	09-Nov-2020 15:07	Time Received	09-Nov-2020 18:27
Time Reported	12-Nov-2020 16:37	Order Number	M,20.5524401.H
Status	Final	Source System	Telepath

Microbiology Final

```
Report issued by NHS GG&C Microbiology South Sector
                        Enquiries 0141 354 9132
** FINAL REPORT **

INVESTIGATION: Blood Culture
SPECIMEN TYPE: B.cult-Hickman line

CONS/GP: Dr Anne Parker       Order No:L17RX8V
LOCATION: Ward 4A Ren. HighAcu QEUH
-----------------------------------------------------

Aerobic   Bottle: POSITIVE
Anaerobic Bottle: No growth 2 days

CULTURE RESULTS:                          FROM BOTTLE:

a)Staphylococcus epidermidis              Aerobic
b)
c)
d)
e)
f)

         ANTIBIOTIC   a) b) c) d) e) f)
 Teicoplanin          S
 Vancomycin           S

Clinical microbiology advice can be obtained by calling
0141 354 (8)9132 or the on-call Microbiologist

-----------------------------------------------------
Senders ref. no.

Authorised by: Dr Alison Balfour
Date/Time authorised: 12.11.2020  16:37
** END OF REPORT **
```

COVERING SHEET – Louise Slorance

LS/06 – appendix 06 : Morbidity & Mortality report

AS [redacted]

Dr Pavlina Spiliopoulou, ST6 Medical Oncology

AS - background

- 49 yo patient
- Referring source: Edinburgh
- Diagnosis of stage IV Mantle cell lymphoma in 2015
- Previously fit and well
- Anxiety/depression – diet controlled NIDDM
- Citalopram and propranolol
- Works for Scottish Government press office
- Married with 3 children

AS - presentation

- Bloody diarrhoea (2015)
- Rectosigmoid lymphomatous disease, widespread lymphadenopathy and hepatosplenomegaly. Bone marrow involvement 20%.
- Nordic protocol and LEAM autograft in May 2016
- **April 2019:** first recurrence with bloody diarrhoea
- Wait and watch approach initially but when symptoms progressed → **Ibrutinib** (Oct'19).
- Whilst on Ibrutinib: referred for allogeneic transplantation by primary consultant

Pre- transplant

- Jan'20: BMT clinic, thought to be fit with good transplant donor options
- Plans for allogeneic transplant delayed to second half of '20 due to COVID-19 pandemic
- Throughout this time patient remained clinically and radiologically stable

Allogeneic transplant

- **Pre-transplant disease status:**

Sigmoidoscopy - no macroscopic/microscopic disease

CT scan only minor changes in area of previous inguinal LNpathy – excellent response to Ibrutinib.

- ECHO: normal-sized LV with overall good systolic/diastolic function
- PFTs: FEV 91% predicted and 100% predicted

- **Conditioning regimen:** Fludarabine – Melphalan - Alemtuzumab

  Matched unrelated donor: 10/10 match, A+/O+, $CMV^{-/-}$

Inpatient

- Admitted on 26/10/2020, day -9 prior PBSC infusion
- Preconditioning regimen starts with Fludarabine on day -7
- Gliclazide (PRN fast-acting insulin) was introduced for better glycaemic control. Propranolol dose increased due to sinus tachycardia (anxiety-related)
- Isolated episode of pyrexia on day -2 was thought to be sec to Alemtuzumab reaction – Tazocin started.

On day -2: SARS-CoV-2 result is positive

Asymptomatic

Date	SARS-CoV-2 PCR result	Pre-conditioning regimen	Day
23/10	Negative	-	-12
26/10	Negative	Hospital admission	-9
28/10	Negative	Fludarabine starts	-7
02/11	POSITIVE*	Alemtuzumab/MP	-2
03/11	POSITIVE	Alemtuzumab/Melphalan	-1
04/11	-	PBSC transplant	0
10/11	POSITIVE		+6
16/11	POSITIVE		+12
20/11	POSITIVE		+16
27/11	POSITIVE		+23
03/12	POSITIVE		+29
05/12	death		+31

* 8 days following admission

Early days post transplant

- **Day -1:** SARS-Cov-2 result reported and discussed with patient, decision to continue with transplant in BMT unit and then move to dedicated ward. *Remains afebrile*
- **Day 0:** asymptomatic of COVID19
- **Day +1:** asymptomatic of COVID19 - Tazocin stopped. Mild liver function derangement
- **Day +2:** asymptomatic of COVID19 - Posaconazole withheld (bilirubin 53umol/L)
- **Day +3:** asymptomatic of COVID19 – no VOD clinically.

Early days post transplant

- **Day +4:** asymptomatic of COVID19 – early mucositis
- **Day +5:** asymptomatic of COVID19 but CRP doubled to **260**, neutropenic (neuts=N/A) - not clinically septic. LFTs static

  ⟹ Tazocin restarted.
- **Day +6:** New pyrexia, **CRP 360. Bilirubin 64 (56).**

Gentamicin added, Viral hepatitis screen, Posaconazole withheld again.

Blood cultures from Hickman line show Gram (+) cocci, Teicoplanin added.

1 dose of G-CSF dose given as per post-BMT protocol

Early days post transplant

- **Day +7:** Pyrexia continues; Hyperbilirubinemia worsens 78 (64)

Clinically looks more "septic" and mildly jaundiced

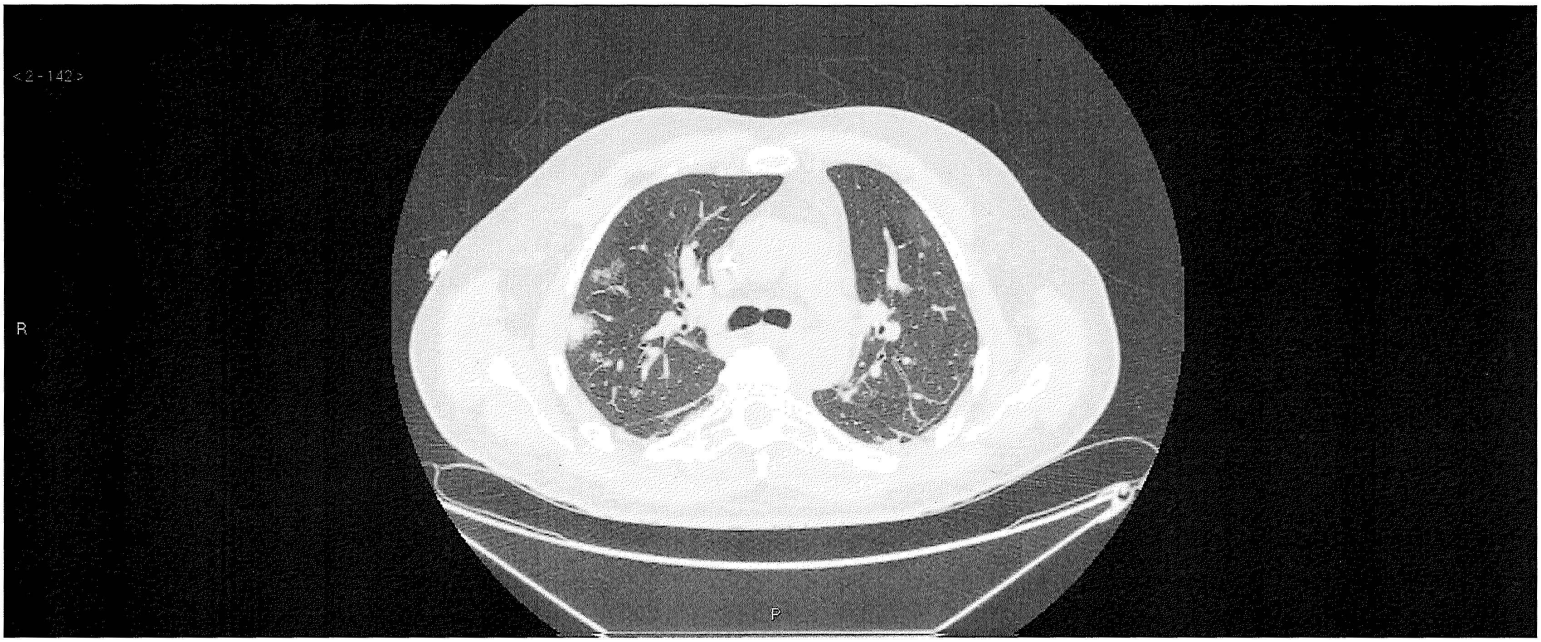
⟹ Antibiotics changed to Mero/Vanc;

plans to remove HL and perform hepatic US.

G-CSF discontinued in view of concurrent COVID19.

- **Day +8:** Pyrexia persists albeit not as high a temperature but develops new O2 requirement

Non-contrast enhanced CT CAP as new AKI on day +8 (though to be secondary to nephrotoxics).


<2-142>
R
P

Day 10 – starting to engraft….neutrophils 0.2

- **Day +10:**
  - Staph. epidermidis sensitive to Abx; CRP improving.
  - Hyperbilirubinemia improving
  - AKI worsens: ciclosporin interrupted, vancomycin changed to teicoplanin
  - First signs of engraftment
  - Discussed with Respiratory: not for BAL
- **Day +11:**
  - Creatinine continues to rise – Remdesivir stopped after d/w ID (4/5 days)

Early days post transplant

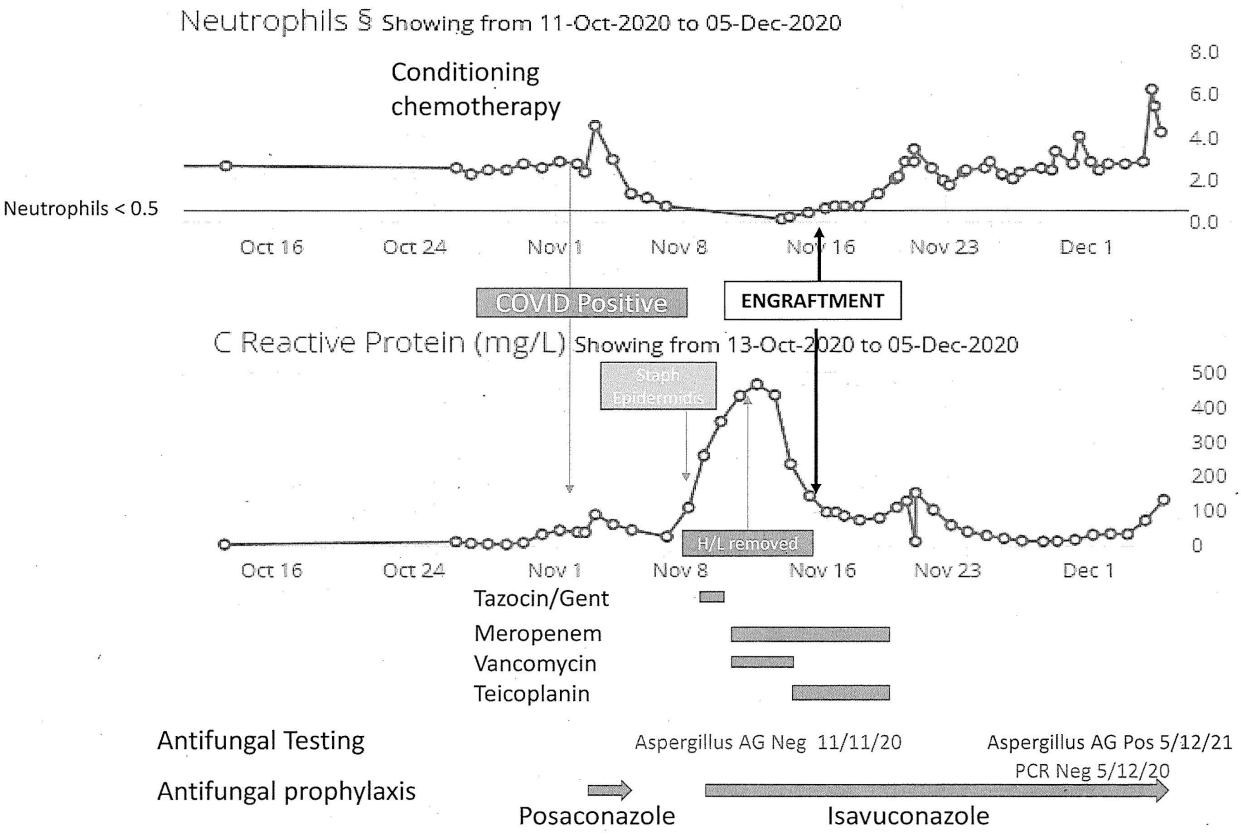
- Dexamethasone and Remdesivir started on Day 8 (ID team). Isavuconazole started too – bilirubin still deranged but static.

  HL removed

- **Day +9: Clinically stable – pyrexia settling;**

On antibiotics, steroids, remdesivir, isavuconazole, prophylactic aciclovir plus ciclosporin for GvHD prevention

Respiratory team review of images: not typical of SARS-CoV-2-induced lung changes, more in keeping with atypical pneumonia….



Antifungal Testing

Aspergillus AG Neg 11/11/20

Aspergillus AG Pos 5/12/21

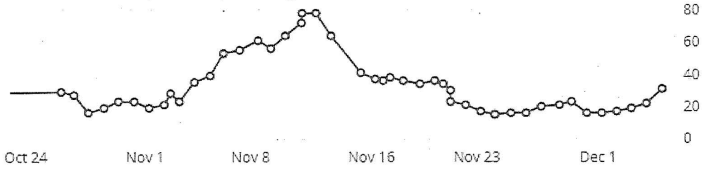
PCR Neg 5/12/20

Antifungal prophylaxis

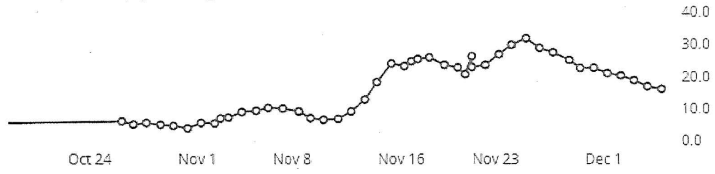
Posaconazole

Isavuconazole

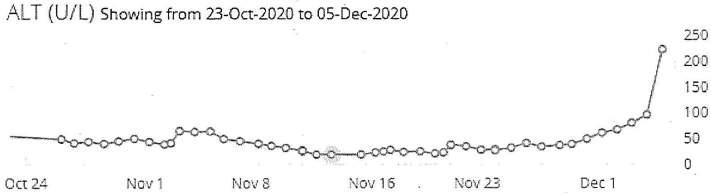
Total Bilirubin (umol/L) Showing from 23-Oct-2020 to 05-Dec-2020



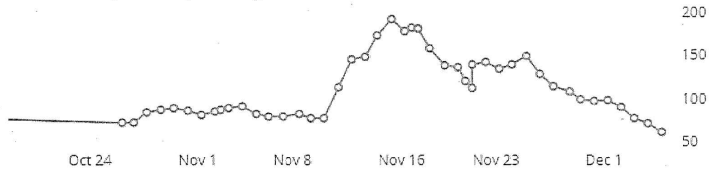
Urea (mmol/L) Showing from 18-Oct-2020 to 05-Dec-2020



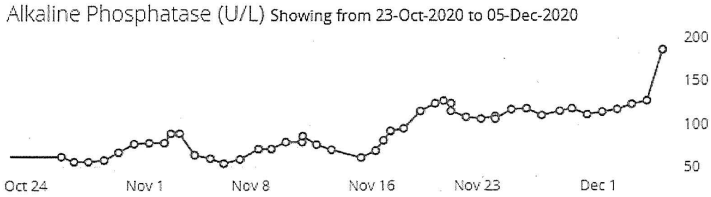
ALT (U/L) Showing from 23-Oct-2020 to 05-Dec-2020



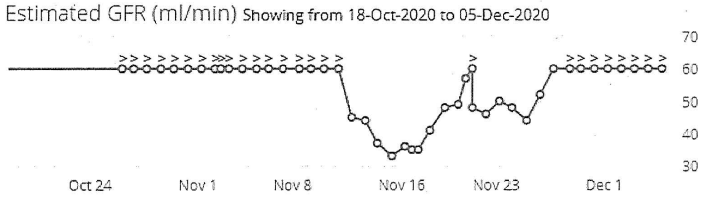
Creatinine (umol/L) Showing from 18-Oct-2020 to 05-Dec-2020



Alkaline Phosphatase (U/L) Showing from 23-Oct-2020 to 05-Dec-2020

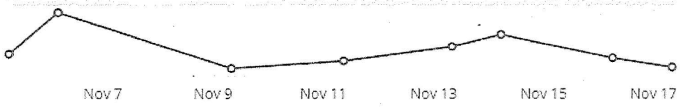


Estimated GFR (ml/min) Showing from 18-Oct-2020 to 05-Dec-2020



Ciclosporin Graph Information is available from 05-Nov-2020 to 17-Nov-2020

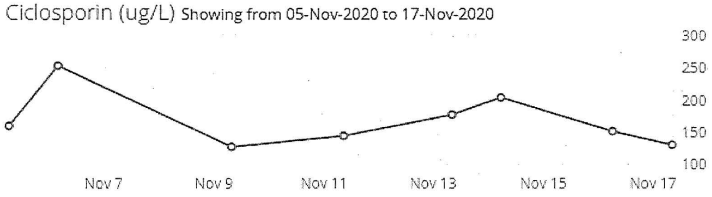
Source Telepath (8)



Ciclosporin

All | Default

Ciclosporin (ug/L) Showing from 05-Nov-2020 to 17-Nov-2020



Medical HDU

- **Day +12:** Oxygen requirements increase, on Venturi mask 35%;
  MMF started (off ciclosporin).
  Continues antibiotics + isavuconazole + steroids + prophylactic aciclovir
  Extensive respiratory viral PCR; negative.
  ID: ? PCP prophylaxis

- **Day 13:** medical HDU transfer in view of O_2 requirements going up
  Engraftment (neut 0.7) – MMF continues + steroids
  CRP improving
  ID team concerned over PCR values (C_t 22) being indicative of on-going viral replication - **Remdesivir restarted**

Medical HDU

- **Day 14:** Renal function improving – CRP reduced even further

Hypoxaemia persists and worsens; target O_2 saturations gradually lowered – some improvement with proning and intermittent CPAP

Neuts = 0.7

Patient remarkably comfortable.

