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International Forum on Transfusion Practices in Haematopoietic Stem-Cell Transplantation: Responses

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Russia

Question 1

250 autologous and 10 allogeneic.

Question 2

We use X-ray as the source of irradiation.

Following are the main technical parameters:

- the exposure time to ensure the absorbed dose from 25 to 35 Gy is 45 min;
- absorbed dose rate level: (in the centre of the camera and tray is 0.62 Gy/min, 2) at the upper and lower levels of the tray 0.72 Gy/min;
- the dimensions of the tray allow irradiation at the same time up to 3 litres of donated blood;
- the tray is oscillated at a frequency of 60 cycles per minute at an angle of up to ±15°;
- the size of the focal spot of the X-ray tube is 1.4 * 1.4 mm;
- the power of the equivalent dose of ionizing radiation at any accessible point at a distance of 0.1 m from the surface of the apparatus does not exceed 1.0 μSv/h.

Question 3

We perform a complete blood count every day during HSCT.

Question 4

Following is our blood transfusion protocol:

- 80 g/l is the haemoglobin threshold for red blood cell transfusion in stable patients during the aplasia period.
- We use 1 red blood cell unit transfusion policy.
- The selection of red blood cells (RBCs) according to the ABO system depends on the period of haematopoietic stem cells (HSC) transplantation. Three periods are distinguished: the period of preparation of the recipient for HSC transplantation (period I), the early period after HSC transplantation until complete donor chimerism occurs, when red blood cells of the host and donor (period II) are determined, and the complete engraftment of the HSC donor (period III). In the first period, transfused RBCs that are identical or compatible with the patient's phenotype. In the second period, starting from +4 day, it is necessary to carry out weekly monitoring of the anti-A and anti-B IgM class, as well as the IgG class: fixed on the surface of the patient RBCs (in direct Coombs test) and circulating in the serum (indirect Coombs test). If the titre of anti-A and/ or anti-B in the pretransplantation period was more than 128 (dilution 1: 128), then IgM and IgG antibodies are measured twice a week after HSC transplantation until the titre decreases to less than 16 (dilution 1: 16), then once a week until the antibodies completely disappear within the next 2 weeks, except for transfusion recipients. Period II lasts until the complete change of blood group, the absence of antidonor antibodies in two sequential blood tests of the recipient for 2 weeks, or the development of transplant rejection. The end of period II means the start of the use of RBCs only with the phenotype of the donor. In the third period, transfused RBCs that are identical in phenotype with an HSC donor [1].

Question 5

Regarding platelet transfusion protocol:

- We use the prophylactic strategy for autologous HSCT.

- As platelet target, we consider 10×10^9/l for platelet prophylactic transfusion in patients undergoing allogeneic and autologous HSCT.
- We use single donor platelets, pathogen reduced (amotosalen + UVA) in additive solution (SSP+). Pooled random platelets are used widely in Russia but still inaccessible for our hospital at local market
- In case of a minor ABO-incompatible platelet transfusion, we do not apply any measure (volume reduction, isoaglutinins titration) due to plasma replacement by additive solution.
- We systematically monitor the efficacy of platelet transfusions by a post-transfusion platelet count at 20 h after transfusion.
- In case of platelet transfusion refractoriness, we manage it with 24-h continuous infusion of platelets [2].

Question 6

We measure the isoagglutinin titres routinely in patients after allogeneic HSCT weekly. If the titre of anti-A and/ or anti-B in the pre-transplantation period was more than 128 (dilution 1: 128), then the isoagglutinin titres are measured twice a week after HSC transplantation until the titre decreases to less than 16 (dilution 1: 16), then once a week until the antibodies completely disappear within the next 2 weeks?

Question 7

See Question 4.

Question 8

We did not have pure red cell aplasia.

References

1 Akselrod BA, Balashova EN, Bautin AE, et al. Clinical guidelines for red blood cell transfusion. Russian Journal of Hematology and Transfusiology (Gematologiya i Transfuziologiya). 2018; 63:372-435.https://doi.org/10.25837/HAT.2019.62.39.006

2 Cid J, Guijarro F, Carbassé G, et al. 24-h continuous infusion of platelets for patients with platelet transfusion refractoriness. Br J Haematol 2018;181:386–9. https://doi.org/10.1111/bjh.14572

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Spain

Question 1

We perform 81 transplants: 21 autologous, 60 allogeneic.

Question 2

For autologous: 6 months, if patient has immunologic recovery.

For allogeneic: 1 year at least. Immunospresors have been withdrawn and total immunologic recovery. If there is doubt, we maintain irradiation.

- I do not know the source of irradiation.
- 25 Gy.

Question 3

Yes, we perform a complete blood count every day for autologous and allogeneic.

Question 4

Protocol for red blood cell transfusion:

- The haemoglobin threshold is <8 g/dl.
- We use 1 unit.
- No. Donor/recipient match units are always used. Engraftment is defined by clinical and complete analytic criteria.

Question 5

Regarding platelet transfusion protocol:

- Prophylactic.
- 10 000/μL if stable and 20 000 if bleeding risk factors.
- Indistinctly. HLA single donor to alloimmunization pts. Yes, the platelets are suspended.
- No.
- No.
- HLA match single donor.

Question 6

No, not routinely. Abo major incompatibility. Haemolysis suspicion. No specific time is defined.

Question 7

Yes. After abo minor and mixed transplants. No Hb responds after transfusion. Haemolysis Suspicion (analytical).

Question 8

Approximately 15%, depending on the number of ABO transplants with major incompatibility. Periodic transfusion mainly. In some very complicated and individual cases, we have used rituximab and also careful review of immunosuppression.

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Tokyo

Question 1

We performed 22 autologous and 33 allogeneic HSCT in 2019 (approximately 50–60 per year).

Question 2

In Japan, all red blood cells and platelets are irradiated.
- X-ray.
- 15–50 Gy.

Question 3

We perform a CBC count every day until engraftment in both cases.

Question 4

- We transfuse two units of red blood cells to maintain a haemoglobin level of 7g/dl.
- One unit of red blood cells is prepared from 200 ml of whole blood in Japan.
- We switch to donor type blood group when anti-donor isoagglutinins are undetectable and RBCs of donor type are present.

Question 5

We transfuse random platelets prophylactically (transfusion threshold is 10 000–20 000/μl). Platelets are suspended in plasma and ACD-A liquid. In case of platelet transfusion refractoriness, we monitor corrected count increment (about 60 min after transfusion). Additionally, anti-HLA antibodies and anti-HPA antibodies are measured.

Question 6

No.

Question 7

No.

Question 8

About 10–15% of recipients who underwent major ABO-mismatched HSCT developed PRCA. We continue red blood cell transfusion until recovery.

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Germany

Question 1

Our centre is a University hospital including a haematology department with an outpatient clinic and a special unit for transplant patients. The collection of autologous and related donor stem cells is performed in collaboration of the haematology clinic, the paediatric haematology clinic and the transfusion medicine department. Allogeneic stem cell transplants from unrelated donors are imported. We perform between 20–30 autologous and 20–30 allogenic stem cell transplantations per year.

Question 2

We follow the guidelines by the British committee of standards in haematology [1]. The guidelines recommend irradiation of cellular blood products after autologous HSCT for 3 months and for 6 months if the patient was treated with irradiation of his body. After allogeneic transplantation, cellular blood products for transfusion are irradiated 3–6 months. It depends on lymphocyte counts and the duration of immunosuppressive therapy.

- Irradiation of RBCs and platelets is performed by caesium
- 30 Gy.

Question 3

During HSCT period, the patient blood count is performed every day until discharge. After discharge, patients are monitored once a week until day 100 after transplantation when no complications occur.

Question 4

Transfusion thresholds for transplant patients do not differ from other patients. Physicians follow the German guidelines for hemotherapy [2]. Transfusions of RBCs are absolutely indicated if the haemoglobin value falls below 3.7 mmol/l (5.7 g/dl). Between 3.7 and 6.0 mmol/l (5.6–9.6 g/dl), RBC transfusions are indicated if the patient shows symptoms of a non-appropriate oxygen supply, for example tachycardia, tachypnea and angina pectoris [2]. Typically, 2 RBCs are transfused in anaemic non-bleeding patients, but since the introduction of patient blood management measures, the number of 1-RBC transfusions became more frequently. One reason for the 2-RBC transfusion strategy is to prolong the period between transfusions, especially for outpatients for increasing their quality of life and to reduce the visits in the outpatient clinic.

Our transfusion strategy for patients after allogeneic HSCT depends on the ABO type of the donor red cells and the anti-A and anti-B antibodies in the patient plasma. For transfusion, we choose red cells which are compatible to the antibodies in the patient plasma, for instance for a patient with blood type A and a transplant of blood type B we further transfuse RBCs of blood type A or O at least as long as anti-B antibodies in the plasma are detectable.

After ABO-incompatible allogeneic transplantation, we change the ABO and RhD blood type of the patient when the majority of the circulating red cells express the blood type of the donor and the serum group is compatible with the donors' red cells. We determine the red blood cell group serologically. Every blood sample that is sent to our laboratory is tested for the ABD type. In case of an engraftment failure, we will recognize changes in the expression of ABD antigens and adapt our RBC transfusion policy individually.