Overall clinical picture increasingly resembles COVID19 respiratory failure.

Efforts to offer convalescent plasma as part of compassionate use not materialised as patient had anaphylactic reaction to PLTs in the past

Medical HDU

- **Day 16:**

Neut 2.1 - Type 1 RF worsens further

Steroids increased to MP 75mg to abrogate hyper acute GvHD affecting lung

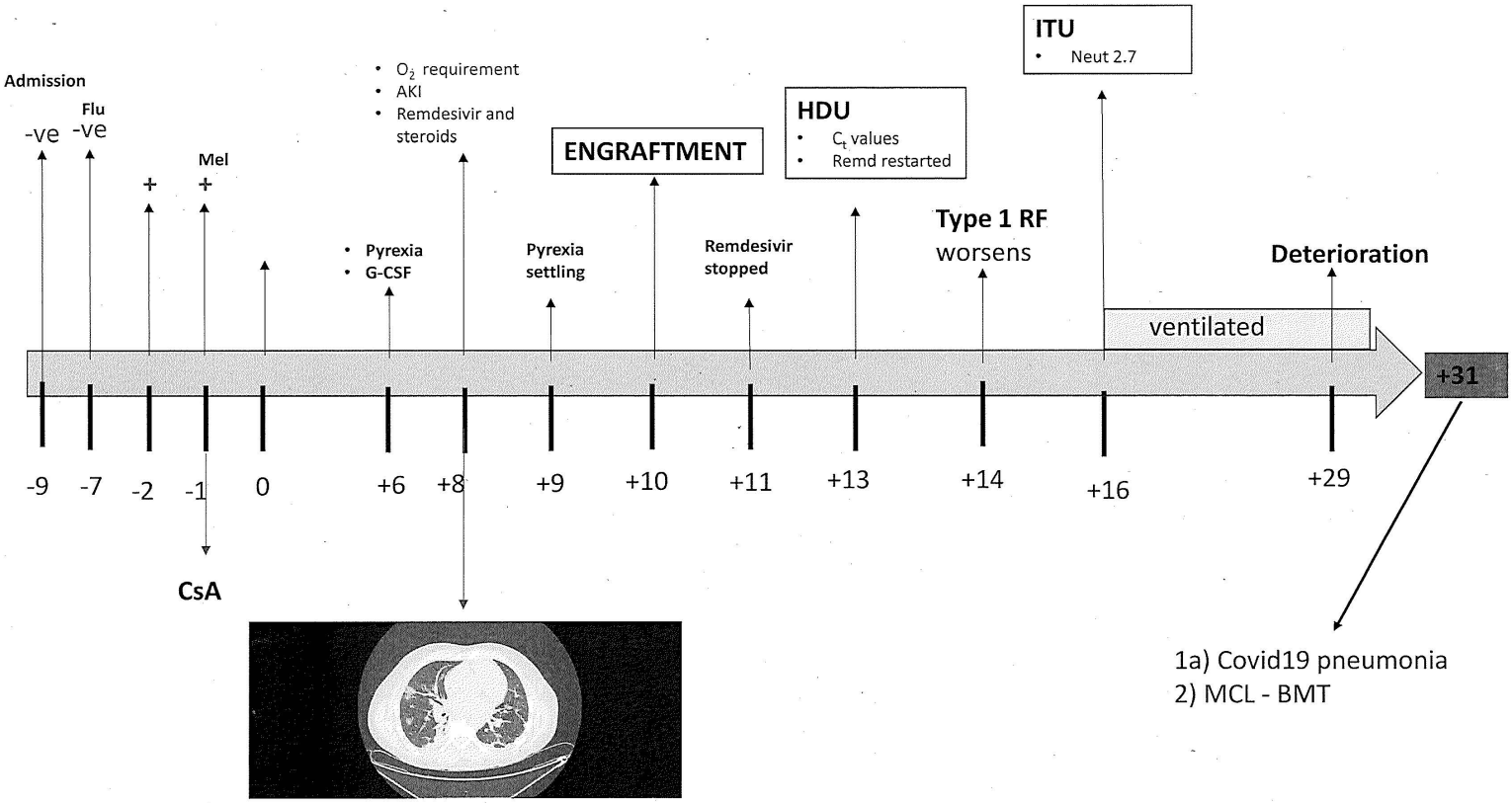
Transfer to ITU and intubation

Although initially was deemed not eligible for RECOVERY trial, eligibility was re-assessed (only for the monoclonal antibody arms of the trial) and recruited study - standard arm (remdesivir and steroids).

ITU

- High-dose steroids - frequent proning – LMWH. No signs of GvHD.
- Throughout admission: procalcitonin normal
- Day +28 Meropenem stopped – Teicoplanin stopped day +29
- Oxygenation deteriorated on day +29
- Day +29 **POSITIVE** galactomannan antigen test ⟹ **Caspofungin added**
- Day +30 **POSITIVE** Beta glucan antigen test (170pg/ml)*
- Day +30: haemodynamically unstable – CRP rise – antibiotics restarted
- Day +31: Patient passed away in the presence of partner

*Aspergillus PCR was NEGATIVE (reported after death)
Beta glucan test reported after death too


Admission
-ve
Flu
-ve
+
Mel
+
• Pyrexia
• G-CSF
• O_2 requirement
• AKI
• Remdesivir and steroids
Pyrexia settling
ENGRAFTMENT
Remdesivir stopped
HDU
• C_t values
• Remd restarted
Type 1 RF
worsens
ITU
• Neut 2.7
ventilated
Deterioration
+31
-9
-7
-2
-1
0
+6
+8
+9
+10
+11
+13
+14
+16
+29
CsA
1a) Covid19 pneumonia
2) MCL - BMT

Considerations - questions

- <u>COVID19 and HCT recipients</u>

  6-week mortality 19% in autologous and 24% in allogeneic HCT (n=500)[1]

- **Remdesivir:** Overall, combined data from a meta-analysis of 4 trials showed no significant impact on death rate ratio (0.91, 95% CI 0.79-1.05) – no reduction in hospitalization duration or initiation of ventilation[2]

  Q: is it beneficial for immunocompromised patients ??

- **Steroids:** meta-analysis showed OR for mortality 0.64 (95% CI, 0.50-0.82; $P < .001$) for dexamethasone[3]

  Q: data on transplant patients ??

[1] EBMT registry [2] WHO Solidarity Trial Consortium, NEJM, Dec '20
[3] The WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group, JAMA Sep '20.

Considerations - questions

- **Convalescent plasma** (high-titre) some benefit when given to older patients within 72 hours of symptoms[1]. No much benefit in overall population in observational studies.

- **Tocilizumab:** On the biggest phase 3 randomised trial, some reduction in the probability of progression to intubation but no effect on overall patient survival[2].

*REMAP-CAP trial (ahead of print) – Tocilizumab (or Sarilumab) have a positive effect on survival of ICU patients

[1] Libster et al, NEJM, Jan '21; [2] Salama et al, NEJM Jan '21;

EBMT guidance

- Limited data: Remdesivir perhaps some benefit; steroids definite benefit in non-transplant patients.

- Anti-coagulants; vitamin D; treatment of co-pathogens

- **Immunosuppressive prophylaxis/treatment to be continued through Covid19 as no data supporting against it.**

❖ **Pre-print (MSK) on G-CSF in cancer patients and Covid19:**

nHL (n=6/36) receiving G-CSF with Covid19 infection

HR 4.62 ($P<0.05$) for respiratory failure in the overall cancer population

Conclusions

- Already received all conditioning regimen by the time first positive result received so facing significant prolonged period of cytopenia unless went ahead with allograft
- Been reported to the procurator Fiscal as possible hospital acquired infection
  - Been reviewed by local infection control team who say indeterminate as was still in window to become positive after admission
- Multiple records of discussion with patient and wife
- Offered entry into all available clinical trials

COVERING SHEET – Louise Slorance

LS/07 – appendix 07 : Communication record galactomannan test

CHI	[redacted]
Patient Name	**Andrew Slorance**
Age (Admission)	**49 years**

[redacted]	Clinical Grade: NNP
	Referred yesterday for PN as high aspirates on enteral nutrition persist. PN 6g as prescribed not administered, RD advised given <24hr not tolerating feed could see how they progress with enteral for longer. Temperature 36.5 degrees. Proned overnight. Fluid balance -ve 253ml. Enteral rate currently at 15ml / hour, yesterday reduced from 65ml following aspirate of 340ml. enteral remained on at 45-50ml until another aspirate of 220ml obtained described as faecal smelling. Propofol infusion reduced to 18ml / hour, atracurium off. For discussion at NST MDT today.
	Date: 03/12/2020 Speciality: Haematology Reviewed By: Dr Parker Clinical Grade: Consultant
	Discussed situation. Little progress. Platelets have fallen, some clots in NG aspirates. Plan Transfuse 1 pool platelets then check FBC 1 hour after to assess for platelet increment. If the platelet count is falling after the platelets then rediscuss with haematology team Withold further clexane dose this evening Reduce methylpred to 40mg
	Date: 03/12/2020 Speciality: Haematology Reviewed By: Dr Parker Clinical Grade: Consultant
	Contacted to discuss galactomannan result and advice of micro re: ambisome. Dr Parker advised will have significant impact on renal function and K. Also likely very poor prognosis if true positive. Dr Parker will d/w haematology ward ?can draw up there to give dose tonight ?need sterile prep. Dr Appleton subsequently d/w micro team- can instead add in caspofungin for now in addition to isavuconazole.
	Date: 04/12/2020 Speciality: Nutrition Reviewed By: P Hood Clinical Grade: NNP
	PN commenced last night at 32mls /hr . Enteral feed reduced to 25mls/hr due to high aspirates . Generally 200mls every 4

CHI	[redacted]
Patient Name	**Andrew Slorance**
Age (Admission)	**49 years**

[redacted]	**Mantle Cell Lymphoma** **NORDIC protocol and LEAM autograft completed May 2016** **Returned to full employment** **Recurrence of GI symptoms April 2019** **Progressive disease evident Nov 2019** **Started on Ibrutinib** **Referred for BMT Jan 2020**

[redacted]

Problems/Diagnosis 1	Problem/Diagnosis: **COVID-19** Status: **Active**
Problems/Diagnosis 2	Problem/Diagnosis: **Relapsed Mantle Cell Lymphoma** **- Admitted 26/10** **- Allogenic BMT 4/11 - NEEDS WASHED PLATELETS + IRRADIATED BLOOD PRODUCTS** Status: **Active**
Problems/Diagnosis 3	Problem/Diagnosis: **AKI** Status: **Active**
Problems/Diagnosis 4	Problem/Diagnosis: **Vitamin D deficiency (new)** Status: **Active**
Problems/Diagnosis 5	Problem/Diagnosis: **Positive galactomannan x2 (3/12)** Status: **Active**
Problems/Diagnosis 6	Problem/Diagnosis: Status:
Problems/Diagnosis 7	Problem/Diagnosis: Status:
Problems/Diagnosis 8	Problem/Diagnosis: Status:
Problems/Diagnosis 9	Problem/Diagnosis: Status:
Problems/Diagnosis 10	Problem/Diagnosis: Status:
Problems/Diagnosis 11	Problem/Diagnosis: Status:
Problems/Diagnosis 12	Problem/Diagnosis: Status:
Problems/Diagnosis 13	Problem/Diagnosis: Status:
Problems/Diagnosis 14	Problem/Diagnosis: Status:
Problems/Diagnosis 15	Problem/Diagnosis: Status:

[redacted]

Operations/Procedures	

[redacted]

COVERING SHEET – Louise Slorance

LS/08 – appendix 08 : Communication record additional infection

CHI	[redacted]
Patient Name	**Andrew Slorance**
Age (Admission)	**49 years**

	EOLC. She understands this and is very realistic regarding continung on whilst there is some reaslistic possiblity of a positive outcome however not persisting when the situation is clearly futile. I explained plan to continue on supportive care whilst keeping under review the prognosis. All questions answered and she was grateful for care and discussion.
Communication 8	Date: 01/12/2020 Persons Present: Louise Spoken to by: Appleton
Communication 8 Note	Explained essentially static last 24 hours. Explained oxygenation at level of considering further episode of proning. Exaplined supportive care including further blood product support, removal of PICC line, rationalisatio of antibioitics. She understands where we are at and the slow nature of changes. All questions answered.
Communication 9	Date: 02/12/2020 Persons Present: Louise Spoken to by: Appleton
Communication 9 Note	Explained remains quite static. We have chenged ETT because of cuff leak. Variable though suboptimal absorption of feed so we are liaising with our dieticians and considering supplemental PN. Ongoing support from haematology and GVH is in our though there are other causes of suboptimal EN absor we are trying to address prior to escalating to increasi We are trialing period off paralysis to assess response, I explained there is a reaosnable chance that this may not be successful and they may need recommenced. Otherwise continuing of support explained, all questions answered.
Communication 10	Date: 03/12/2020 Persons Present: Louise Spoken to by: Appleton
Communication 10 Note	Update of last 24 hours. Paralysis had to be restarted last evening with deterioratino in gas exhange and then ANdrew was turned prone. This had little if any benefit on oxygenation. Now supine. His platelet count has dropped with some blood clots in NGS apsirate so risk/beenfit we are witholding this evenings dose of clexane. Haematology support with Andrews care and we are reducing his methylpred. I explained the concerns regarding a lack of progress and the risks associated with this and need for Andrew to begin to improve soon if there is any chance for him to survive. She is understanding of this and the poor prognosis. All questions answered.
	Date: 04/12/2020 Persons Present: Louise Spoken to by: Doherty
Communication 11 Note	Andrew less well. Potential for additional infection. Oxygen levels

COVERING SHEET – Louise Slorance

LS/09 – appendix 09 : Death certificate form

MEDICAL CERTIFICATE OF CAUSE OF DEATH (Form 11) ***Serial number:*** [redacted]
(Section 24(1) of the Registration of Births, Deaths and Marriages (Scotland) Act 1965)

The completed certificate should be taken to the Registrar of Births, Deaths and Marriages and will be retained by them.

GUIDANCE FOR COMPLETION OF THIS FORM IS AVAILABLE AT www.nrscotland.gov.uk/MCCDGuidance

PLEASE PRINT CLEARLY IN BLOCK CAPITALS AND DO NOT ABBREVIATE

PART A - DETAILS OF DECEASED

Name of deceased	ANDREW SLORANCE
Date of death *(dd/mm/yyyy)*	05/12/2020
Time of death *(24-hour clock – hh:mm)*	1136
Place of death	INTENSIVE CARE UNIT 4 QUEEN ELIZABETH UNIVERSITY HOSPITAL
Health Board area in which death occurred	GREATER GLASGOW AND CLYDE
Community Health Index (CHI) number	[redacted]
Date of birth *(dd/mm/yyyy)*	[redacted]1971

PART B - DETAILS OF CERTIFYING DOCTOR

Name	KATHRYN HARPER
GMC number	6073025
Business address	C/O ANAESTHETIC DEPT / QEUH / 1345 GOVAN ROAD / GLASGOW / G51 4TF
Business contact telephone number	0141 201 1100
For a death in hospital **Name of the consultant** responsible for the deceased	DR P DOHERTY

I hereby certify that to the best of my knowledge and belief the information contained in this Medical Certificate of Cause of Death is correct.

Signature of certifying doctor	[redacted]
Date	05/12/2020

For registration office use	RD Number	Year	Entry number

PART C - CAUSE OF DEATH

PLEASE PRINT CLEARLY IN BLOCK CAPITALS AND DO NOT ABBREVIATE

	Approximate interval between onset and death		
	Years	Months	Days
I Disease or condition directly leading to death *			
(a) COVID PNEUMONIA		1	9
Antecedent causes – Morbid conditions, if any, giving rise to the above cause, stating the underlying condition last			
due to (or as a consequence of) **(b)**			
due to (or as a consequence of) **(c)**			
due to (or as a consequence of) **(d)**			
II Other significant conditions contributing to the death, but not related to the disease or condition causing it			
MANTLE CELL LYMPHOMA	4		
BONE MARROW TRANSPLANT		1	

* *This does not mean mode of dying, such as heart or respiratory failure; it means the disease, injury or complication that caused death.*

PART D - HAZARDS

To the best of your knowledge and belief;		Y	N
DH1	Does the body of the deceased pose a risk to public health: for example, did the deceased have a notifiable infectious disease or was their body "contaminated", immediately before death?	✓	✓
DH2	Is there a cardiac pacemaker or any other potentially explosive device currently present in the deceased?		✓
DH3	Is there radioactive material or other hazardous implant currently present in the deceased?		✓

PART E – ADDITIONAL INFORMATION

Post mortem examination by a pathologist (*tick one*)		
PM1	Post mortem has been done and information is included above	
PM2	Post mortem information may be available later	
PM3	No post mortem	✓

Attendance on deceased (*tick one*)		
A1	I was in attendance upon the deceased during last illness	✓
A2	I was not in attendance upon the deceased during last illness: the doctor who was is unable to provide the certificate	
A3	No doctor was in attendance on the deceased	

Procurator Fiscal (*tick if applicable*)		
PF	This death has been reported to the procurator fiscal	✓

Extra information for statistical purposes (*tick if applicable*)		
X	I may be able to supply the Registrar General with additional information	

Maternal Deaths (*tick if applicable*)		
M1	Death during pregnancy or within 42 days of the pregnancy ending	
M2	Death between 43 days and 12 months after the end of pregnancy	

COVERING SHEET – Louise Slorance

LS/10 – appendix 10 : Nicola Sturgeon letter

Rt Hon Nicola Sturgeon MSP
First Minister of Scotland

St Andrew's House, Regent Road, Edinburgh EH1 3DG
T: 0300 244 4000

Scottish Government
Riaghaltas na h-Alba
gov.scot

25 November 2021

Dear Louise

I cannot begin to imagine the grief that you and your family have endured in the last year since Andrew's death. While I know there are not words I can express that can help ease that pain, I hope you know that you continue to have my heartfelt condolences.