Question 5

The indication for prophylactic platelet transfusions depends on the bleeding risk assessment of the individual patient. In our hospital, the prophylactic platelet transfusion strategy is absolutely indicated in patients with platelet counts lower than 10 G/L without other bleeding risks. In the majority of cases, platelets are transfused for treatment of bleeding. Our transfusion medicine department provides predominantly platelet concentrates pooled from buffy coats of 4 donors of the same blood type suspended in additive solution. Platelet apheresis is performed for patients with rare blood types or platelet transfusion refractoriness because of HLA class I antibodies. In these products, platelets are suspended in plasma of the donor. No special procedures are performed to detect or reduce isoagglutinins in the donors' plasma. To decrease the risk for haemolytic episodes and clinical symptomatic transfusion reactions after minor incompatible platelet transfusions, we specially consider ABO plasma compatibility in children with low body weight and patients with high transfusion frequency. Platelet transfusion efficacy is monitored typically on the next day after transfusion. If there is no appropriate increment in the platelet count, laboratory testing for HLA class I antibodies is initiated. When the antibody screening is positive, only antibodies with lymphocytotoxic effects are considered as clinically relevant and HLA class I compatible donors are chosen for platelet apheresis. Other reasons than HLA antibodies can induce platelet transfusion refractoriness in non-bleeding patients. To distinguish immunological from non-immunological reasons, we transfuse 2 platelet concentrates at the same time and measure the platelet increment 1 h after transfusion. If there is no increment, an immunological reason is likely.

Question 6

We defined a standard for immunohematology laboratory testing before HSCT including the patients ABO and Rhesus type (CcDEe), K antigen, red cell antibody screening, isoagglutinin IgM and IgG titration performed by a microcolumn gel centrifugation technique and a direct antiglobulin test. After HSCT, we clearly state the transfusion strategy in the patient database that the laboratory assistants have a guideline for choosing blood products for this patient. When we observe changes in the ABD antigen expression

of the patient, we repeat isoagglutinin testing of the patient but without titration. If ABD antigen expression has changed to the donors group and the presence of isoagglutinins is compatible to the donors ABO type, we change the blood type of the patient in the patient database.

Question 7

This is already stated in answer 6 we perform a standard of immunohematology investigations before HSCT including the direct antiglobulin test. The result before HSCT is the benchmark for results after HSCT but we do not perform the antiglobulin test routinely after HSCT in a defined frequency. As long as the red cell antibody screen and crossmatches are negative, we do not repeat the direct antiglobulin test except there is a clinical suspicion for haemolysis. If the antibody screen is positive, all further investigations including the direct antiglobulin test and elution procedures of the autologous red cells are directed to detect or exclude clinically relevant alloantibodies. But this is the same for all patients not only after HSCT.

Question 8

The incidence of pure red cell anaemia (PRCA) is very low with less than one case per year in our institution. When the diagnosis of a PRCA is suspected, a complete haematological work-up is carried out. It includes the physical examination, peripheral blood smear, reticulocyte count, iron parameters, vitamin B12 and folic acid levels and a metabolic panel. Additionally, antibodies against viruses are determined to exclude viral infections associated with anaemia. A bone marrow examination is mandatory with smear, histology, cytogenetics and molecular genetics to exclude a myelodysplastic syndrome. Therapeutic options include red cell transfusions, steroids and immunosuppressive agents, when necessary. The choice of therapy in absence of associated causes depends upon severity of the disease and patients' age and constitution. Allografts for PRCA were not used in our institution so far.

References

1 Treleaven J, Gennery A, Marsh J, et al. Guidelines on the use of irradiated blood components prepared by the British Committee for Standards in Haematology blood transfusion task force. Br J Haematol 2011;152:35–51

2 Bundesärztekammer. Querschnitts-Leitlinien zur Therapie mit Blutkomponenten und Plasmaderivaten Deutscher ÄrzteVerlag; 2009. Available from: https://www.bundesaerztekammer.de/fileadmin/user_upload/downloads/QLL_Haemotherapie_2014.pdf.

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Switzerland

Question 1

100 allogeneic, 45 autologous.

Question 2

Autologous: principally for 1 year, in clinical practice lifelong.

Allogeneic: as long as there are signs of GvHD, or if patients are under immunosuppressive treatment, in clinical practice lifelong.

- Caesium 137.
- 30 Gy.

Question 3

Complete blood count is performed every day, once a week there is also a microscopic blood film analysis, in certain circumstances additional blood smears at the discretion of the treating physician.

Question 4

Transfusion protocol:

- 70 g/l.
- 1 RBC unit.
- We change RBC blood groups to donor type usually after 6 months. AB0 antigens must be donor type, and also RH, K, JK, FY and MNS (extended phenotype). The DAT should be negative. Criteria for RBC engraftment

are an absolute reticulocyte count of >30 ×G/l and the absence of RBC transfusion requirements. The detection of donor AB0 blood group is not part of the criteria. (Neutrophil engraftment is defined as the first of three consecutive days of an absolute ANC count of >0.5 G/l; PLT engraftment is defined as PLT > 20 G/l without transfusions in the last 7 days).

Question 5

Regarding platelet transfusion protocol:

- Prophylactic.
- 10 G/l in stable clinical situation, 20 G/l when there are risk factors for bleeding such as fever, aGvHD, 30 G/l in case of systemic anticoagulation due to thrombosis.
- We use both single donor and buffy coat pooled PLT, all are pathogen reduced using the Intercept Blood system from CERUS (since 2011) all are in platelet additive solution (Intersol). No, considering also the suspension in platelet additive solutions (PAS).
- Yes. 15–60 min post-transfusion.
- Assess if non-immunological reason for refractoriness, check for HLA –Antibodies (Luminex). If HLA –Ab are present, we try to prevent transfusion of single donor PLT bearing the relevant antigens, in special cases we transfuse HLA-matched platelet concentrates.
- In case of no success, we use PLT drip infusion (described by J.Cid and M. Lozano): [1] adult doses are divided into 4 split doses, and each dose will be continuously infused over a 4–5 h period of time in order to have a constant (small) amount of PLT in the circulation supporting endothelial integrity.

Question 6

Yes.

- Before HSCT, at day 30 and at day 180.
- More frequently in case of pure red cell aplasia or relapse.

Question 7

Yes, we use DAT and Elution techniques (incl. elution against A and/or B panel cells).

Question 8

The PRCA incidence is about 20% of the HSCT with major or bidirectional AB0 incompatibility (about 3% of all allogeneic HSCT).

Management information:

(i) red blood cell transfusion (Hb threshold 70 g/l).
(ii) we try to taper immunosuppression as fast as possible.
(iii) daratumumab and/or rituximab in cases not resolving spontaneously or not responding to the reduction of immunosuppression.

Reference

1 Cid J, Guijarro F, Carbassé G, et al. 24-h continuous infusion of platelets for patients with platelet transfusion refractoriness. Br J Haematol 2018;181:386–9.

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Italy

Question 1

We perform 20 autologous and 15 allogeneic haemopoietic transplantations per year.

Question 2

We irradiate all blood products for autologous and allogeneic recipients except platelet concentrates (both from single donors and from pooled buffy coats) for which irradiation has been replaced by Amotosalen/UV pathogen inactivation.

Irradiation is applied using a dedicated Caesium-137 source and the energy of 2500 cGy.

Question 3

All patients, after autologous or allogeneic transplantation, have a daily complete blood count and leucocyte differential till full haemopoietic recovery.

Question 4

The haemoglobin threshold to perform red blood cell transfusion in stable allografted or autografted patients is 80 g/l. In routine practice, we use a single-unit red blood cell transfusion policy. In ABO-incompatible transplants, we change the red blood cell group of RBC concentrates to donor cell group when stable full engraftment is obtained and monitored: engraftment is in general defined by molecular full-donor chimerism and, for red blood cells, by globular/plasmatic tests (including titrations) combined with negative results of direct/indirect antiglobulin tests and, finally, with the ABO genotyping confirmation.

Question 5

We use a prophylactic strategy for platelet transfusion. In stable patients, the prophylactic threshold is 10×10^9/L in both autologous and allogeneic transplantation. We transfuse both single donor and pooled buffy-coat platelet concentrates. Our platelet concentrates are produced in platelet additive solution with a poor plasma content. In any case, in most of our transfusion episodes, we release ABO identical/compatible platelet concentrates for all patients, including haemopoietic transplant recipients. We monitor platelet transfusion efficacy with a complete blood count the morning after transfusion. We do not perform routinely blood counts 15–60 min after transfusion.

In recipients with serologically detected immune platelet refractoriness by ELISA (anti-HPA platelet antibodies) and Luminex (anti-HLA platelet antibodies) tests, if the patient is bleeding and the transfusion is urgent, we assign fresh pooled buffy-coat platelet concentrates, and otherwise, we perform platelet cross-match with SPRCA technology on ABO, rarely HPA/HLA, compatible single donor concentrates. For these patients, we monitor routinely blood counts 60 min after transfusion.

Question 6

We routinely monitor isoagglutinin titres during ABO-incompatible haemopoietic transplantation. Isoagglutinin titres are performed prior transplantation, before and after plasma-exchange in case the recipient undergo isoagglutinin removal. After transplantation, isoagglutinin titres are performed every week until engraftment and then every 15 days, with ABO blood group checked every month.

Question 7

The basic immunohematologic monitoring of ABO-incompatible recipients includes also direct/indirect antiglobulin tests and isoagglutinin titration. The direct antiglobulin test is performed 2 times a week for 3 weeks, 1 time a week for 2 weeks and then monthly until the DAT will be negative. We also test LDH and haptoglobin.