As you know, Andrew was a friend and colleague to a huge number of people across the Scottish Government and we all still miss him.

I am writing today to set out some of the initial actions we have instructed to try and get answers to the questions you have asked.

Our Interim Chief Nursing Officer, Professor Alex McMahon, has commissioned the Medical Director of NHS Lothian to provide an external review of Andrew's care and treatment and the communication of his care with your family. This is distinct from any internal process being carried out by NHS Greater Glasgow and Clyde. Both the external and internal case note review will be reported directly to Professor McMahon and will, of course, be shared with you.

In addition, we have tasked Healthcare Improvement Scotland (HIS) to carry out a more general review of aspergillus in the Queen Elizabeth University Hospital to assess and determine if there are any broader concerns requiring action.

We will of course keep you updated as these reviews proceed and I understand that Professor McMahon has asked NHS Lothian to undertake its part of the review as a matter of urgency. Should you have any further questions, please do not hesitate to get in touch.

I know that none of these steps will, of themselves, immediately resolve the issues you have raised - but I hope the action that will flow from this work will help do so.

You and the children are in my thoughts.
With my best wishes

NICOLA STURGEON [redacted]

COVERING SHEET – Louise Slorance

LS/11 – appendix 11 : NHSGGC Case Review

Mr Andrew Slorance
DOB [redacted]/1971
CHI [redacted]

The below review is a summary of the care of the above patient based upon information available via Clinical Portal ,TrakCare and ICU ICCA (Careview) systems.

*The review has been conducted by **Dr Andrew Mackay** (Clinical Director, Critical Care, QEUH) and **Dr Andrew Clark** (Clinical Lead, Bone Marrow Transplant Unit, QEUH) with additional information from IPCT and microbiology teams.*

Summary of Mr Slorance's care prior to ICU

Andrew was admitted to hospital on 26/10/20 electively ahead of transplantation for mantle cell lymphoma (MCL). He also had a past medical history of anxiety, depression, diet-controlled diabetes mellitus and had initially had MCL treated in 2016 (NORDIC protocol and LEAM autograft) with recurrence in April 2019 (GI symptoms - progressed in November so started on Ibrutinib to control his disease ahead of referral for BMT in Jan 2020).

He received an allograft from a well matched 10/10 HLA antigen matched unrelated donor. CMV status was host negative / donor negative. Andrew was Toxoplasma IgG negative, HIV negative, Hep B/C negative. He required washed platelets in Edinburgh.

He was admitted on 26/10/20. He started transplant conditioning on 28/10/20, using fludarabine/ melphalan chemotherapy and alemtuzumab (anti-CD52 monoclonal antibody). This antibody is used for T cell depletion (to deplete recipient T-cells), to prevent graft rejection and ameliorate post-transplant graft versus host disease (GVHD). This is a 7-day course. The condition therapy renders patients profoundly pancytopenic for 7-14 days but more profound deficiencies in B and T cell function last for 6-18 months after transplant.

Andrew tested negative for COVID on PCR sampling on 26/10/20 and 28/10/20. He was first noted to be COVID positive on 3/11/20 from a sample taken the day before. This was his 8th day in hospital and 7th day from admission with no outside contact.

By the time the COVID result was known he had received all his conditioning chemotherapy. As such, he would be rendered pancytopenic within 2-3 days and this would be life threatening without stem cell rescue. He required to proceed to the stem cell reinfusion which he received on 4/11/20. It was felt important to deliver these cells within the transplant unit, in a controlled specialist environment but it was also decided to transfer the patient out of this unit following successful reinfusion to protect remaining patients. Post infusion he was treated in a single room in ward 4A. He was managed by the BMT team during this admission but nursed by 4A staff.

Andrew became febrile at day +5 (9/11/20) when he was profoundly neutropenic (neutrophils undetectable). He was started on tazocin and gentamicin. This is standard therapy for neutropenic sepsis. Blood culture on this day grew *Staph.epidermidis*. His CRP was 261. He became increasingly unwell over the next few days, with fever and increasing respiratory

symptoms. He developed an acute kidney injury (AKI) and hepatic impairment. His antibiotics were changed to meropenem and vancomycin once the blood culture results were known. Vancomycin was changed to teicoplanin when extended sensitivities were known in the face of renal impairment. His CRP peaked at 468. His Hickman line was removed.

A non-contrast CT scan was performed to avoid compounding his AKI with nephrotoxic contrast medium. This scan was reported as:
Consolidation in the right lower lobe and widespread pulmonary infiltrates throughout both lungs. Appearances are concerning for atypical infection. Viral and fungal (inclusive invasive aspergillosis) pathogens should be considered in the differential diagnosis. Respiratory review and potentially bronchoalveolar lavage (BAL) were recommended.

Serum aspergillus antigen (by virtue of the galactomannan antigen assay) was negative at this time, but antifungal therapy was started using isavuconazole on 12/11/20. Posaconazole had been discontinued due to abnormal LFTs. An extended panel of respiratory viruses were negative on PCR. He was discussed with respiratory medicine and in particular their opinion on his suitability for broncho- alveolar lavage was sought. It was felt this was not required. His case was discussed with the infectious diseases team, and he was discussed at the QEUH COVID escalation MDT. They confirmed his suitability for escalation to HDU/ITU if symptoms dictated and suggested he started corticosteroids and a 5-day course of remdesivir. He was treated with methylprednisolone as he had had his ciclosporin stopped due to AKI and the MDT was concerned about GVHD prophylaxis. His fever and CRP settled after his Hickman line (Tunneled central venous catheter) was removed and as he engrafted but he remained hypoxic.

He was transferred from Haematology BMT Unit to Medical HDU on 17/11/20 due to increasing oxygen requirements and developing further renal impairment. He remained on meropenem and teicoplanin as cover for neutropenic sepsis alongside empirical isavuconazole and prophylactic aciclovir. He started MMF and continued steroids as initially there was some concern that he was having a brisk engraftment syndrome/ hyperacute GVHD, although no other manifestations of GVHD were subsequently seen. His neutrophil count slowly improved. He was given only one dose of G-CSF. He was treated as part of a multidisciplinary/multispecialty team.

The infectious diseases team became concerned over SARS-CoV-2 PCR values (CT 22) being indicative of ongoing viral replication. Remdesivir was restarted on 17/11/20. His renal function improved, and CRP reduced even further but hypoxaemia persisted and worsened. Target O2 saturations were gradually lowered. Andrew experienced some improvement with proning and intermittent CPAP. He remained remarkably comfortable considering the degree of hypoxia. His case was discussed with SNBTS directly regarding non-trial use of convalescent plasma for compassionate reasons, but this was refused as patient had had an anaphylactic reaction to platelets in the past. His condition continued to deteriorate, and he required high flow nasal oxygen with a non-rebreathing O2 mask and intermittent CPAP.

Summary of Mr Slorance's care whilst in ICU

He was reviewed by an ICU consultant on 20/11/20. He was struggling at this point on maximum oxygen therapy and a discussion was had with Andrew about the risks and benefits of invasive ventilation with a quoted mortality of up to >90%. His wife was also updated via phone and invited to attend. Following this discussion, he was admitted to ICU in the evening on 20/11/20. He was intubated and ventilated for progressive respiratory failure due to COVID. He was paralysed and ventilated using standard lung protective ventilation. He received otherwise standard ICU care of stress ulcer prophylaxis, thromboprophylaxis (COVID dosing), and physiotherapy.

His condition initially improved, and his oxygen requirements decreased, and his paralysis was removed. His ongoing haematological care of immunosuppression, regular blood, and platelet infusion and standard post-BMT care were directed by the haemato-oncology team. He had aciclovir and isavuconazole added on 24/11/20 empirically as per microbiology and haematology advice. He developed polyuric renal failure causing a rise in urea and creatinine which settled over a few days and was accompanied by hypernatremia. This trend of gradual and slight improvement continued until 28/11/20 when he had an acute deterioration overnight and his oxygen requirements increased. He required an FiO2 of 1.0, paralysis and proning to achieve adequate ventilation and oxygenation. He became very labile with intermittent tachycardia and hypertension. His oxygenation was variable with a further requirement to be proned overnight from 2/12/20 into 3/12/20, with limited improvement in oxygenation.

Throughout Andrew's stay in ICU, he did not have any positive microbiology from 21/11/20 until 3/12/20 and after discussion with microbiology colleagues, his meropenem and teicoplanin were stopped on 3/12/20. He remained positive for SARS-CoV-2 throughout his stay but was negative for other respiratory viruses. He had serology sent for aspergillus antigen (galactomannan assay) on 11/11/20 which was negative, further samples on 1/12/20 were both positive but results were not available until 3/12/20. As he was already on isavuconazole, microbiology advice was to add caspofungin, send samples for aspergillus PCR and consider a bronchoalveolar lavage (BAL). On 4/12/20, in the face of worsening tachycardia and a rising CRP, he was restarted on teicoplanin with aztreonam. A blood (plasma sample) for aspergillus PCR was sent on 4/12/20 and was negative but was not reported until 9/12/20.

His condition deteriorated on 3/12/20 and he had a further significant increase in his FiO2 with dramatic worsening of his P/F ratio. He would not have been fit for BAL sampling. Despite ongoing ventilation, his condition worsened on 4/12/20. At 1900 he was reviewed by two ICU consultants who felt that he would not be suitable for further proning (tachycardia and previous failure to improve with it). By 2230, he was reviewed by two ICU consultants and a senior trainee, and a decision was made that it was likely that Andrew would continue to deteriorate and his wife was called to attend.

On 5/12/20, Andrew was reviewed on the ward round and felt that given the likelihood of a new infection (noting the positive galactomannan results, rising CRP and tachycardia) despite appropriate antimicrobial treatment alongside persistent COVID pneumonitis with critical hypoxia and recent stem cell transplantation, Andrew was now dying on maximal support. His wife was in attendance and, following MDT discussion, a decision was made to move to end-of-life care.

Andrew died at 1136 on 5/12/20.

Patient journey through QEUH

Mr Slorance was admitted to the QEUH Wd 4B (Bone Marrow Transplant) on 26th October 2020. Ward 4B is a Bone Marrow Transplant Unit comprising of 24 Single Rooms with ensuite facilities. He had a nose and throat swab undertaken on admission for COVID-19 on 26/10/20 which was negative as was his screen on 28/10/20. A further screen on 02/11/20 returned a positive result. IPCT were alerted to this on 03/11/20 and Ward 4B was contacted and advised that the patient was at the time pyrexial but no other COVID-19 symptoms. Ward 4B was contacted initially by phone and was advised on IPCT Transmission Based Precautions (TBP) as per national guidance, but due to complex chemotherapy treatment the patient was to remain in Ward 4B overnight. Ward 4B was visited the following morning to discuss the movement of the patient to Ward 4A. Medical staff have agreed for patient transfer out of Ward 4B, but currently was being nursed by a member of nursing staff on a 1:1 ratio. Patient was transferred to Ward 4A on 05/11/20 and continued to be nursed in a single room with TBP as per national guidance. Mr Slorance continued to screen positive for COVID-19 throughout his stay until he passed away on 05/12/20.

Time Line / Ward Movements

Ward	From	To	Bed	Room type
Wd 4B	26/10	04/11	78	BMT room. 1-2-1 nursing following positive result on 02.11.21
Wd 4B	04/11	05/11	76	BMT room.
Wd 4A	05/11	17/11	9	SSR used for isolation of Ward 4b Haem-onc isolation
Unit 7 HDU	17/11	20/11	78	COVID Hub
Unit 4 ICU	20/11	05/12	31	Isolation PPVL

Acquisition of COVID-19

Andrew was tested for COVID-19 by PCR on 26/10/20 and 28/10/20. He was tested again on 2/11/20 and PCR was now positive and remained positive until his death. The interval from admission to testing positive was 7 days. Andrew would be classified as a probable healthcare associated COVID-19 infection. Within the BMT unit, Andrew was cared for in a positive pressure HEPA filtered room. There were no visitors during his stay, standard PPE was used, social distancing was enforced, and every attempt was made to prevent transmission from staff to patients. Over an 18-month period, the BMT unit has had 3 cases of COVID-19 on the ward. All were sporadic with no more than one patient at any time testing positive. Some staff did become positive. Unavoidable contact between asymptomatic positive staff and patients prior to staff members testing positive almost certainly occurred at times but the measures listed were successful in protecting both patients and staff and minimising transmission of the virus.

Aspergillus assessment and antifungal treatment

Andrew was initially on Posaconazole as prophylaxis during his admission for transplant but this was stopped due to derangement of liver function tests. Aspergillus antigen serology was sent on the 11/11/20 which was negative. A CT scan performed due to persistent pyrexia on

12/11/20 (as above) showed appearances suggestive of atypical infection and it was suggested that fungal pathogens (including aspergillus) should be considered. Andrew was started on isavuconazole on 12/11/20 empirically. Respiratory consultant opinion at the time was that a BAL was unnecessary and microbiology and infectious disease colleagues were comfortable with his current antimicrobial therapy. Repeat aspergillus antigen serology was performed on 1/12/20 which was reported 48h later as positive.

On 3/12/20, upon receiving these results, his treatment was amended upon microbiology advice to add caspofungin to his isavuconazole. They suggested sending samples for aspergillus PCR and a BAL sample (for culture and galactomannan antigen testing). The blood sample sent for PCR on 4/12/20 was negative although not reported until 9/12/20 and Andrew was too hypoxic for a BAL to be undertaken. Given the clinical picture, radiological appearance and positive galactomannan, Andrew's presentation was suggestive but not diagnostic of COVID-19 associated pulmonary aspergillosis. The absence of BAL or tissue sampling makes confirmation very difficult. The subsequent negative aspergillus PCR serology is of unclear significance. Overall, Andrew may have either been colonised or had a secondary infection with aspergillus as up to 33% of critically ill COVID-19 patients do. He was treated with appropriate antifungal therapy under microbiological advice throughout his stay.

Communication with patient / next of kin

Prior to intensive care, there are multiple entries in the note describing discussions with Andrew's wife and Andrew but without extensive detail of the contents of these discussion beyond an update regarding treatment. In ICU, there are communication entries from medical staff on all but 3 days of his stay. These conversations were primarily over the phone due to the ongoing restrictions on visiting. Andrew's wife was kept up to date with his current condition, prognosis, and treatment throughout.

With regards an update regarding aspergillus infection, there is a communication entry on 4/12/20 detailing "potential for additional infection". It would not be routine practice to differentiate between groups of microorganisms unless the family member had clearly demonstrated some subject matter knowledge or had asked for specific details. There are also daily entries of communication with relatives documented in the nursing notes section of ICCA. Overall, the standard of documented communication appears to be of the same high level that is expected for all our critical care patients.

Death Certification

A death certificate was issued with cause of death as:
1a) COVID Pneumonia
2 - Mantle Cell Lymphoma, Bone Marrow Transplant

As was standard practice, a death certificate was completed on 5/12/20 but not issued until 7/12/20 when it could be discussed with the Procurator Fiscal's office. This discussion took place due to concerns regarding the timing of COVID positivity and the potential for this to be a case of nosocomial acquisition. Although there is no record of the discussion with the PF,

the certificate was issued the same day which suggests that the PF was happy with the case and the absence of any concerns regarding care being expressed by the family.

Addendum

Serological testing for Aspergillus (Dr Cottam, Consultant microbiologist)

There are caveats/limitations to any diagnostic test, with the Galactomannan antigen/ Beta-D-Glucan assays being no exception in the assessment of aspergillus infection.

Unfortunately, no respiratory tract specimens were received for either culture or fungal biomarker/PCR testing.

An important caveat to consider when interpreting serum GM and the beta-D-glucan assay, is that they are non-specific.

False positive results can be seen in patients with gastrointestinal tract mucositis caused by chemotherapy or GVHD, with the postulated mechanism being that galactomannan in food or bacteria can behave as cross-reactive epitopes and may translocate across the intestinal mucosa if there is compromise to the mucosal integrity. Furthermore studies have demonstrated false positive results in patients who have received immunoglobulin therapy and/or transfused blood products. Lastly, and equally important, is that the beta-D-glucan assay can be positive in patients with candidiasis.

Overall, my understanding is that the diagnostic utility of serum biomarkers in the setting of COVID-19 and IPA/CAPA is less certain, particularly in this case it is additionally challenging as we have no respiratory tract samples. As it stands, in my opinion, the diagnosis of invasive aspergillosis would seem possible, with appropriate empirical antifungal treatment being instigated.

COVERING SHEET – Louise Slorance

LS/12 – appendix 12 : Angela Wallace and Christine Peters e-mail

[redacted]

From: Peters, Christine
Sent: 18 November 2021 17:54
To: Angela Wallace (NHS Forth Valley)
Subject: Press today

Tracking: **Recipient**
Angela Wallace (NHS Forth Valley)

Hi Angela,

I am sure the last 24 hours have been difficult for you and the IPCT regarding the adverse publicity and headlines once again, as I know this is so difficult for the clinical teams as well. I hope you are all ok.

I was involved in the microbiology advice for the patient that is being discussed in the press and recall the case very clearly.

We were treating the patient for presumed Aspergillosis based on clinical findings and galactomannan (antigen) positive tests. This is not a definitive diagnosis, but was the most likely cause of infection at the time of demise and he was on full treatment with antifungal agents. The negative PCR that came back after death does not rule out the diagnosis.

There are a few issues to bring to your attention as I recall we discussed the case extensively at the time in handovers and Buzz meeting:

1. Re hospital acquired COVID, at 8 days the probability of it being hospital versus community is very high (up to 0.75), being immune compromised the incubation could be quicker and I recall discussing this particular case at the time and given the negative testing and isolation prior to admission HOCI seems highly likely. I do recall there were staff in the unit infected in 2020 but unsure as to the timing or the when policy to screen was put in place. There was discussion re WGS, and I am not sure if that could really be interpreted fully without screening being in place.

2. Re aspergillus I am aware that in Nov 2020 there was a paediatric haemonc case who died of aspergillosis who had also been housed in 4B, and we highlighted fungal infections in the paeds group to the IPCT at the time. I think this may be relevant in any retrospective assessment of the fungal infection risk as well as the fact that he was not housed in a positive pressure room throughout his neutropenic stage. Of course this was at the peak of the second wave when beds were very tight, but I assume that one of the reports that claimed he had been housed in a negative pressure room was wrong as that would be against the patient placement policy.

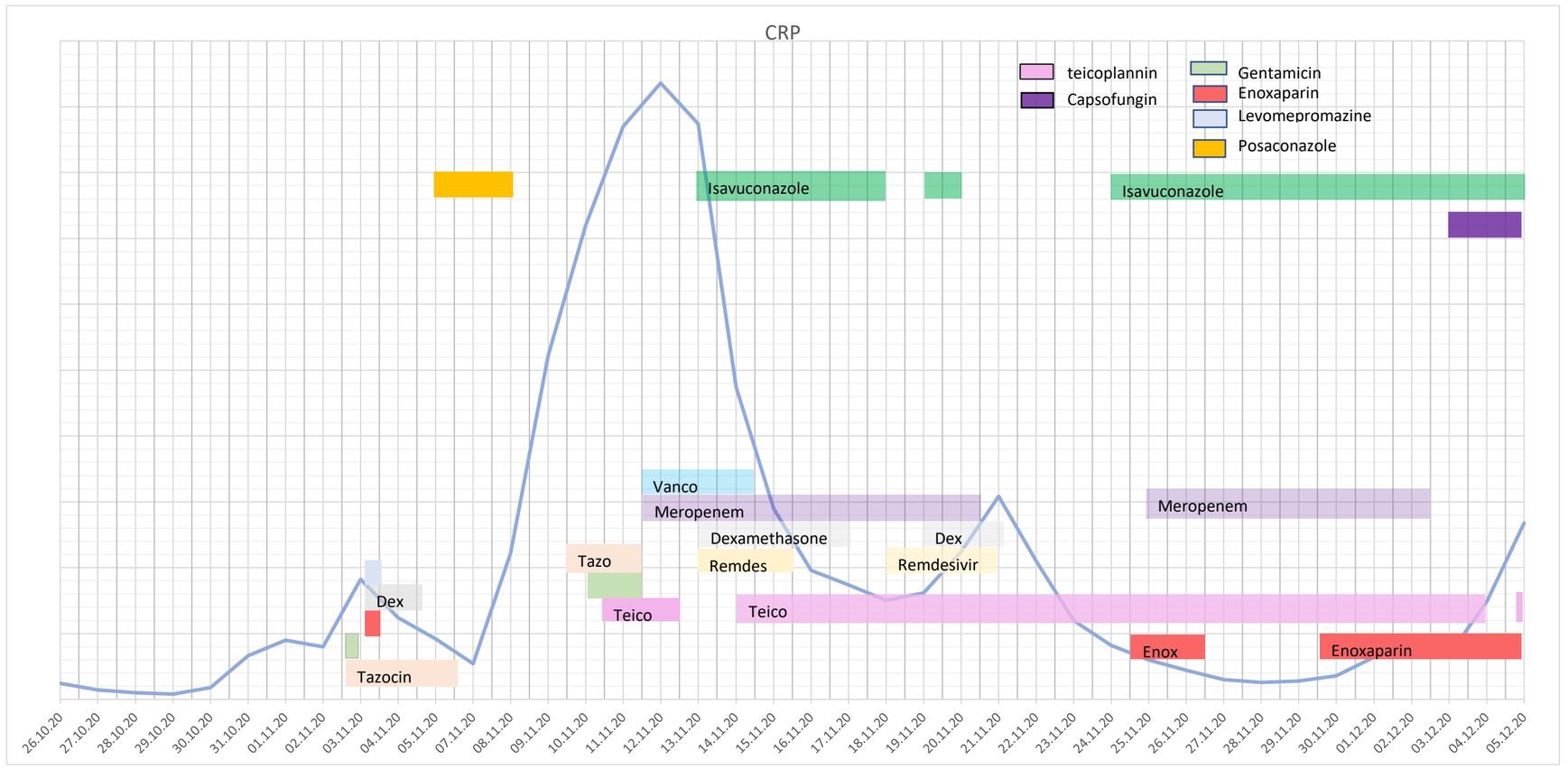
It is so sad to hear of the passing of any person from COVID and its complications and thoughts are with the family and also the teams who work so hard throughout the whole pandemic to treat and save patients' lives.

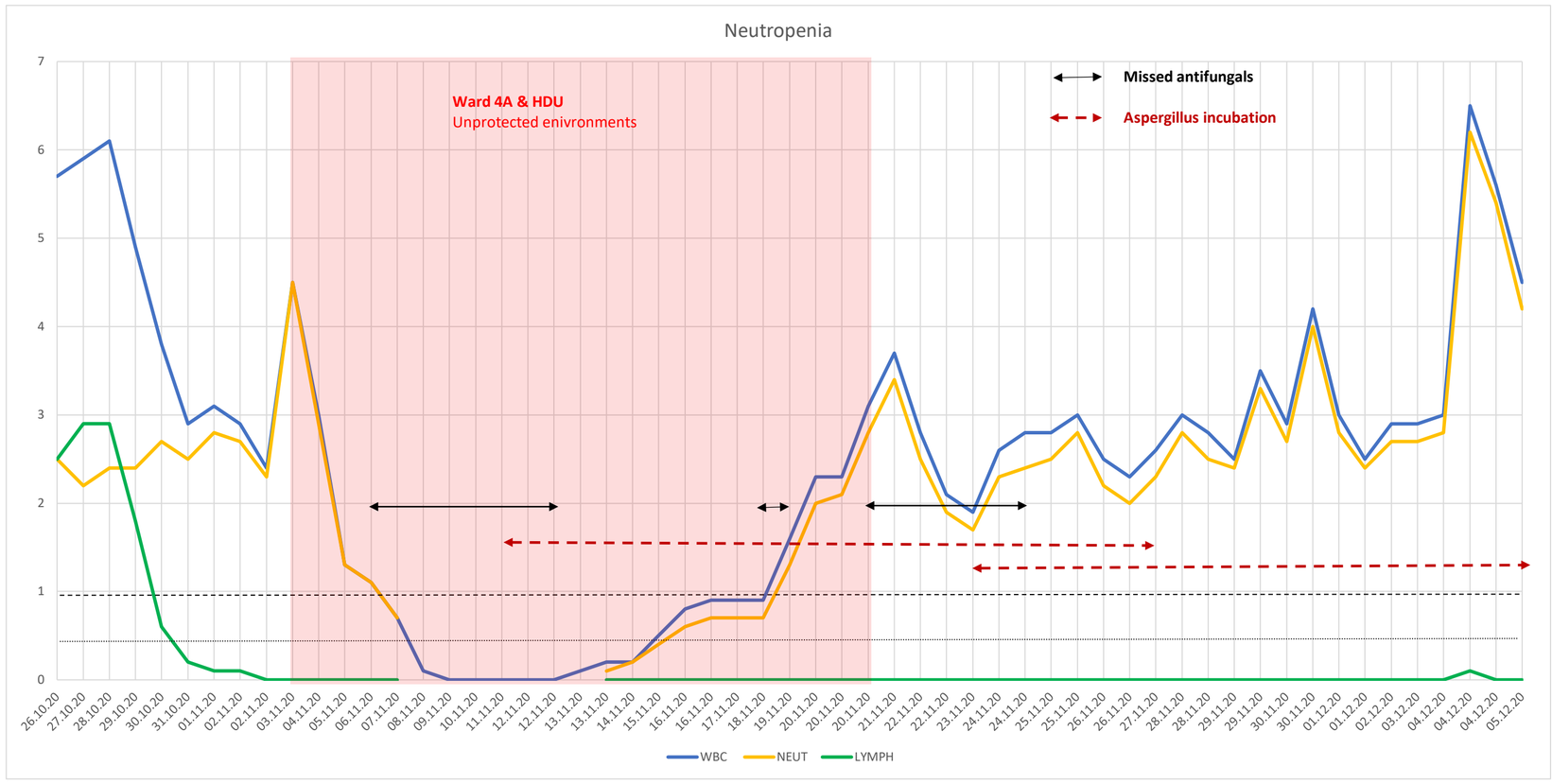
Kind regards,

Christine

Dr Christine Peters
Clinical Lead
Consultant Microbiologist
QEUH

Date	CRP
26.10.20	12
27.10.20	7
28.10.20	5
29.10.20	4
30.10.20	9
31.10.20	33
01.11.20	45
02.11.20	40
02.11.20	39
03.11.20	91
04.11.20	62
05.11.20	46
07.11.20	27
08.11.20	111
09.11.20	261
10.11.20	360
11.11.20	435
12.11.20	468
13.11.20	437
14.11.20	237
15.11.20	145
16.11.20	98
16.11.20	98
17.11.20	87
18.11.20	75
19.11.20	81
20.11.20	112
20.11.20	130
21.11.20	154
22.11.20	105
23.11.20	60
24.11.20	41
25.11.20	30
26.11.20	22
27.11.20	15
28.11.20	13
28.11.20	13
29.11.20	14
30.11.20	18
01.12.20	32
02.12.20	35
03.12.20	34
04.12.20	74
05.12.20	134




Neutropenia
Ward 4A & HDU
Unprotected enivronments
Missed antifungals
Aspergillus incubation
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WBC
NEUT
LYMPH

COVERING SHEET – Louise Slorance

LS/15 – appendix 15 : Internal Report: Summary of care

Brief clinical history and commentary - AS CHI [redacted]

Compiled by- Dr Andrew Clark. BMT Programme Director.

There is a powerpoint presentation which accompanies this word document- first presented 21/1/21 by haem/Onc Fellow and presented at the unit morbidity and mortality meeting. Update by A.Clark 20/11/21. Original scanned onto portal.

History pre- stem cell reinfusion.

A.S. was a 49 year old man with mantle cell lymphoma. He was treated with ibrutinib pre transplant to control his lymphoma and had good disease control at time of transplant. He received an allograft from a well matched 10/10 HLA antigen matched unrelated donor. CMV status was host neg / donor neg. AS was Toxoplasma IgG neg, HIV neg Hep B, C neg. He required washed platelets in Edinburgh. He had diabetes mellitus.

He was admitted on 26/10/20. He started transplant conditioning on 28/10/20, using Fludarabine/ Melphalan chemotherapy and Alemtuzumab anti CD52 monoclonal antibody. This antibody is used to T deplete the recipient, to prevent graft rejection and ameliorate post-transplant graft versus host disease (GvHD). This is a 7 day course. The condition therapy renders patients profoundly pancytopenic for 7-14 days but more profound deficiencies in B and T cell function last for 6-18 months post transplant.

A.S.was noted to be COVID positive on 3/11/20 from a sample taken the day before. Positive sample collected on 2/11/21. This was the 8th day in hospital and the 7th day from admission with no outside contact.

> ***Comment- BMT unit and staff protocols*** The BMT unit comprises positive pressured HEPA filtered single rooms. These provide a constant stream of clean air but do push air into the corridors making it dangerous for staff (at that time unvaccinated) and other patients to look after a COVID 19 positive patient in these rooms. We had a 'No visitors' policy at that time and a raft of measures to protect staff and patients alike. These included the use of PPE at all times, as laid down by contemporaneous government rules- at least mask, apron and gloves. Social distancing was enforced with patients and social distancing and masks mandated to be worn during all breaks and mealtimes. Staff were discouraged from meeting socially with each other to avoid direct transmission. In 18 months we have had 3 cases of COVID 19 on the ward, none of whom were demonstrated to be hospital acquired. All cases were sporadic with no more than one patient at any one time positive, no patient to patient transfer and no outbreaks. Some staff did become positive. Unavoidable contact between asymptomatic positive staff and patients prior to staff members testing positive almost certainly occurred at times but the measures listed were successful in protecting both patients and staff and minimising transmission of the virus. In AS's case I think one staff member did subsequently become positive but I do not know the full details.

By the time the COVID result was known he had received all his conditioning chemotherapy. As such, he would be rendered pancytopenic within 2-3 days and this would be life threatening without stem cell rescue. He required to proceed to the stem cell reinfusion which he received on 4/11/20. It was felt important to deliver these cells within the transplant unit, in a controlled specialist environment but it was also decided to transfer the patient out of this unit following successful reinfusion to protect remaining patients. This followed our emergency SOPs , which were informed by NICE and BSBMT guidance

Pancytopenic management

A.S. became febrile at day +5 (9/11/20) when he was profoundly neutropenic (neutrophils undetectable). He was started on Tazocin and Gentamicin. This is standard therapy for neutropenic sepsis. Blood culture on this day grew Staph. Epidermidis. His CRP was 261. He became increasingly unwell over the next few days, with fever and increasing respiratory symptoms. He developed acute kidney injury (AKI) and hepatic impairment. His antibiotics were changed to Meropenem and vancomycin once the blood culture results were known. Vancomycin was changed to Teicoplanin when extended sensitivities were known in the face of renal impairment. His CRP peaked at 468. His Hickman line was removed. A non-contrast CT scan was performed to avoid compounding his AKI with nephrotoxic contrast medium. This scan was reported as

' Consolidation in the right lower lobe and widespread pulmonary infiltrates throughout both lungs. Appearances are concerning for atypical infection. Viral and fungal (inclusive invasive aspergillosis) pathogens should be considered in the differential diagnosis. Respiratory review and potentially BAL were recommended'.

Aspergillus Ag was negative at this time but antifungal therapy was started using Isavuconazole on 12/11/20. Posaconazole had been discontinued due to abnormal LFTs. An extended panel of respiratory viruses were negative by PCR. He was discussed with respiratory medicine and in particular their opinion on his suitability for broncho- alveolar lavage (BAL). It was felt this was not required. His case was discussed with the ID team and he was discussed at the QEUH COVID escalation MDT. They confirmed his suitability for escalation to HDU/ITU if symptoms dictated and suggested he started corticosteroid and a 5 day course of Remdesivir. We used methylprednisolone as he had had his ciclosporing stopped due to AKI and we were concerned about GvHD prophylaxis. His fever and CRP settled after his Hickman line (Tunneled central venous catheter) was removed and as he engrafted. However, he remained hypoxic

Comment- Management during pancytopenic phase.

This period of pancytopenia was particularly stormy for AS. This was, almost certainly, not directly related to COVID. He engrafted neutrophils promptly (day +12). It may be important to say that I felt that the complications that he suffered during this period were to be expected and most likely bacterial, though other atypical infections can never be excluded 100%. This is the most common clinical scenario at this stage. We see this pattern often. His infective episode came on suddenly, was associated with multifocal consolidative changes in his lungs and we grew Staphlococcus Epidermidis. The fact that he became so much better so quickly- from the point of view of the acute septic episode- after line removal and engraftment, is more in keeping with this diagnosis (Staph Epidermidis pneumonia with multiple emboli from line) rather than viral, fungal or PCP diagnoses. Of note Aspergillus Ag was negative at a time of likely septicaemia. No definitive CT changes were seen (but it was non contrast) and the respiratory viral screen was negative. BAL was discussed but the respiratory team felt that BAL was not necessary, as he was on optimal antimicrobial therapy and there was a risk of performing an aerosolising procedure and transmitting virus when no change in management would ensue. Isavuconazole was chosen as antifungal therapy at this stage as it is less hepatotoxic, while retaining good anti mould activity. <u>All our patients would have been on an azole at this stage post-transplant, most commonly Posaconazole and we did not start Isavuconazole because we thought it likely A.S. had Aspergilllus.</u>

Progressive Respiratory decline Day +12 to day + 16

Despite engraftment and an improvement in A.S's inflammatory markers, his oxygen requirements increased. He continued on all antimicrobial therapy, namely antibiotics (meropenem and teicoplanin) + isavuconazole + prophylactic acyclovir. He was transferred to medical HDU transfer in view of further increase in oxygen requirement. He started MMF and continued steroids as initially there was some concern we may be seeing a brisk engraftment syndrome/ hyperacute GVhD, although no other manifestations of GvHD were seen. His neutrophil count slowly improved. We gave only one dose of G-CSF. He was treated as part of a multidisciplinary/mutispecialty team. It was essential that A.S. was considered for all available therapeutic options so we liaised regularly with ID and pushed for him to be discussed for trial eligibility and review at the hospital COVID MDT meetings.

ID team became concerned over PCR values (CT 22) being indicative of on-going viral replication - Remdesivir restarted on 17/11/20. His renal function improved and CRP reduced even further but hypoxaemia persisted and worsened. Target O2 saturations gradually lowered. Some improvement with proning and intermittent CPAP. Patient remarkably comfortable. Discussed with SNBTS directly off trial convalescent plasma as part of compassionate. This was refused as patient had had an anaphylactic reaction to PLTs in the past.

On day +16 (20/11/20) Type 1 RF worsens further. Steroids increased to MP 75mg to abrogate hyper acute GvHD affecting lung .Transfer to ITU and intubation. Although initially was deemed not eligible for RECOVERY trial, eligibility was re-assessed (only for the monoclonal antibody arms of the trial) and recruited study - standard arm (remdesivir and steroids).

Comment - Management after engraftment

At the time we felt that, although he continued to improve from his acute post- transplant septic illness, another process was declaring itself. Overall clinical picture increasingly resembled COVID19 respiratory failure. We continued antimicrobial agents including antifungals. We looked into trial involvement and convalescent plasma but were unsuccessful. There was a co-ordinated multispecialty team approach. He did receive high doses of steroid. Antifungal therapy – prophylaxis but same dose as has been used in previous treatment studies (SECURE).