Question 8

In our practice, the incidence of pure red cell aplasia in ABO-incompatible haemopoietic transplantation is around 5%. In general, patients are supported with carefully cross-matched red cell transfusions and corticosteroids. During treatment and support, immunohematologic monitoring includes direct/indirect antiglobulin tests, serological and genomic blood group typing as well as isoagglutinin titration.

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The Netherlands

Question 1

In our academic hospital, we perform about 60–80 autologous and 60–70 allogeneic HSCT's in adults per year.

Question 2

After an autologous HSCT, patients have an indication for irradiated blood products for a period of 1 year. Patients undergoing an allogenic HSCT receive irradiated blood products 4 weeks before until 5 years after transplantation. In our country, institutes normally not irradiate products themselves. This is performed by Sanquin, the

only institute (foundation) in the Netherlands allowed to and responsible for the blood supply.
-X-ray is used as source of irradiation
-at an energy dose of 25–50 Gy.

Question 3

We perform a complete blood count in autologous and allogeneic HSCT every 2nd day, until repopulation. In case of pre-treatment with anti-thymocyte globulin (ATG), a complete blood count is performed daily.

Question 4

In stable patients, an haemoglobin threshold of 8 g/dl is used for red blood cell transfusion. We use an one red blood cell transfusion policy, in the outpatient ward occasionally a two red blood cell unit transfusion policy. Patients receiving a non ABO identical transplant, receive both patient and donor ABO compatible red cell units starting from two weeks before HSCT. We do not change to donor ABO compatible units after engraftment. However, we do change the patient's ABO blood group to the donor blood group, once we are sure engraftment is reached. For that, the patient must be transfusion independent for three months and his/her blood group must match the donor ABO blood group, based on antigen typing, without discrepancies. For treatment purposes, engraftment is determined by white cell donor chimerism detection.

Question 5

In our institution, a prophylactic platelet transfusion protocol is used in case of an autologous HSCT. The prophylactic platelet transfusion trigger is $>10 \times 10^9$/l both in patients undergoing allogeneic as autologous HSCT. The standard platelet product for this purpose is a 5-donor random platelet product containing PAS-E/plasma. In case of transfusion refractoriness with proven HLA class 1 antibodies, there is an indication for an HLA-A and HLA-B typed (identical) single donor platelet product, again suspended in PAS-E/plasma. Because we use platelets suspended in PAS-E/plasma, iso-agglutinins concentrations are lowered. Therefore, we don't apply any measure in case of a minor ABO-incompatible platelet transfusion. We systematically monitor the efficacy of platelet transfusions in patients undergoing HSCT by a post-transfusion platelet count about an hour after finishing the transfusion. In case of transfusion refractoriness, we first check for the presence of HLA class 1 antibodies (by use of a Luminex technique). In case they are present, the patient has an indication for HLA-A and HLA-B typed (identical) single donor platelet products. Waiting for the result of the HLA class 1 antibody screening, and in case of bleeding, the patient will receive HLA-A and HLA-B typed (identical) single donor platelet product(s) on a trial basis. In case of severe platelet refractoriness and absence of HLA class 1 antibodies, we screen for HPA antibodies (following an HPA typed single donor platelet product transfusion).

Question 6

Isoagglutinin titres are not determined routinely in patients after allogeneic HSCT. They do are determined before HCST in case of major ABO blood group antagonism. Furthermore, we perform ABO typing (antigen and antibody) after HSCT on a regular basis, and anti-A and/or anti-B agglutination strengths are sometimes used to evaluate aplastic anaemia due to major ABO blood group antagonism.

Question 7

After HSCT, ABO blood group typing (antigen and antibody) and an irregular antibody screen is performed on a regular basis. At first every three days, thereafter with each visit to the outpatient department, until engraftment is reached. The direct antiglobulin test is not performed routinely, however, is done whenever there are discrepancies in the ABO blood group typing or when the irregular antibody screening is positive. Of course, the direct antiglobulin test is also performed in case of clinical signs of (auto-immune) haemolytic anaemia.

Question 8

We see about three cases of pure red cell aplasia in HSCT patients per year. In case of major ABO blood group, antagonism anti-A and/or anti-B agglutination strengths can be used for monitoring. Patients receive red blood cell and platelet transfusions when needed. Further treatments of AA are in line with the Dutch guideline for AA (ATGAM, allo SCT).

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Australia

Question 1

120 autografts and 100 allografts for adult patients.

Question 2

Irradiated cellular blood products are provided indefinitely after both autologous and allogeneic HSCT.