Management in ITU

Comment ITU care

I was not directly involved in this part of his care. I can see that Dr Parker and Dr McQuaker gave advice. I am happy to discuss with them next week. In my opinion he had COVID as the major driver of illness. It looks as if he could have developed a co –infection with Aspergillus, which has been described to complicate a significant number of cases worldwide. This mould is everywhere – including potentially in the gut flora- but microbiology would be better to comment on this aspect. The Ag test can also be falsely positive but his levels were high as was Beta –D- Glucan. This combination of Aspergilllus co-infection in COVID patients seems to have become an increasingly recognised combination since AS 's death. The fact that these tests became positive, despite being on Isavuconazole, could mean resistance of fungis to azoles, but more likely reflects his profound T cell immunity post- transplant His case was discussed with the Procurator Fiscal after his death. I am not clear of the content of that call.

As I discussed above he had been in hospital for only 8 days and had had no outside contact for 7 days. So he was well within the incubation period.

Communication

We spoke to his wife everyday, with AS's permission and often while in his room as a three way call.

I offered to come to discuss matters with his wife

After he died, (13/12/20) I wrote to his wife Louise asking if she wanted to come and discuss any aspect of his care with us. I did say " I am very sorry that Andrew eventually lost his fight against COVID recently". This is because I knew he had COVID, I didn t know, at that time, that he had the positive Aspergillus Ag, despite Isavuconazole therapy (I did know he had previously negative). I thought he had died of progressive COVID, and I still do. This may have been complicated by a fungal infection, as is common with COVID or Flu, but I do not think that was why he died. I did not intend to be deceptive. I have no recollection of knowing this and only found out at the mortality and morbidity meeting in January. I did not think it changed what happened significantly so I did not rediscuss with his wife.

COVERING SHEET – Louise Slorance

LS/16 – appendix 16: Internal version of NHSGGC

Case Review

Mr Andrew Slorance DOB [redacted]/1971 CHI [redacted]

The below review is a summary of the care of the above patient based upon information available via Clinical Portal ,TrakCare and ICU ICCA (Careview) systems.

*The review has been conducted by **Dr Andrew Mackay** (Clinical Director, Critical Care, QEUH) and **Dr Andrew Clark** (Clinical Lead, Bone Marrow Transplant Unit, QEUH) with additional information from IPCT and microbiology teams.*

1. Summary of Mr Slorance's care prior to ICU –

Andrew was admitted to hospital on 26/10/20 electively ahead of transplantation for mantle cell lymphoma (MCL). He also had a past medical history of anxiety, depression, dietcontrolled diabetes mellitus and had initially had MCL treated in 2016 (NORDIC protocol and LEAM autograft) with recurrence in April 2019 (GI symptoms - progressed in November so started on Ibrutinib to control his disease ahead of referral for BMT in Jan 2020).

He received an allograft from a well matched 10/10 HLA antigen matched unrelated donor. CMV status was host negative / donor negative. Andrew was Toxoplasma IgG negative, HIV negative, Hep B/C negative. He required washed platelets in Edinburgh.

He was admitted on 26/10/20. He started transplant conditioning on 28/10/20, using fludarabine/ melphalan chemotherapy and alemtuzumab (anti-CD52 monoclonal antibody). This antibody is used for T cell depletion (to deplete recipient T-cells), to prevent graft rejection and ameliorate post-transplant graft versus host disease (GVHD). This is a 7-day course. The condition therapy renders patients profoundly pancytopenic for 7-14 days but more profound deficiencies in B and T cell function last for 6-18 months after transplant.

Andrew tested negative for COVID on PCR sampling on 26/10/20 and 28/10/20. He was first noted to be COVID positive on 3/11/20 from a sample taken the day before. This was his 8th day in hospital and 7th day from admission with no outside contact.

By the time the COVID result was known he had received all his conditioning chemotherapy. As such, he would be rendered pancytopenic within 2-3 days and this would be life threatening without stem cell rescue. He required to proceed to the stem cell reinfusion which he received on 4/11/20. It was felt important to deliver these cells within the transplant unit, in a controlled specialist environment but it was also decided to transfer the patient out of this unit following successful reinfusion to protect remaining patients. Post infusion he was treated in a single room in ward 4A. He was managed by the BMT team during this admission but nursed by 4A staff.

Andrew became febrile at day +5 (9/11/20) when he was profoundly neutropenic (neutrophils undetectable). He was started on tazocin and gentamicin. This is standard therapy for neutropenic sepsis. Blood culture on this day grew *Staph.epidermidis*. His CRP was 261. He became increasingly unwell over the next few days, with fever and increasing respiratory

symptoms. He developed an acute kidney injury (AKI) and hepatic impairment. His antibiotics were changed to meropenem and vancomycin once the blood culture results were known. Vancomycin was changed to teicoplanin when extended sensitivities were known in the face of renal impairment. His CRP peaked at 468. His Hickman line was removed.

A non-contrast CT scan was performed to avoid compounding his AKI with nephrotoxic contrast medium. This scan was reported as:
Consolidation in the right lower lobe and widespread pulmonary infiltrates throughout both lungs. Appearances are concerning for atypical infection. Viral and fungal (inclusive invasive aspergillosis) pathogens should be considered in the differential diagnosis. Respiratory review and potentially bronchoalveolar lavage (BAL) were recommended.

Serum aspergillus antigen (by virtue of the galactomannan antigen assay) was negative at this time, but antifungal therapy was started using isavuconazole on 12/11/20. Posaconazole had been discontinued due to abnormal LFTs. An extended panel of respiratory viruses were negative on PCR. He was discussed with respiratory medicine and in particular their opinion on his suitability for broncho- alveolar lavage was sought. It was felt this was not required. His case was discussed with the infectious diseases team, and he was discussed at the QEUH COVID escalation MDT. They confirmed his suitability for escalation to HDU/ITU if symptoms dictated and suggested he started corticosteroids and a 5-day course of remdesivir. He was treated with methylprednisolone as he had had his ciclosporin stopped due to AKI and the MDT was concerned about GVHD prophylaxis. His fever and CRP settled after his Hickman line (Tunneled central venous catheter) was removed and as he engrafted but he remained hypoxic.

He was transferred from ~~Haematology BMT Unit~~ward 4A to Medical HDU on 17/11/20 due to increasing oxygen requirements and developing further renal impairment. He remained on meropenem and teicoplanin as cover for neutropenic sepsis alongside empirical isavuconazole and prophylactic aciclovir. He started MMF and continued steroids as initially there was some concern that he was having a brisk engraftment syndrome/ hyperacute GVHD, although no other manifestations of GVHD were subsequently seen. His neutrophil count slowly improved. He was given only one dose of G-CSF. He was treated as part of a multidisciplinary/multispecialty team.

The infectious diseases team became concerned over SARS-CoV-2 PCR values (CT 22) being indicative of ongoing viral replication. Remdesivir was restarted on 17/11/20. His renal function improved, and CRP reduced even further but hypoxaemia persisted and worsened. Target O2 saturations were gradually lowered. Andrew experienced some improvement with proning and intermittent CPAP. He remained remarkably comfortable considering the degree of hypoxia. His case was discussed with SNBTS directly regarding non-trial use of convalescent plasma for compassionate reasons, but this was refused as patient had had an anaphylactic reaction to platelets in the past. His condition continued to deteriorate, and he required high flow nasal oxygen with a non-rebreathing O2 mask and intermittent CPAP.

Questions of clarification

1. On what date did AS first become hypoxic

   AS had occasional isolated readings at 93% saturation by finger probe (2-3 readings, spontaneously returned to normal by next set of standard observations, over time from admission 27/10/20 – 11/11/20)

   On night of 11/11/20 into the morning of 12/11/20 he became more hypoxic with 3 readings at 94% followed by a reading of 89%. Oxygen therapy was started at 35% by venturi mask at 0200 on 12/11/20. His oxygen requirement fell during that day to 24% , then 3L by nasal cannulae by 1900h on the same day.

   He remained stable for 4 days before deteriorating and requiring increased flow by NC on 16/11/20. This was the start of a progressive deterioration, albeit with a stuttering and partially responsive initial phase.

2. When was remdesvir and steroids first started and what was the plan for duration of therapy

   He was started on Remdesvir and steroids on 12/11/20. Until that time he had not been hypoxic and had had an alternative cause for his illness. Plan was for 5 days of therapy as that was standard of care at the time. This aspect of his care was co-ordinated by our colleagues in ID.

   Is Posaconazole the only antimicrobial prophylaxis recommended for this type of treatment?

   Post allogeneic stem cell transplant there are a variety of regimens used as fungal prophylaxis. We have chosen posaconazole as it is a very active, well tolerated azole antifungal. However, during a period of neutropenic sepsis if liver function tests are abnormal and the cause of sepsis is felt to be much more likely to be bacterial (rapid rise in CRP with a pro inflammatory clinical picture that usually settles on use of correct antimicrobials and engraftment) , then a short pause in the antifungal posaconazole (which worsens liver function) can be indicated, although early re-institution of treatment is indicated as soon as possible. This is what happened with Mr AS. We sometimes use caspofungin or ambisome if there is not early clinical response to antibiotics.

3. Please clarify the statement "He required washed platelets in Edinburgh", was this the reason for the delay in admission and the beginning of treatment?

AS had had transfusion reactions to platelets in Edinburgh (referring team). He had been investigated there and a decision made to use washed platelets, if he was thrombocytopenic. This is a treatment usually used if the patient is experiencing a reaction to plasma in the platelet product, rather than platelets themselves. There are several causes but often the exact nature of the reaction is not elucidated. He did not need platelets in Glasgow before he started conditioning and it was not the reason for the delay. The reason for mentioning this is that it was that he was considered for convalescent plasma later in the admission but the requirement for washed platelets excluded him from receiving that treatment.

4. Why did the patient require admission 2 days prior to commencing transplant conditioning?

   The delay was to allow for a second pre transplant COVID PCR test to be performed, and for us to get the result prior to starting conditioning chemotherapy. At the time, we mandated that all patients had two negative tests prior to starting chemotherapy. One was done by the referring team and one on admission. Turnaround times were slower and no POC machines were available in Oct 2020.

5. It would be necessary to understand the nursing and medical staff arrangements (including staff testing etc) and visiting access for relatives prior to patient testing positive for COVID 19.
   This is a summary of precautions. There was an SOP outlining precautions attached:

   All nursing, medical and AHP staff were tested weekly by PCR.
   This was before the introduction of lateral flow testing
   All staff had to use Gloves, mask and apron at all times in the rooms and wore masks in the corridors.
   Masks were worn at all times in the communal areas of the ward
   Social distancing was enforced in all communal areas and mealtimes
   Staff were encouraged to eat alone when on shift
   Contact with patients was reduced and numbers of doctors entering the rooms on ward rounds was reduced to a single person.
   Allied healthcare professionals contact was cut to a minimum.
   Any symptomatic staff self-isolated until a negative test returned
   All contacts of COVID 19 positive patients or staff isolated for 14 days.

   All staff had to have a NEGATIVE PCR prior to returning to work and had to be asymptomatic for 7 days. This was an exception to the standard hospital policy which we fought to be able to introduce in the stem cell transplant unit.

   No relatives were allowed unless the patient was terminal and even then we looked to move patients out of the ward.

The following is for the contemporaneous unit SOP:

Minimising risk of staff exposure to and transfer of SARS-CoV-2 in the Adult Haemopoietic blood and marrow stem cell transplant unit (BMT unit.

1.0 General procedures

1.1 Staff must follow all national UK and Scottish Government rules

1.2 Personal protective equipment will be worn at all times

1.3 Social distancing and masks will be worn during all breaks and mealtimes

1.4 Staff are encouraged to download the NHS protect Scot App

1.5 Staff are discouraged from meeting socially with each other to avoid direct transmission

1.6 Staff are encouraged to engage with Trak and Trace services whenever they go out to hospitality premises

1.7 Any staff who have had 'significant' contact with positive cases of COVID i.e. > 15 mins of contact < 2m apart, must self-isolate for 14 days. There is no utility of testing in asymptomatic cases in this context.

1.8 Symptomatic staff with a new cough, fever or anosmia will require testing and self isolation until test results are known.

1.9 Asymptomatic staff will be regularly tested in a screening programme

2.0 Screening programme

2.1 All staff who work on the BMT unit (Ward 4B at QEUH) will be asked if they would be tested weekly for the presence of COVID 19 by nasal and oropharyngeal swabs. This test is voluntary, but refusal may necessitate temporary redeployment.

2.2 Test results are sent by text message to the individual who has been tested. Ideally results should be available within 24 hours but often take 48-72 hours to return.

2.3 Staff continue to work normally if asymptomatic

2.4 All BMT patients are also tested twice prior to admission prior to chemotherapy commencing and weekly thereafter to prevent 'retrograde' transmission

2.5 No relatives are allowed to visit during high risk periods when restrictions are in place

3.0 Managing staff who test positive

3.1 Staff must self-isolate for at least 10 days if they test positive

3.2 Staff are given a dedicated telephone number to support their mental wellbeing and are encouraged to communicate their progress to clinical managers during their absence

3.3 Staff will receive a self-testing kit through the post or will be given a kit prior to leaving work.

3.4 Following a positive test staff will be removed from the screening programme for 90 days. Thereafter they may be re-enrolled as it is not yet clear if second infections occur.

4.0 Return to work

4.1 Strict criteria must be met prior to staff returning to patient contact activities in the BMT unit.

- Staff must be symptom free for 7 days
- Staff must test NEGATIVE for SARS-CoV- 2 prior to return to direct patient contact on the BMT unit. (NICE Guidance: COVID19 rapid guideline: Haemopoietic stem cell transplant)

4.2 To minimise extended absence after self-isolation BMT staff will self-test on the day of their proposed return

4.3 Sealed, alcohol wiped sample bags will be collected from the front door by a member of ward staff wearing a mask and gloves

4.4 Samples will be analysed using a rapid test with a 4 hour turnaround or point of care testing if this becomes available. Testing will be arranged by email using the clinical virology service, west-ssvc@nhs.net or west-ssvc@nhs.scot after migration

4.5 Alternatively, staff could be redeployed to other clinical areas or work from home after self-isolating in line with UK government guidance (COVID19) on management of staff and exposed patients or residents in health and social care settings (July 2020)

4.6 Asymptomatic staff who continue to test positive will be tested weekly

4.7 All cases who are persistently positive will be discussed with the occupational health team on a case by case basis. Asymptomatic shedding is a recognised feature of the disease but is less likely in young fit staff members. In addition, the

longer the individual sheds the less likely this is to represent transmissible disease.

As was stated in the initial report it was impossible to avoid contact between asymptomatic staff and patients.

A timeline of staff who tested positive after AS was admitted was looked at:

One staff member had protected contact on 28.10.2020 and tested positive on 5.11.2020. One other staff member had contact on 3/11/20 and subsequently tested positive on 9/11/20

6. More clarity on acuity of Ward 4A. Is it an HDU or Level 1 area? Is the single side room that the patient was nursed in a negative or positive pressure room?

   Ward 4A is a single room on the renal unit. The room is neither positively nor negatively pressurised. In contrast, the rooms in ward 4B (BMT Unit) where Mr AS was being treated prior to testing positive for COVID, are positively pressurised and would have resulted in potential contamination of the corridor areas with virus if he had stayed in that area- potentially cross-contaminating the unit. The aim of moving Mr AS was primarily to protect other patients in the transplant unit.

   Ward 4A is next to ward4B and was chosen for several reasons. AS would be close to medical and nursing staff with transplant experience day and night who could both review the patient and advise the ward nursing team quickly in the case of a problem. The ward is also a renal ward. The renal team have a very strong clinical background with a high quality nursing team with experience of managing patients on immunosuppression and post renal transplant.

   AS was reviewed each day by a dedicated registrar and was seen by the attending consultant after an MDT discussion on a near daily basis

7. More information on the patient's status between the 4th and the 9th of November. Was his respiratory status and other blood results stable?
   As noted in response to Q1, AS did not become hypoxic until 12/11/20.

   Haematology 4/11/20 -9/11/20
   He rapidly became pancytopenic, as is to be expected. See summary slide.
   Neutrophils fell from normal on 4/11/20 to $< 0.5 \times 10^9$/l by Day +5 on 9/11/20.
   He was 'well' during this time. He experienced mild mucositis and lethargy.
   Afebrile. NEWS 0-2 (3 max on rare occasions)

He then entered a period of 1 week where he was profoundly neutropenic with neutrophils not detectable. He engrafted to neutrophils > 0.5 x 10^9/l on 16/11/20 and a further 3-4 days when he had Neut < 1.0 x 10^9/l
It was during this time that he became acutely unwell
This is a classical episode of neutropenic sepsis and is most likely bacterial

Liver function 4/11/20 -9/11/20
During this initial period post-transplant (Day 0 – Day +5), his bilirubin rose from 20 to 60 . There is often a concern about Liver function at his time post-transplant, as some patients can develop veno-occlusive disease (VOD) of the liver. AS had had the risk factor of significant previous chemotherapy including a previous autologous PBSC transplant in 2016. So we were careful with hepato toxins – including posaconazole. An ultrasound scan of liver was requested to exclude hepatomegaly, ascites and reverse flow in portal veins – signs of VOD

Renal function 4/11/20 -9/11/20

Renal function was normal during this time

8. When was the Hickman Line inserted and removed? Were antibiotics given down the Hickman line?

   The Hickman line was inserted by the referring team in Edinburgh on 23/10/20, 3 days prior to admission and was removed during the episode of neutropenic sepsis on day +8 – 12/11/20.

9. Is it possible that the *Staph Epidermidis* was a blood culture contaminant? Were samples taken via the Hickman line and was the line itself sent for culture when removed?

   Staph epidermidis is a potential contaminant.
   On the other hand, this was a Hickman line culture, not direct contact with skin. In addition, staph epidermidis infections including pneumonia are well described in immunocompromised hosts with indwelling, tunnelled central venous catheters. Colonisation of lines with this bacteria are quite common. The CT images would be consistent with septic emboli from an infected line. The time course of rapid onset of infection during the neutropenic phase, rapidly rising CRP and resolution with antibiotics, line removal and engraftment of neutrophils strongly argues for a bacterial cause. (See attached powerpoint slide)

10. More information on the extent of the initial AKI would be desirable. In particular did this have any influence on the number of doses of Gentamicin given.

    AS became septic on 9/11/20 when profoundly neutropenic. His condition deteriorated, in terms of worsening sepsis for 48-72 h before stabilising

Renal function deteriorated from the time of this septic insult and deteriorated as the infection caused more profound fever, suggesting an element of pre- renal hypovolaemia. However, he was on concurrent nephrotoxins- initially Ciclosporin A and Gentamicin. The gentamicin was stopped and vancomycin added.
The decision to stop Gentamicin was not based on renal function.
Ciclosporin level were within the range 150-250 except 1 reading of 253 on 6/11/20
Gentamicin levels were not 'toxic' and can be seen on the gentamicin prescription chart. Vancomycin levels were not high either at any time.

After this toxic insult the renal function initially deteriorated and then slowly recovered.

11. It is unclear on what date the antibiotic change to Vanc and Mero was made and the rationale. Was it better sensitivity for a Staphlococcal infection?

AS became septic and developed a temperature overnight 9/11/20 – 10/11/20 NEWS 3-4. He started Tazocin and Gentamicin as this is our first line therapy for neutropenic sepsis and he was not profoundly unwell. Initially, even though his temperature did not fully settle, it looked like it might be settling so he stayed on these antibiotics but he re-spiked to 39.4 on 12/11/20. His NEWS at this time had deteriorated to 7-8. It is standard practice to make a change in antibiotics in neutropenic patients after 48 hrs if no improvement and in this case when there was actually deterioration, so his antibiotics were 'escalated'. This process of escalation takes into account several factors including:

- The most likely organisms involved and the most dangerous- even when we have no cultures. In neutropenic sepsis we only grow an organism from cultures 35-50% of the time.
- Any positive cultures

Rationale for escalation- Gram negative sepsis is a feared complication so Tazocin and gentamicin were changed to meropenem due to its' broader spectrum of activity on 12/11/20.
The vancomycin was added, again on 12/11/20, because we had grown a Staph. Epidermidis , but also to broaden the gram positive cover. The hickman line was also removed. It is standard practice to remove indwelling catheters if sepsis is worsening or resistant to fist line antibiotcs.

12. It is not clear if the isuvaconazole was started to replace Posaconazole and were any dose considerations e.g. prophylactic versus treatment dose.

Posaconazole was given from 4/11/20- 6/11/20 inclusive. This was discontinued in the face of a rising bilirubin and concerns about veno-occlusive disease, as discussed in more detail above.

Isavuconazole was started on 12/11/20. This drug is less hepatotoxic. The drug dose we use is the same whether used for treatment or prophylaxis. Our policy is to use this drug at the same dose that was used in treatment trials. There is limited good quality data from using the drug as prophylaxis at a lower dose. It is better tolerated than Posaconazole, specifically it is less hepatotoxic and has good efficacy versus Voriconazole in treatment trials.
Isavuconazole was not primarily started as a treatment but as prophylaxis, as bacterial infection is much more likely to describe the events that AS presented with but would ensure fungal pathogens were treated if occult. This is again standard practice. CT reports for transplant patients not infrequently include a statement about aspergillus, as this falls within the radiological differential diagnosis- but on this occasion no characteristic lesions associated with fungal infections were seen and the findings are non-specific. The aspergillus antigen test was negative at this stage.

13. . Given Remdesivir is postulated to be more efficacious earlier in COVID 19 disease was any consideration given to starting it in an immunosuppressed patient at the time of diagnosis?

The optimal management using this drug was not known at that time. For instance, breaking news was presented in The New England Journal of Medicine on 5/11/20 which carried at least two high quality publications and an updated editorial on the

AS was treated for 5 days, initially, which was abbreviated by 1 day due to concerns about renal function. Remdesivir was restarted on 17/11/20, as CT values were rising- both interventions were advised by ID.

14. What date was the extended panel of respiratory virus testing undertaken?

An extended respiratory virus screen was sent on 10/11/20 and 16/11/20

Summary of Mr Slorance's care whilst in ICU

He was reviewed by an ICU consultant on 20/11/20. He was struggling at this point on maximum oxygen therapy and a discussion was had with Andrew about the risks and benefits of invasive ventilation with a quoted mortality of up to >90%. His wife was also updated via phone and invited to attend. Following this discussion, he was admitted to ICU in the evening on 20/11/20. He was intubated and ventilated for progressive respiratory failure due to COVID. He was paralysed and ventilated using standard lung protective ventilation. He received otherwise standard ICU care of stress ulcer prophylaxis, thromboprophylaxis (COVID dosing), and physiotherapy.

His condition initially improved, and his oxygen requirements decreased, and his paralysis was removed. His ongoing haematological care of immunosuppression, regular blood, and platelet infusion and standard post-BMT care were directed by the haemato-oncology team. He had aciclovir and isavuconazole added on 24/11/20 empirically as per microbiology and haematology advice. He developed polyuric renal failure causing a rise in urea and creatinine which settled over a few days and was accompanied by hypernatremia. This trend of gradual and slight improvement continued until 28/11/20 when he had an acute deterioration overnight and his oxygen requirements increased. He required an FiO2 of 1.0, paralysis and proning to achieve adequate ventilation and oxygenation. He became very labile with intermittent tachycardia and hypertension. His oxygenation was variable with a further requirement to be proned overnight from 2/12/20 into 3/12/20, with limited improvement in oxygenation.

Throughout Andrew's stay in ICU, he did not have any positive microbiology from 21/11/20 until 3/12/20 and after discussion with microbiology colleagues, his meropenem and teicoplanin were stopped on 3/12/20. He remained positive for SARS-CoV-2 throughout his stay but was negative for other respiratory viruses. He had serology sent for aspergillus antigen (galactomannan assay) on 11/11/20 which was negative, further samples on 1/12/20 were both positive but results were not available until 3/12/20. As he was already on isavuconazole, microbiology advice was to add caspofungin, send samples for aspergillus PCR and consider a bronchoalveolar lavage (BAL). On 4/12/20, in the face of worsening tachycardia and a rising CRP, he was restarted on teicoplanin with aztreonam. A blood (plasma sample) for aspergillus PCR was sent on 4/12/20 and was negative but was not reported until 9/12/20.

His condition deteriorated on 3/12/20 and he had a further significant increase in his FiO2 with dramatic worsening of his P/F ratio. He would not have been fit for BAL sampling. Despite ongoing ventilation, his condition worsened on 4/12/20. At 1900 he was reviewed by two ICU consultants who felt that he would not be suitable for further proning (tachycardia and previous failure to improve with it). By 2230, he was reviewed by two ICU consultants and a senior trainee, and a decision was made that it was likely that Andrew would continue to deteriorate and his wife was called to attend.

On 5/12/20, Andrew was reviewed on the ward round and felt that given the likelihood of a new infection (noting the positive galactomannan results, rising CRP and tachycardia) despite appropriate antimicrobial treatment alongside persistent COVID pneumonitis with critical hypoxia and recent stem cell transplantation, Andrew was now dying on maximal support. His wife was in attendance and, following MDT discussion, a decision was made to move to endof-life care.

Andrew died at 1136 on 5/12/20.

Questions for clarification

1. It may be accurate but what was the "Mortality of 90%" based on.
2. Would be useful to know the degree of hypoxia and how long patient had been on non-invasive respiratory support prior to the decision to intubate.
3. Patient was paralysed and ventilated suggesting severe hypoxaemia. Was prone ventilation considered at this time? It would be useful to have a timeline of when paralysis was stopped and the severity of hypoxamia on each day e.g. PF ratios. Was ECMO considered (published data suggest very low survival if ECMO required following BMT, this is pre-COVOD).
4. Inconsistency in the start and stopping dates of antibiotics, particularly the isavuconazole which it says was started on the 17th and also the 24th of November. Separate courses or the same course?
5. Useful to know more on severity of AKI and whether either drug toxicity OR requirement to reduce antibiotic doses were a feature.
6. Usefully to know the severity of hypoxaemia which prompted decision to prone the patient and could proning have been considered earlier.
7. It is unclear what respiratory sampling was sent from the time of intubation until the 3rd of December. Of relevance here is whether a BAL, miniBAL were sent, given the patient was immunosuppressed and failing to improve. It is stated that the patient was too hypoxaemic for a BAL on 5th December. There is a known association of invasive aspergillosis and COVID 19 (as well as in immunosuppressed patients) but other opportunistic infections may have been a possibility.
8. Was a repeat CT considered to either exclude PE or further identify cause of hypoxamia between 20/11 and 3/12.
9. Was patient anticoagulated?
10. More detail in the timeline with regard to conversations with next of kin might be useful.

Patient journey through QEUH

Mr Slorance was admitted to the QEUH Wd 4B (Bone Marrow Transplant) on 26th October 2020. Ward 4B is a Bone Marrow Transplant Unit comprising of 24 Single Rooms with ensuite facilities. He had a nose and throat swab undertaken on admission for COVID-19 on 26/10/20 which was negative as was his screen on 28/10/20. A further screen on 02/11/20 returned a positive result. IPCT were alerted to this on 03/11/20 and Ward 4B was contacted and advised that the patient was at the time pyrexial but no other COVID-19 symptoms. Ward 4B was contacted initially by phone and was advised on IPCT Transmission Based Precautions (TBP) as per national guidance, but due to complex chemotherapy treatment the patient was to remain in Ward 4B overnight. Ward 4B was visited the following morning to discuss the movement of the patient to Ward 4A. Medical staff have agreed for patient transfer out of Ward 4B, but currently was being nursed by a member of nursing staff on a

1:1 ratio. Patient was transferred to Ward 4A on 05/11/20 and continued to be nursed in a single room with TBP as per national guidance. Mr Slorance continued to screen positive for COVID-19 throughout his stay until he passed away on 05/12/20.

Time Line / Ward Movements

Ward	From	To	Bed	Room type
Wd 4B	26/10	04/11	78	BMT room. 1-2-1 nursing following positive result on 02.11.21
Wd 4B	04/11	05/11	76	BMT room.
Wd 4A	05/11	17/11	9	SSR used for isolation of Ward 4b Haem-onc isolation
Unit 7 HDU	17/11	20/11	78	COVID Hub
Unit 4 ICU	20/11	05/12	31	Isolation PPVL

Acquisition of COVID-19

Andrew was tested for COVID-19 by PCR on 26/10/20 and 28/10/20. He was tested again on 2/11/20 and PCR was now positive and remained positive until his death. The interval from admission to testing positive was 7 days. Andrew would be classified as a probable healthcare associated COVID-19 infection. Within the BMT unit, Andrew was cared for in a positive pressure HEPA filtered room. There were no visitors during his stay, standard PPE was used, social distancing was enforced, and every attempt was made to prevent transmission from staff to patients. Over an 18-month period, the BMT unit has had 3 cases of COVID-19 on the ward. All were sporadic with no more than one patient at any time testing positive. Some staff did become positive. Unavoidable contact between asymptomatic positive staff and patients prior to staff members testing positive almost certainly occurred at times but the measures listed were successful in protecting both patients and staff and minimising transmission of the virus.

Questions for this section/missing info

1. **Did any of the patients close household contacts develop symptoms/test positive for COVID between 23rd Oct and 8th Nov?** no information is provided on any probable or confirmed out of hospital exposure.
   AS had three children, aged 13/11/10. It is not clear if they were at school.
   We do not know if he isolated for any time prior to admission.
   Prior to admission but within the incubation period AS attended an Edinburgh hospital for procedures.
   12 days before diagnosis on 21/10/20 – Colonoscopy
   10 days before diagnosis on 23/10/20 – Hickman line insertion
2. **Did the patient attend any other department outside of Ward 4 (e.g. Xray, CT, ECG etc) between admission and 2nd Nov?**
   AS had a CXR performed as a mobile/ portable procedure ON 26/10/20. ECG was done by ward team. He did not leave any ward for investigations until his CT scan.
3. **Why was a COVID screen taken on 2nd Nov?**
   Was there a local COVID testing regime in place or was the patient symptomatic/unwell? Test taken on admission & day 2 (pre-treatment) and again at day 8 (the positive test) which does not align with national guidance at, or since that time.

   The test taken on 2/11/20 was in response to a fever more likely to be caused by Campath/alemtuzmab than COVID but this fever triggered the swab.

   The other two tests were taken as a second screening test (admission) and then as part of a routine screening programme (day2)

   Patients were tested more than was recommended because we were trying to prevent COVID entering the ward or spreading in this highly vulnerable group and we obtained special dispensation to be able to screen more than most areas as we had small numbers of highly vulnerable patients. All our patients were tested twice prior to commencing conditioning chemotherapy, once at the base hospital and then once on admission. Subsequently patients were tested once a week if asymptomatic and at any times they exhibited typical or atypical symptoms.

4. **If the test was taken because the patient was symptomatic, what was the earliest onset date of symptoms recorded?**
   AS was tested on 2/11/20 because he had spiked a fever. This was the first day he had been febrile. He had received a monoclonal antibody called campath/alemtuzumab that day. This almost universally causes fever, especially on the first day of therapy (2/11/20). This can be quite a high fever and in our practice, patients may be started on antibiotics as a precaution, although this course is usually significantly abbreviated, as was the case with AS who received a short course of Tazocin.
   This fever is very unlikely to have been a symptom of COVID and very much more likely to be a side effect of the antibody therapy.

Note that in the narrative states the patient was reported as febrile on IPCT reporting of the positive result on day 9 (3rd Nov). The sample was taken on Day 8 (2nd Nov) but the timeline & remaining review does not show the patient becoming febrile until 9th Nov. The onset is on the cusp of the definition between 'Indeterminate hospital onset (Days 3-7) and Probably hospital onset (Day 8-14).

5. **Narrative states "*patient had no other Covid symptoms*" on return of the positive result- what case definition was being applied, and was atypical presentation considered given the patients underlying health conditions/immunosuppression?**
   Patient had a fever but no loss of taste or smell, no new cough and no respiratory symptoms at all. As noted, we were very well aware that immunocompromised patients should be managed with a high index of suspicion re- development of COVID.
   In this respect that justified the 4 tests described above in a short time frame.
   The patient had a fever. They were not Standard case definition is pyrexia, new persistent cough, loss/alteration of taste or smell. National guidance at states " *It is important to take into account atypical and non-specific presentations in older people with frailty,* ***those with pre-existing conditions and those who are immunocompromised.***"
6. **Can GGC confirm if weekly PCR testing was in place in Ward 4B, and what the weekly compliance rate was this this?**
   Yes weekly testing by PCR was in place for staff and patients. (discussed in more detail in answer to question 3)
   This was the extant policy position at the time of the patient's admission (implementation date of 8th July 2020 as per CMO letter of 3rd July)
7. **Can GGC confirm if all substantive staff regularly working in the unit were included in testing, specifically domestic, AHP, phlebotomy, pharmacy, radiology/radiography staff.**
   We do not have phlebotomists and we did not have control of radiology staff. Large numbers of radiology staff all had a small chance of performing portable films on the ward but we could not test all of these at the time. All other staff groups mentioned were tested weekly.
8. **Were there any staff shortages at the time this case was identified and how were these addressed? Redeployment of staff within the hospital/use of bank agency?**
   Three shifts were cross-covered by ward staff. This overtime will show as 'Bank shifts' but the bank staff were ward staff so covered by screening policies discussed
   See point above about testing of staff – in line with SGov letter dated 3rd July 2020.
9. **Can GGC confirm if any Bank/agency staff were used during the period 26/10/2020 and 03/11/2020, and if so, were these staff included in weekly PCR testing?**
   No external staff used.

10. **Why was the patient moved from bed 78 to bed 76 in Ward 4B?**

This was done to move the patient to the most remote room on the unit to minimise transfer of virus pending reinfusion of stem cell graft, which it was felt should be delivered by transplant unit staff. So the patient was kept on the unit for one further day in the most remote room. The rooms 76-80 are in a slightly separate area to the rest of the ward. In the main body of the ward two banks of rooms run parallel and opposite each other, albeit separated by a wall – best seen on a diagram

Noting the move took place the day after the positive Covid result was known and before a move to Ward4A. No rationale for this move is provided in the narrative

11. **Please confirm the type of room and ventilation specifications of a 'BMT' room in Ward 4B**

BMT rooms are HEPA filtered, positive pressure rooms with no lobbies.

Patient placement appears appropriate on admission – the narrative suggests this is a single bedroom (although unclear if this is a lobbied single room/PPVL) with HEPA filtered air supply and positive pressure. This would be appropriate for the provision of protective isolation for a vulnerable/immunocompromised individual.

12. **What is ward 4A, and what type of rooms (single rooms, PPVL, other?) are provided. Can GGC confirm the ventilation specification for room 9.**

The room on 4A was a single, ensuite room with no HEPA filtration.

This is listed as a single side room (SSR) in the narrative. It would be helpful to understand if this was designed/provided as a single en-suite room (6 air changes balanced pressure) or something else.

13. **Did the accommodation provided in Ward 4B take account of the need for ongoing protective isolation for this patient in addition to source isolation?**

AS was not neutropenic at the time the move took place, on 5/11/20. His counts did fall rapidly and he was neutropenic for the first time on 9/11/20, corresponding with a period of neutropenic sepsis, discussed in depth in previous sections. The answer to this question and question 15 are linked.

Noting the patient was pancytopaenic by the time this move took place

14. **Can more information be provided on the 'COVID Hub' and specifically bed 78.**

The COVID hub is in HDU. I can not speak to this part properly as I do not know the specifications. I can say that the room was a single room with ensuite. There is no HEPA filtration in this area.

Is this a single room or bed space within an open area? If this is a single room, what are the ventilation parameters of this room (air change rate, pressure differential, filter type).

15. **Was there an agreed escalation & management plan to manage any COVID positive patients identified within the BMT via a defined 'High risk' pathway as per August 2020 remobilisation guidance?**

It was felt that the best way to manage the small number of positive transplant patients was on an individual basis, co-ordinated at consultant level. The person who knew these patients best was the consultant Haematologist who was covering the transplant ward (The attending consultant). If a patient became positive for COVID 19 then the attending

consultant on the transplant unit would discuss the case with the ID team, and all other relevant teams (e.g. nursing , ITU, infection control), on an individual, case by case, basis. This meant consultant level discussion of vulnerable patients took place. This was to ensure that the 'high risk' nature of these patients was highlighted and the best available care delivered at any given time.