Gamma irradiation is performed by the Australian Red Cross Lifeblood prior to product issue to hospitals. This is undertaken according to Australian and New Zealand Society of Blood Transfusion 'Guidelines for Prevention of Transfusion-Associated Graft-Versus-Host Disease', 2011.

A minimum 25 Gy with no part of the component receiving more than 50 Gy. [1]

Question 3

Full blood counts are performed every day after both allogeneic and autologous HSCT until count recovery/discharge.

Question 4

The typical threshold for red cell transfusion in a stable post-transplant patient is Hb < 80 g/l. We note the recent publication by Tay and colleagues reporting similar quality of life and other outcomes in HSCT patients using restrictive (Hb 70 g/l) compared with liberal (Hb 90 g/l) thresholds for RBC transfusion [2].

If red cell transfusion is required on the combination of clinical features and haemoglobin result, 1–2 units of RBCs are usually transfused.

Allogeneic HSCT recipients requiring RBC transfusion receive RBCS which are compatible with both donor and recipient blood groups until engraftment. Following engraftment, according to our protocol, the patient's blood group is changed to donor type in the laboratory information system when, after 3 months without RBC transfusion, testing is performed that shows their forward group is consistent with donor group with no mixed field, the reverse group demonstrates no anti-donor isoagglutinins, the DAT is negative, and the RBC phenotype is consistent with donor phenotype. From this point, if the patient requires further transfusions, this will be with RBCs of donor blood type.

Question 5

A prophylactic platelet transfusion strategy (i.e. transfusion in the setting of thrombocytopenia but without bleeding, in an effort to prevent bleeding) is still routine. A few consultants (10%) follow the TOPPS trial findings [3] and transfuse only for clinically significant bleeding rather than using a prophylactic strategy in the stable autograft cohort.

For both autograft and allograft, a platelet threshold of $<10 \times 10^9$/L routinely is used, or $<20 \times 10^9$/L if febrile and/or bleeding.

The majority (~70% of units transfused) of platelets supplied by our local blood service are derived from pooled random platelets (pool of 4) suspended in additive solution. Single donor/apheresis units are provided in ~30% cases and on request, for example platelet transfusion reactions or poor incrementation. One to three adult doses of platelets may be prepared from a single apheresis platelet donation. Since March 2019, these platelets are suspended in an additive solution.

No measure is applied for a minor ABO-incompatible platelet transfusion.

The efficacy of platelet transfusions is not routinely measured by a post-platelet transfusion increment (PPI), however if there are any concerns regarding the daily platelet counts (e.g. persisting low counts after prior transfusion such that the patient is requiring very frequent transfusions), we would perform platelet increment testing at 30–60 min post-transfusion.

For platelet transfusion refractoriness, post-platelet increment measurements are undertaken to demonstrate potential refractoriness. Subsequently, a trial of single donor/apheresis platelets with increment testing is performed, and if there are continued concerns about refractoriness, then anti-HLA/HPA antibodies are tested. If HLA-antibodies are demonstrated, then HLA-matched platelets are trialed and further PPI testing undertaken.

Question 6

Isoagglutinin titres are routinely measured pre-transplant, as well as at day 100, and other time points (if clinical concerns) for ABO-mismatched HSCT recipients.

Question 7

Red blood cells phenotype and DAT are performed routinely at day 100 for all allogeneic HSCT recipients. They are also performed at other time points as needed, according to risk assessment and clinical requirements.

Question 8

Based on a definition of complete absence of erythroid precursors in the bone marrow in the presence of donor engraftment (as determined by myeloid chimerism) and

persistence of granulopoiesis and thrombopoiesis, our incidence of post-transplant red cell aplasia is approximately 1–3%.

Our general approach to treatment is supportive care with transfusions and EPO and waiting for resolution.

Acknowledgements

We acknowledge valuable contributions from Mr Michael Haeusler, Dr Giles Kelsey and Professor David Ritchie to preparation of these answers.

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Question 1

We performed 110 autologous HSCT and 125 allogeneic HSCT in the most recent calendar year. The allogeneic transplants could be further broken down to include 54 marrow transplants, 44 cord blood transplants and 27 peripheral blood stem cell transplants.

Question 2

We continue to irradiate cellular blood components for one year after an autologous stem cell transplant. After an allogeneic transplant, we continue to irradiate for the life of the patient.

- X-ray.
- 25 Gy.

Question 3

Yes, a CBC is completed each day for an inpatient undergoing HSCT. Many autologous HSCT are done as outpatients.

Question 4

Regarding the red blood cell transfusion protocol:

- 8 g/dl.
- 1 RBC.
- We do change the blood group of the patient based on the following: (1) 120 days without a RBC transfusion; (2) molecular studies showing full engraftment; (3) back type is compatible with the front type.