In the small number of patients who became positive, several factors came into play when deciding whether to move patients out of the transplant unit (Ward 4B) and where they were to move to.

The first consideration was whether it was safe for all other transplant patients (24 bedded unit) to allow positive cases to stay on the unit. In all cases it was deemed that the risk of cross-contamination to other patients outweighed the benefit, to the individual with COVID, of being nursed in ward 4B. This is because the rooms in ward 4B (BMT Unit) where Mr AS was being treated prior to testing positive for COVID, are positively pressurised, but do not have anterooms and would have resulted in potential contamination of the corridor areas with virus if he had stayed in that area.

The next consideration is where to move patients. There are very few effective negative pressure rooms or positive pressure rooms with anterooms in the hospital. These rooms are always under intense pressure. There are no other HEPA filtered areas outside theatres and ITU, which again was under intense bed pressures. All patients were, however, moved to ensuite side rooms The other 4 patients presenting over the last 18 months (3 before and one after AS) were transferred to the ID ward on the 5th floor. These other 4 cases were further out from transplant.

AS was otherwise well, asymptomatic, not neutropenic and not requiring active intervention at the time he was moved out of ward 4B. AS was moved to a single room on ward 4A, part of the renal unit. Ward 4A is next to ward4B and was chosen for several reasons. AS would be close to medical and nursing staff with transplant experience day and night who could both review the patient and advise the ward nursing team quickly in the case of a problem. While in ward 4A, he was managed medically by the transplant team but nursed by renal unit staff. This proved very helpful when managing his subsequent neutropenic sepsis. The renal team have a very strong clinical background with a high quality nursing team with experience of managing patients on immunosuppression and post renal transplant.

Did this escalation plan take into account the continued need for protective isolation in significantly immunocompromised patients in addition to source isolation or cohorting need? Was this plan followed?

16. Please confirm the dates of any positive staff cases associated with Ward 4B and their last known date at work in the 7 days prior to the patient's admission on 26th October.

Staff member	Symptomatic (Y/N)	Diagnosed	Last working day
1	N	Staff testing 20/10/20	19/10/20
2	N	Staff testing 30/10/20	30/10/20
3	N	Staff testing 05/11/20	05/11/20
4	N	Staff testing 09/11/20	13/11/20
5	Y	Community test 15/11/20	11/11/20

Summary of direct contact

One staff member had protected contact (with appropriate PPE) on 28.10.2020 and tested positive on 5.11.2020. One other staff member had contact (with appropriate PPE) on 3/11/20 and subsequently tested positive on 9/11/20

17. If there were staff cases identified in this period, were these linked to a plausible household/non work exposure.

The staff involved did have non work / household exposures. This has not been forensically dissected yet. More information could be obtained.

This would inform the inclusion or exclusion of staff cases and risk of staff to patient transmission as part of an outbreak hypothesis.

18. Were any staff or patient cases identified with an epidemiological association to Ward 4B in the 14 days after the 2nd November 2020?

NO OTHER PATIENTS DEVELOPED COVID ON WARD 4B AFTER AS until Oct 2021

As noted , 2 staff did test positive in this timeframe but no definite epidemiological association to Ward 4B was identified in this time frame and alternative explanations existed.

How many staff, and how many patients?

19. Please confirm the dates of previous positive patients over 18 months and the case definitions applied to these cases (non-hospital onset/indeterminate onset/probable onset/definite hospital onset)

Patient	date	Classification
1. AB	30/03/20	Probable hospital – day 16 admission 4B
2. JP	05/04/20	Non hospital - day 2 re- admitted with fever
3. BM	27/05/20	Non Hospital – day of admit with cough
4. FP	18/10/21	Indeterminate – day 6 post admit day 1 on 4B

20. Can GGC provide any audit data or documented feedback from IPC observation of staff practice within ward 4B, and specifically compliance with PPE, Hand Hygiene, equipment decontamination or environmental cleaning for October and November 2020.

By October 2020 all non essential footfall had been stopped, so handhygene audits and environmental monitoring had been put on hold. Last hand hygene audit June 2020 highly

satisfactory. Annual infection control audit June 2020 gold award. The ward has a strong background record of successful infection control audits in many areas. Runs charts of hospital acquired infections show no hospital transfer in 2year period.

21. Have GGC considered any other risk factors for potential acquisition of Aspergillus from the hospital built environment for this patient?

No identifiable site. No building works. Rooms that AS was in functioning well, no leaks.

Aspergillus assessment and antifungal treatment

Andrew was initially on Posaconazole as prophylaxis during his admission for transplant but this was stopped due to derangement of liver function tests. Aspergillus antigen serology was sent on the 11/11/20 which was negative. A CT scan performed due to persistent pyrexia on 12/11/20 (as above) showed appearances suggestive of atypical infection and it was suggested that fungal pathogens (including aspergillus) should be considered. Andrew was started on isavuconazole on 12/11/20 empirically. Respiratory consultant opinion at the time was that a BAL was unnecessary and microbiology and infectious disease colleagues were comfortable with his current antimicrobial therapy. Repeat aspergillus antigen serology was performed on 1/12/20 which was reported 48h later as positive.

On 3/12/20, upon receiving these results, his treatment was amended upon microbiology advice to add caspofungin to his isavuconazole. They suggested sending samples for aspergillus PCR and a BAL sample (for culture and galactomannan antigen testing). The blood sample sent for PCR on 4/12/20 was negative although not reported until 9/12/20 and Andrew was too hypoxic for a BAL to be undertaken. Given the clinical picture, radiological appearance and positive galactomannan, Andrew's presentation was suggestive but not diagnostic of COVID-19 associated pulmonary aspergillosis. The absence of BAL or tissue sampling makes confirmation very difficult. The subsequent negative aspergillus PCR serology is of unclear significance. Overall, Andrew may have either been colonised or had a secondary infection with aspergillus as up to 33% of critically ill COVID-19 patients do. He was treated with appropriate antifungal therapy under microbiological advice throughout his stay.

Communication with patient / next of kin

Prior to intensive care, there are multiple entries in the note describing discussions with Andrew's wife and Andrew but without extensive detail of the contents of these discussion beyond an update regarding treatment. In ICU, there are communication entries from medical staff on all but 3 days of his stay. These conversations were primarily over the phone due to the ongoing restrictions on visiting. Andrew's wife was kept up to date with his current condition, prognosis, and treatment throughout.

With regards an update regarding aspergillus infection, there is a communication entry on 4/12/20 detailing "potential for additional infection". It would not be routine practice to differentiate between groups of microorganisms unless the family member had clearly demonstrated some subject matter knowledge or had asked for specific details. There are also daily entries of communication with relatives documented in the nursing notes section of ICCA. Overall, the standard of documented communication appears to be of the same high level that is expected for all our critical care patients.

Death Certification

A death certificate was issued with cause of death as:

1a) COVID Pneumonia
2 – Mantle Cell Lymphoma, Bone Marrow Transplant

As was standard practice, a death certificate was completed on 5/12/20 but not issued until 7/12/20 when it could be discussed with the Procurator Fiscal's office. This discussion took place due to concerns regarding the timing of COVID positivity and the potential for this to be a case of nosocomial acquisition. Although there is no record of the discussion with the PF, the certificate was issued the same day which suggests that the PF was happy with the case and the absence of any concerns regarding care being expressed by the family.

Addendum

Serological testing for Aspergillus (Dr Cottam, Consultant microbiologist)

There are caveats/limitations to any diagnostic test, with the Galactomannan antigen/ BetaD-Glucan assays being no exception in the assessment of aspergillus infection.

Unfortunately, no respiratory tract specimens were received for either culture or fungal biomarker/PCR testing.

An important caveat to consider when interpreting serum GM and the beta-D-glucan assay, is that they are non-specific.

False positive results can be seen in patients with gastrointestinal tract mucositis caused by chemotherapy or GVHD, with the postulated mechanism being that galactomannan in food or bacteria can behave as cross-reactive epitopes and may translocate across the intestinal mucosa if there is compromise to the mucosal integrity. Furthermore studies have demonstrated false positive results in patients who have received immunoglobulin therapy and/or transfused blood products. Lastly, and equally important, is that the beta-D-glucan assay can be positive in patients with candidiasis.

Overall, my understanding is that the diagnostic utility of serum biomarkers in the setting of COVID-19 and IPA/CAPA is less certain, particularly in this case it is additionally challenging as we have no respiratory tract samples. As it stands, in my opinion, the diagnosis of invasive aspergillosis would seem possible, with appropriate empirical antifungal treatment being instigated.

COVERING SHEET – Louise Slorance

LS/17 – appendix 17 : Lothian Peer Review

NHS Lothian case review of the care of Mr Andrew Slorance (AS)

This section sets out the introduction and the method followed.

The CNO asked NHS Lothian to review the care of Mr Andrew Slorance (CHI [redacted]) and provided a copy of the internal case review carried out by NHS GGC.

The case review was shared with a small number of clinical experts in the relevant fields. None had looked after Mr Slorance or had a conflict of interest in providing the review. This is relevant as Mr Slorance was a Lothian resident and had been treated by NHS Lothian.

Initial reading generated a number of questions that NHS GGC provided further information in answer to these where possible.

Individual reviewers provided commentary and opinion and these were shared between the group. No reviewer had the opportunity to examine the records of care and construct their own timeline or evidence drawn directly from GGC policies and protocols. With that caveat, all reviewers have had an opportunity to discuss and to disagree with any of the high level conclusions being drawn.

The method used has limitations, most notably that case notes and the actual records were not seen, which would be the way an expert opinion is usually given. Nor were any GGC staff spoken to for clarification of the clinical intention or preceding discussion, which can sometimes be captured incompletely in a case review, prior to writing the report.

The level of this review has therefore been kept at a high level and focussed on whether the care provided met the expected standards.

The following documents have been used:

- CNO commissioning letter, asking for a case note review
- Reply letter to the CNO (by TG which sets out the individuals who would be asked to review based on their relevant expertise)
- Case review from GGC, comprising text assembled by named clinicians summarising the care
- Responses to additional questions from GGC and the documentation of family communication in ITU

The review by NHS Lothian has been assembled and checked with contributing participants that they are in agreement with the overall summary.

A commentary, observations and conclusions marked as opinion have been noted under each section. Where further information would have been helpful, or where assumptions have been made, this is noted.

The overall findings have been set out as a summary at the beginning.

Two clinical papers have been highlighted as being relevant to the questions considered and these are provided separately. Extant guidance documents at the time of Mr Slorance's admission are also referred to with links.

The report was submitted in the agreed timeframe to the CNO, and at their request NHS Lothian and NHS GGC met on 05 January 2022 to clarify outstanding questions in the document, recognising the limitations of the method and to provide an opportunity for discussion. The points of clarification were agreed by email and incorporated into a paragraph at the end of the report. No overall change to the findings resulted from this discussion.

Summary of findings

Overall care in Haematology ward

- The care received by Mr Slorance from the Haematology team was good and no significant gaps in care were identified.
- The therapeutic management of the infections, actual and suspected, including Covid, were appropriate.
- The pattern of disease and possible sources of infection are similar to those seen in other immunosuppressed patients in other units.

Acquisition of Covid

- On the balance of probability this was acquired in hospital but that is not proven.
- It may not be possible to determine exactly how, when or where it was acquired.
- Although gene sequencing of the samples from the patient and asymptomatic staff may be considered, this will not determine the direction of infection and so is unlikely to add anything further.
- In the documentation provided all reasonable precautions appear to have been taken in the care of Mr Slorance and extant Infection Prevention Control guidance followed.

Care in critical care

- AS received appropriate care during his ICU admission with several examples of good quality care.

Journey through the hospital

- Mr Slorance's placement was appropriate to his underlying condition and developing needs throughout his journey, and was in line with extant policy and good practice.

Management of clinical infection

- The administration of prophylaxis for infection of Mr Slorance was broadly in line with that expected based on his underlying condition and treatment.
- Standard bone marrow transplant protocols were followed for Mr Slorance and these included prophylaxis for *Pneumocystis jirovecii* pneumonia.
- The management of Mr Slorance's Covid infection was appropriate.
- Consideration was given to all classes of organisms (bacterial, viral, fungal) that may have caused his underlying pneumonia in addition to Covid and therapeutic cover was provided for these

Diagnosis of Aspergillus infection

- A single positive galactomannan serology result does not prove infection. In the clinical context, this could not be ignored, although there is the possibility of a false positive result.

- Secondary fungal infection is common in Covid patients and in immunosuppressed patients after bone marrow transplant but on the evidence presented, the diagnosis of invasive Aspergillus infection is not certain given the differential diagnoses.
- The patient was too unwell for a broncho-alveolar lavage (BAL) when in critical care but there were some other opportunities to test other samples which with hindsight may have helped support or refute the diagnosis.
- The patient was already receiving appropriate antifungal medication and therefore the correct therapeutic intervention.

Discussion with family

- Communication with all families during Covid has been particularly difficult despite efforts (video calls etc) throughout the NHS.
- In the light of the patient's overwhelming illness, and the lack of any other useful therapeutic intervention, reference to additional infection rather than by a specific name was not unreasonable in the circumstances.

Cause of death

- The completion of the death certificate is in line with the clinical course described

Overall conclusion

The care provided to Mr Slorance was good and met expected standards of care

Detailed review of aspects of care (these follow the same structure as the GGC case review)

Haematology care prior to ITU- review by haematologist

- AS had Mantle cell lymphoma treated with first line chemotherapy in 2016 with NORDIC protocol and LEAM autograft. His disease relapsed in 2019. At a consultation with his Haematology consultant in October 2019, there was a decision to treat his lymphoma with the chemotherapy drug ibrutinib but given that this was only a way of temporarily controlling disease to then go on to consolidate this response with an allogeneic haematopoietic stem cell transplant.
- Allogeneic haematopoietic stem cell transplant was the only curative option for treating this condition and given AS's relatively young age and lack of significant co-morbidity, this was an appropriate treatment course.
- AS had a first consultation with one of the Glasgow transplant physicians in January 2020 who agreed that allogeneic transplant was appropriate. A provisional transplant date of March 2020 was proposed at that consultation. However as this coincided with the start of the covid-19 pandemic in UK it appears as if the allogeneic transplant was deferred to later in the year.
- AS had a second consultation with a different member of the Glasgow transplant consultant team in October 2020. At that consultation there is documentation on the potential impact on the covid-19 pandemic on the risk of transplant. AS was advised that it would be better to proceed to transplant rather than delay until after the pandemic was over because there was a high chance that delay could lead to disease progression which would make AS ineligible for transplant.
- In terms of the risk of severe outcome of covid-19 in transplant recipients a recent EBMT publication provides data on outcomes of covid-19 in haematopoietic stem cell transplant recipients. A mortality of 25.2% was directly attributable to covid-19 infection in this population. (https://doi.org/10.1038/s41375-021-01302-5)
- AS had a covid-19 swab checked 2 days prior to admission to QEUH and was negative. A further swab taken on the day of admission was also negative. The first positive result as obtained on the 2nd November on the 8th day in hospital. Therefore I would agree with the case report that this was hospital acquired.
- Remdesivir and steroids were commenced on 12th November based on the finding of persistent hypoxia first recorded on the evening of 11th November. The timing and appropriateness of this intervention was consistent with the then NHS Scotland guidance on use of corticosteroids and remdesivir. (https://www.sehd.scot.nhs.uk/publications/DC20200903Corticosteroids.pdf, https://www.sehd.scot.nhs.uk/publications/DC20201106REMDESIVIR.pdf)
- I note that AS was entered into the RECOVERY trial but was randomised to standard of care. Toculizamab was a further option for therapy although guidance on its use was only published on 6th November.

(https://www.sehd.scot.nhs.uk/publications/DC20201106REMDESIVIR.pdf)

- A further option that was considered was convalescent plasma but this was discounted because AS had had previous severe reactions to blood components.
- In relation to other aspects of the transplant care prior to ICU admission AS developed neutropenic sepsis with blood cultures taken on 9th November with growing *S. epidermidis*. From his records it appears as if he was quite unwell with a CRP of 450. Once the results of cultures were known his Hickman line was removed and his antibiotics were changed to meropenem and vancomycin. Because of developing renal impairment vancomycin was changed to Teicoplanin. This was an appropriate combination to cover both the *S. epidermidis* bacteraemia and the potential of other unidentified bacterial sepsis. In terms of the appropriateness of Hickman line removal this is not always required in *S. epidermidis* bacteraemia, but given how unwell AS was, this does appear to have been an appropriate action. He improved following removal.
- In order to look for alternative causes for ongoing sepsis a CT scan was performed which demonstrated widespread pulmonary infiltrates throughout both lungs concerning for atypical infection. As patients are profoundly immunosuppressed post allogeneic transplant they are at risk of bacterial, fungal and viral infections.
- Fungal infections in particular are difficult to diagnose and often treatment with systemic antifungals is given on an empiric basis. AS had been on prophylactic posaconazole but this was stopped on 11th November due to hepatic impairment. Isavucoazole was started on 12th November and this is appropriate for aspergillus infection. Intravenous liposomal amphotericin B would be the first line choice for treatment of possible or probable invasive fungal infection but may not have been appropriate due to the combination of renal and hepatic impairment

Opinion

- In relation to the significance of the galactomannan results these are only helpful to a degree in the diagnosis of pulmonary aspergillosis, as there is a relatively high false positive and false negative rate with these tests.
- In relation to the question as to whether to perform a BAL it is documented that this was discussed with respiratory medicine and it was felt this was not required. Whilst it is likely that the BAL would not have given positive microbiology given that AS was already at that time on a broad combination of antibacterial and antifungal drugs, if AS had been fit enough to undergo the procedure this probably would have been the most appropriate course. However, in this clinical scenario often a BAL is not possible due to hypoxia and sometimes this procedure is only undertaken once the patient has been started on invasive ventilation in the ICU.
- In relation to GVHD (Graft versus Host Disease) management I note that there was clinical concern about the possibility of engraftment syndrome/hyperacute GVHD. The standard GVHD prophylaxis with Ciclosporin had been discontinued due to renal impairment, and Methylprednisolone had been given,

I am assuming as treatment for covid-19 and to cover for possible GVHD. MMF is a very standard second line treatment option for GVHD treatment so this was an appropriate therapeutic choice at that time.

- In relation to escalation to ICU it was apparent that AS was critically unwell with multiorgan failure. The only question would be whether given that the likelihood of recovery was very low, whether his care should have been palliative at that stage and not escalated to ICU. That however is a very difficult decision to make in a relatively young patient with a potentially treatable condition.

Care Prior to ICU: review by critical care experts

- AS was admitted to QEUH on 26th October 2020 prior to bone marrow transplantation for mantle cell lymphoma.
- AS treatment commenced on 28th October 2020 following two negative COVID tests taken 26th and 28th October 2020.
- AS tested positive for COVID on a sample taken on 2nd Nov 2020. By the time this result was known he had received all his conditioning chemotherapy, so it was necessary to proceed to the stem cell reinfusion, which occurred on the 4th of November. Posaconazole was initiated as antifungal prophylaxis at this time.
- AS became febrile and neutropenic on the 9th of November. Piperacillin-tazobactam and gentamicin were started at this time as standard therapy for neutropenic sepsis. Blood cultures on this day taken from the Hickman Line grew *S. Epidermidis.*
- Posaconazole was discontinued due to concerns about nonocclusive disease and deteriorating liver function. A less hepatotoxic replacement, isavuconazole was started on the 12th of November. This continued until AS' death.
- In the face of continued clinical deterioration with a sepsis-like picture, antibiotics were changed to vancomycin and meropenem on the 12th of November and AS' Hickman line was removed.
- A non-contrast CT chest on the 12th of November was consistent with a viral pneumonitis, but the report also recommends consideration of fungal infection.
- An extended panel of respiratory virus testing was sent on the 10th and 16th of November 2020.
- Aspergillus serology sent on the 11th of November was negative.
- AS had a respiratory medicine, infectious diseases consult at this time and was discussed at COVID MDT. Of note a broncho-alveolar lavage (BAL) was considered but not felt to be indicated at this time.
- AS' renal function deteriorated from the 9th of November, and this was thought to be multifactorial: sepsis, hypovolaemia, and nephrotoxic drugs.
- AS became increasingly hypoxaemic from the 12th of November. Dexamethasone and Remdesivir were started on this date. Respiratory function deteriorated requiring high flow nasal oxygen (HFNO) and admission to Medical HDU on the 16th of November.
- Between 17th November and 20th November AS was managed with HFNO, CPAP (Continuous Positive Airways Pressure) and conventional oxygen therapy. He also underwent self-proning trials.

Opinion

- From a critical care perspective AS received standard treatment based on what was considered best practice in the management of COVID at that time.
- Other aspects of AS' care were appropriate in our opinion.
- He was investigated appropriately. We agree with the decision not to BAL as it may have precipitated a deterioration in this patient who was already receiving appropriate antibiotic therapy including antifungals.
- He was managed in an appropriate level of care setting based on severity of illness during this period.

Clinical care prior to ITU by microbiological experts

- If there remains significant contention over the time of acquisition of Covid, it may be useful to establish which PCR platform for SARS Co-V 2 diagnosis was used and a virology view as to how much trust to put in a negative result.
    - Some of the initial testing platforms only looked for a single SARS CoV2 gene whereas later ones had more targets.
    - Knowing the PCR Ct value of this result may be helpful to establish if it was a low positive which became stronger, i.e. likely early infection.
- Hickman line: the microbiological sampling that would be required to clearly diagnose a Hickmann line infection are sets of blood cultures from each line lumen plus a peripheral set and the line tip once removed. It is still unclear what microbiological sampling took place to investigate whether there was a line infection or blood culture contamination.
- The lung CT images were consistent with septic emboli from the line. There is a balance of risk in undertaking further tests (BAL) to attempt to establish the diagnosis further. The decision to remove the Hickman line and treat appropriately is a reasonable clinical one overall but one which would best be made in discussion with microbiological colleagues.
- The rise in CRP (C Reactive Protein) during this period from 261 to 468 would not necessarily support the diagnosis of a bacterial line infection in this patient as it could be attributable to worsening Covid which may lead to a rising CRP.
- No issues are identified with the decision making regarding the empirical escalation and choice of antimicrobials if neutropenic sepsis was not resolving. The use of posaconazole and then isavuconazole at this stage in the admission would align with ESCMID (European Society Clinical Microbiology and Infectious Diseases) guidance for treatment of invasive aspergillosis.

Summary of Mr Slorance's care while in ITU: review by critical care experts

- Prior to intubation AS was being managed in an HDU environment and was reviewed by the ICU team including a consultant. He and his next of kin were appropriately counselled about what Intensive Care treatments would involve and the limited chance of a successful outcome.
- AS was intubated after a 72-hour trial of non-invasive respiratory support. This would be considered best practice in management of COVID pneumonitis.
- Prone ventilation was undertaken at appropriate points in his ICU admission, and it is noted that he responded poorly to this.
- From the information provided, other aspects of ICU care were appropriate for an immunosuppressed critically ill patient with COVID, and consistent with best practice at this time, including Factor Xa guided anticoagulation.
- Endotracheal secretions and other microbiological samples were sent on admission. He remained positive for SARS CoV-2 during his ICU admission
- Galactomannan Assay sent on the 1st of December 2020 returned a positive result however this was not available until 3rd December.
- AS received appropriate antimicrobial therapy throughout the duration of his ICU admission and this included antiviral and antifungal therapy.
- AS was too hypoxaemic for a BAL on the 5th of December 2020.
- AS continued to deteriorate on maximal support. Following review by senior clinicians and discussion with AS' wife a decision was made to move to end-of-life care, and he died later that day.

Opinion

- AS received appropriate care during his ICU admission with several examples of good quality care.
- From the documentation provided, communication with AS family was accurate and appropriate.
- Invasive Pulmonary Aspergillus (IPA) is associated with immunosuppression, Haematopoietic Stem Cell Transplant (HSCT) and COVID (COVID 19 Associated Pulmonary Aspergillosis - CAPA). Some case series report a rate of CAPA of 15% of patients with SARS CoV2 infection who require mechanical ventilation.
- There is nothing contained within the information I have reviewed that would concern me that there was an environmental source for AS' IPA if this was the underlying diagnosis.
- From the documentation provided AS had moderate to severe ARDS for the duration of his ICU admission. A recent review of CAPA suggests that sputum or endotracheal aspirate can both be used to diagnose IPA although not as sensitive as BAL (Koehler et al, Lancet Infectious Diseases, 2021). To undertake a BAL in AS while ventilated would have been a balance of risks between diagnosis of new infection and precipitating a further deterioration in respiratory function.
- AS continued to test positive for SARS CoV2 and was receiving antimicrobial treatment which included antifungals. It is our opinion that the ICU team's approach was reasonable in this regard.

- Patients admitted to ICU with multiple organ failure following HSCT have a high mortality, without SACS CoV2 infection. Although there is limited data on outcome of patients with both HSCT and SARS CoV2 who become critically unwell, we would expect the mortality in this group to be extremely high and consistent with the figure of 90% quoted to the family. CAPA is associated in a doubling in mortality in ventilated patients with SARS CoV2.

Commentary from microbiological experts-

- It would be very helpful to see renal biochemistry results from the period 28/11 to 3/12 to understand the nature of renal impairment as these will have guided the choice of antifungal agents. Use of liposomal amphotericin B is preferable as second line treatment, however the addition of an echinocandin (i.e. caspofungin) to isavuconazole as a salvage regimen in management of invasive aspergillosis is also appropriate. Liposomal amphotericin B may have been avoided because of potential toxicities.
- The decision making behind the antibiotic prescribing at this point was the subject of clarification with NHS GGC. The therapeutic choices made reflect the overall patient condition and progress and were made in consultation between different disciplines in critical care.
    - In the table provided in the supplementary information, on 3/12 Gram positive cover (teicoplanin) is continued but Gram negative cover (meropenem) is stopped, with aztreonam which has a narrower spectrum of activity started 24 hours later.
    - These therapeutic choices reflect the lack of progress in response to meropenem which was stopped after a full two week course and reflects a therapeutic change to intensification of empirical antifungal treatment which can be undermined by maintaining broad spectrum antibiotic cover.

Patient journey through QEUH: review by Infection Prevention and Infection Control colleagues

- AS was cared for in single room accommodation throughout his admission.
- The single ensuite bedroom on admission was provided with HEPA filtered air and mechanical supply and extract ventilation under positive pressure. This is designed to protect the room occupant from unfiltered air and ingress of airborne contaminant from the hospital corridor and appropriate to this patient group.
- Admission COVID PCR screening was completed (and negative) in line with extant policy at that time.
- Additional precautionary screening over and above the frequency required by national policy was in place – this reflects & acknowledges an understanding of the vulnerability of this patient group to infection.
- There was no delay in PCR testing in response to initial symptoms (pyrexia).
- A risk-based approach to patient moves within ward 4B was adopted following AS' positive COVID result. This is in line with good practice in order to mitigate risk to others within the ward.
- Attempts to minimise patient movement (and potential for exposure outside of the protective ward environment) were taken and are considered good practice – e.g. chest x-rays were carried out in the ward.
- A detailed rationale is provided to explain the overall management of patients with COVID within the transplant unit. This reflects a balanced consideration of individual patient risk factors, clinical need and the needs of the wider patient population and is line with good practice.
- Protection from opportunistic infection was provided in HDU. The air supplied to this ward is not (and is not required to be) HEPA filtered, but positive pressure air flow from mechanical ventilation systems was maintained (protecting AS from 'contaminated' air ingress from the corridor/wider unit).

Opinion

- It is our view that patient placement was appropriate to AS's underlying condition, planned treatment and subsequent COVID infection throughout his admission and was in line with extant policy and good practice at that time.
- Transfers and patient placement following his diagnosis with COVID on 2nd November took account of both the need for source and protective isolation for this patient. This is in line with good practice.

COVID acquisition: review by Infection Prevention and Infection Control colleagues

- AS had a negative COVID PCR test on 23rd October 2020 in NHS Lothian where his Hickman line was inserted (day case procedure).
- On admission to QEUH his PCR on 26th October and subsequent precautionary PCR screening on 28th October were also negative.
- There were no COVID positive cases associated with the Cancer Assessment Unit at WGH Edinburgh between 20th and 23rd Oct 2020 meaning it is less likely that AS was exposed to COVID 19 during his visits there on these dates for insertion of Hickman line and colonoscopy and prior to admission to QEUH.
- There was no known exposure to COVID prior to his admission to hospital.
- Appropriate steps were taken to minimise the risk of transmission within the hospital environment – this included provision of routine diagnostic tests such as plain Xray within the ward rather than the wider radiology department.
- The staff who participated in weekly asymptomatic staff PCR screening **and** had a positive PCR result in late October or early November 2020 **and** had confirmed contact with AS between 26th Oct and 2nd Nov were confirmed as PCR negative at the time of that contact. This means it is less plausible that there has been staff to patient transmission of the virus from these individuals to AS.
- A plausible non workplace exposure was identified for all staff who tested positive for COVID on routine asymptomatic screening. However patient to staff transmission through an unknown mechanism and time remains a plausible hypothesis.
- The direction of infection transmission (staff to patient, patient to staff, staff to staff) cannot be asserted beyond all reasonable doubt on the basis of descriptive epidemiology.
- Whole genomic sequencing of staff and patient samples (if available) would also only be able to confirm or exclude that the virus in each sample was genetically linked (indistinguishable) or not. It would not provide evidence of the direction of transmission.
- AS had some contact with a small number of staff for whom no COVID screening information is available in both hospitals. AS had, or may have had, contact with a small number of staff for whom no COVID screening was required or is available. This would include for example, radiographers. Asymptomatic staff to patient transmission is plausible from this cohort of staff over this period.
- There were no known breaches in the use of PPE although this is reliant on self-reported compliance from staff. No structured observational data is available due to the temporary suspension of formal audit programmes. This approach is consistent with that taken in other large Boards including NHS Lothian to allow IPC and clinical resource to be prioritised.
- PPE is considered the lowest level of protection in the hierarchy of control (as defined by national policy). Fluid resistant surgical face masks, whilst effective in reducing risk, do not provide 100% protection from droplet or short-range aerosol dispersal.

- Masks are not close fitting or sealed to the face. There can be natural gapping at the sides and top of the mask. Movement of the mask is not uncommon during normal use and speech. It is plausible that AS was inadvertently exposed to droplet or aerosols of this highly transmissible virus from an asymptomatic member of staff during care even if a FRSM was worn.
- The adequacy of IPC control measures within ward 4B is supported by the fact there was not subsequent transmission of COVID following AS diagnosis.
- Over the duration of the pandemic, there is no epidemiological link between the 4 other patient COVID infections in ward 4B, and 2 of these 4 infections were defined as non-hospital onset (exposure occurred prior to admission).

Opinion

- It is probable that AS acquired COVID 19 from an unknown person, between his admission on 26th October and 2nd November 2020.
- There is no indication of systemic failings in IPC or COVID control – all known cases appear to have been managed well with no further transmission within the ward environment.

Aspergillus assessment and treatment: expert opinion from medical microbiology

- The assessment **as written** places more diagnostic certainty on the galactomannan serology results being genuine than I am comfortable with. Galactomannan serology may give false positives. Many penicillin based antibiotics have generated false positives including piperacillin-tazobactam but more recent kits may avoid this. The positive galactomannan results are after exposure to piperacillin-tazobactam and are not supported by a negative blood Aspergillus PCR. Neither test alone is robust enough to diagnose or exclude pulmonary Aspergillosis.
- IDSA guidance from 2016 for management of pulmonary aspergillosis says that galactomannan should not be performed from blood (only BAL) if already on antifungals, and this patient was already on antifungals at the point of the Galactomannan testing which tested positive.
- Discussion with GGC has clarified that this (the validity of a single galactomannan serology sample) is widely known amongst the clinical teams and formed part of the discussion about management of care. The limitations of the test and the risk of overinterpretation were understood.
- The CT appearances may have been from a viral aetiology (this is difficult to know without seeing the CT scan). He was known to have Covid at the time.
- The absence of deep respiratory sampling does not help exclude a bacterial cause of Ventilator Associated Pneumonia which may not have been covered by teicoplanin and aztreonam. It could have been tested either for galactomannan or cultured for fungi or tested by PCR for Aspergillus species and other pathogens so there might have been opportunity to gain greater diagnostic certainty if it had been possible to get a deep respiratory sample.
- The diagnosis of aspergillosis is not proven from the data we have, but there was awareness of this potential infection not just in a BMT patient, but also in Covid patients.
- He was managed empirically for aspergillus infection. Antifungal management seems broadly appropriate in terms of prophylaxis and empiric treatment, although possibly resistance and fungi other than aspergillus are not mentioned
- Accepting that there was too great a risk to perform a BAL after 3/12, deep respiratory samples can be both cultured and/or be used for molecular detection of pathogens to help diagnose whether a second organism is present. It would have been a better sample type to use to look for fungal hyphae directly by microscopy, test galactomannan or perform aspergillus PCR to further investigate whether there is pulmonary aspergillosis or a false positive serum galactomannan. This is not a failure in clinical care but a learning point.
- A sputum sample sent on 20 November could have been used for other tests.
- It could have been used to test (or re-test with greater positive predictive value than throat swab after 16/11) for a wider panel of respiratory viruses, Legionella, Chlamydia, Pneumocystis.
- The possibility of secondary Pneumocystis pneumonia does not seem to have been considered although would have been in the differential for a neutropenic

patient with a progressive pneumonitis. Appropriate prophylaxis was given and the clinical picture did not fit with this for the clinical team – see clarification.

- By 3/12 a BAL would have likely been too risky to perform given the precarious ventilation but other "blind" sampling of respiratory secretions or even throat swabs might have helped improve diagnostic uncertainty with regard to presence of other pathogens. Current European (ESCMID) and American (IDSA) guidance for investigation and management of invasive aspergillosis strongly advocates use of BAL for diagnosis.
- Note the ESCMID (2018) guidance and IDSA (2016) guidance do not support use of serum galactomannan in patients to make the diagnosis who are already receiving antifungal prophylaxis.

Communication with family: review by critical care colleagues (lead doctor and previously lead nurse) and others

- In the light of the patient's overwhelming illness, and the lack of any other useful therapeutic intervention, reference to additional infection rather than by a specific name was not unreasonable in the circumstances. It was also acknowledged that communication over the telephone due to very restricted visiting would have been difficult for both clinical staff and family.
- In communication 3 26/11, there is acknowledgement that there is a risk of secondary lung infection. Communication note 7 on 30/11 says that there was at that stage not thought to be any suggestion of a secondary lung infection but only Covid pneumonitis.

Clarification from NHS GGC

This covered a number of areas following discussion on 05 January 2022:

- PCP prophylaxis was given - protocol is that this is not due to start until day 28 post BMT (02/12/20) and the clinical picture on CT was not one of PCP. Septrin would have been avoided in the light of the toxicity profile. The Haematology team did not consider this to be PCP.
- Choice of antimicrobials - the decision to change antimicrobials is made as part of the daily consideration of patient care and reflects the overall clinical picture, therapeutic options, side effect profile and patient progress. Specifically the narrowing of antibacterial cover on 3/12/21 reducing Gram negative cover reflects the overall patient condition and was a considered decision made by the whole team.
- On balance of risk, all were in agreement that the decisions not to undertake BAL were the correct ones,
- Additional information was provided by Dr Clark about a letter he had written to Mrs S after AS's death, expressing condolences, agreeing that the main cause of death in his opinion was Covid and offering to meet to discuss any questions Mrs S had.

Tracey Gillies

11 January 2022