Question 5

Regarding platelet transfusion protocol:

- Prophylactic.
- 10 000 plts/μl.
- Single donor. We use both plasma and additive solution interchangeably.
- We have a 1000 ml limit (recently raised to 1500 ml, but not fully implemented) per week. If we reach the incompatible plasma limit, we perform a DAT. If DAT is negative, the medical director may allow more incompatible plasma. If DAT is positive or medical director does not waive, then we volume reduce incompatible units.
- We try but often the nurses do not draw the post-count. Ideally, it would be drawn 10–60' after each transfusion.
- First, we try to rule out non-immune causes for refractoriness. If we cannot find other reasons for refractory state, then we order a cross-match assay. If approximately >1/3 are incompatible, we order compatible units and monitor the next three transfusions closely (if <1/3 incompatible we stay with random units.) to

see if CCI improves and is >5000. If either trial of random or of XM-compatible fails, then we test for HLA antibodies against class I HLA. We then talk to our local blood centre to find either 4/4 direct HLA match or we try to avoid antibodies. When we get HLA-matched (or antibody avoidance) units, we do a three transfusion trial. If this also does not increase the CCI >5000, we return to using random units.

Question 6

We do not measure isoagglutinin titres. We look at the back type and grade the strength of the reaction 0-4 and follow trends.

Question 7

We perform a DAT after a transfusion reaction (which are frequently reported in this population due to neutropenic fevers) and if we suspect antibody-mediated haemolysis after a drop in haemoglobin.

Question 8

I do not know the exact incidence, but it is rare. Most frequently (and classically), we see PRCA after a group O patient receives a group A transplant. Initially, PRCA is managed by the clinicians conservatively, with the expectation that it will 'burn itself out'. The clinician might try a trial of steroids or rituximab. If the patient has an extended course, they will come to transfusion medicine for apheresis to reduce the titre of isohemagglutinins. We have done this aggressively on some patients and it has always worked.

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United Kingdom–London

Question 1

Our centre performs 30 autologous and 30 allogeneic.

Question 2

1 year after autologous and lifelong for allogeneic
-X-RAY.
-25 Gy.

Question 3

Daily FBC is routine for both autologous and allogeneic transplants.

Question 4

Regarding the red blood cell transfusion protocol:
- 70 g/l.
- 1 unit.
- This statement is confusing. Is this asking for engraftment of the stem cells (I assume not) or whether this is full donor blood group change (we do not term this engraftment). In this case, engraftment is by full grouping and antibody screen which will include a antiglobulin test.)

Question 5

Regarding platelet transfusion protocol:
- Prophylactic.
- In both 10×10^9/l unless other circumstances (bleeding, fever, on other anti-coagulants, etc).
- Single donor in additive solution.
- None.
- Not routinely unless platelet refractory. Then, a count check is done 60 min post-transfusion.
- HLA-matched platelets.

Question 6

Only prior to transplant and before stem cell infusion. Not routinely after except once every year to detect blood group change.

Question 7

Generally not unless there is a clinical indication – high bilirubin, delayed engraftment.

Question 8

Transient hypoplasia post-major ABO-incompatible transplant more common (about 10%). Actual red cell aplasia much less common. Managed with transfusion support until the aplasia/hypoplasia recovers.

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Canada

Question 1

The University Health Network performs HSCT at Princess Margaret Cancer Centre, one of its three main (acute care) hospitals. Annually, 350 autologous and 190 allogeneic HSCTs are performed (540).

Question 2

Though we are in medical agreement with the principles of Canada's National Advisory Committee on Blood and Blood Products (https://www.nacblood.ca/resources/guidelines/downloads/Recommendations_Irradiated_Blood_Components.pdf_), which specify 3–6 months after autologous HSCT and for as long as immune suppressant therapies and/or (chronic) graft versus host disease may be present after autologous HSCT (with annual reviewer thereof). At our institution, the instruction to irradiate invariably remains in place indefinitely for the following reasons:

(a) Disease relapses or de novo indications, which themselves are indications for irradiation, have arisen after the NAC term conditions or intervals have elapsed, and
(b) it has not been feasible to expeditiously obtain sufficiently indubitable case details on the NAC term conditions or intervals, as patients may have health information in more locations than we are able to access, interpret and verify

We use Cesium-137 as our irradiation source at a minimum central dose of 25 Gray.

Question 3

A complete blood count occured daily during HSCT admissions, with the exception of reduced-frequency testing scenarios (to every other day, in lower-volume tubes), in patients with stronger blood conservation mandates (i.e. transfusions relatively or absolutely contraindicated). More recently, with the shift of autologous SCT to the outpatient setting, CBC frequencies have decreased. At least one count check is prescribed in the first week post-discharge, and patients are seen 3–10 times in the first 30 days after discharge with laboratory testing at those times.

Question 4

The haemoglobin threshold for red blood cell transfusion in stable, non-bleeding inpatients during the aplasia period is single unit red blood cell orders at ≤70–75 g/l.

We are able to change the red blood cell group of RBC concentrates to the donor's group when engraftment occurs. This occurs when the forward group reflects exclusively donor erythropoiesis, without confounding by transfusion, and by demonstration of the absence of anti-graft isoagglutinin activity (on reverse type or by DAT). However, we tend not to encode the group change for a variety of reasons:

(a) Grouping samples in the post-engraftment period, after sufficiently lengthy transfusion-free periods, may not be drawn (due to the associated absence of need for transfusion); and
(b) Experience with a number of 'impermanence anecdotes' (i.e. disease relapses and/or evidence of delayed recurrences of host erythropoiesis), perhaps as a function of the increased proportion of reduced intensity/non-myeloablative conditioning regimens, with reversion to the hybrid type designation and permissible component-specific ABO exposure truth tables.

Question 5

In autologous HSCT, the platelet transfusion protocol is permissive on the use of prophylactic platelet transfusions, that is it is not restricted to treatment only. The Platelet Transfusion Requirements in Hematopoietic Transplantation (PATH) trial (https://clinicaltrials.gov/ct2/

show/NCT02650791), which is investigating outcomes by either strategy, is active at our centre. Both approaches can be seen in audits by virtue of enrolments or clinician equipoise (with the institutional policy permitting prophylaxis at platelet counts of ≤10 for auto- or allo-HSCT). In times of (and in accordance with extent of) platelet shortage, stricter triggering is enforced.

Our adult dose platelet concentrates are predominantly buffy coat pools (four whole blood donor derived) with single donor apheresis platelets. The ratio delivered to our centre by Canadian Blood Services is presently 10:1, which has been rising from previous ratios (3:1) over the last several years [1].

Apheresis platelet stocks are enriched for those that have been selected by HLA- (and/or HPA-)-type in the care of sensitized and otherwise platelet transfusion refractory patients.

Our platelet concentrates are suspended in the plasma of a contributing male donor in pooled concentrates.

In the case of minor ABO-incompatible platelet transfusion, a room temperature (immediate spin) 1:50 titre is performed on group O platelets if this is the only available type left in inventory for non-O recipients. The product is unmodified if titre negative. If titre positive, the platelet undergoes a plasma volume reduction (PVR).

We advise monitoring of post-transfusion platelet counts (15–60 min post) in 'high-use alert cases' (three consecutive days with ≥1 platelet transfusion per day), or in the evaluation of immune-selected single donor apheresis platelets (to assess the in vivo efficacy of products which had been selected to circumvent the last known array of HLA- and/or HPA-specific antibodies).

Our hospital transfusion laboratory receives its testing and product support through Canadian Blood Services, with a local (Toronto-based) HLA Histocompatibility laboratory, a national (Winnipeg-based) Platelet and Leukocyte Reference laboratory, and the associated apheresis/donor management programmes.

Platelet transfusion refractoriness is managed by identifying suspicious cases (with the aforementioned [automated] high-use alert placed in the patient's electronic medical record), and a clinical policy which supports immune refractoriness testing and the coordinated provision of selected platelets. Suitable options for the latter reflect a hierarchy of potentially available 'matches,' (i.e. HLA-identical, HLA-'similar' [software-modelled/structurally-predicted tolerance], HLA-'negative' [with respect to the patient's last-determined specificities] or 'low MFI' [HLA-mismatched with respect to the lowest mean fluorescence intensity antibody specificities on PRA]).

Due to the preparation time entailed in sourcing and delivering preferred platelets (especially for the lower frequency profiles commanded by certain cases), the anticipated needs are reported a week in advance by the most responsible physician. An active list of sensitized patients with platelet transfusion needs is coordinated in the blood transfusion laboratory and amended with clinician input and pertinent emerging laboratory results.

For the latter, serologic profiles predicting for refractoriness come to the transfusion physician's attention for clinical review. Retesting the antibody repertoire is encouraged quarterly and/or when patients exhibit refractoriness to matched products (should this be sooner [or later/after missed rescreening opportunities]).

Question 6

We do not routinely measure isoagglutinin titres routinely in patients after allogeneic HSCT, though we provide this service on request. Requests are usually limited to those cases with suspected pure red cell aplasia/delayed red cell engraftment from ABO major mismatch.

Question 7

The transfusion laboratory does not prescribe or enforce a prospective schedule of monitoring by direct antiglobulin tests or other measures to detect early immunohematologic complications after ABO-incompatible HSCT. However, the transplant teams consult closely with the transfusion laboratory medical directors to obtain investigative advice and interpretation.

Question 8

We do not have information on our incidence of pure red cell aplasia. Management is on a case-by-case basis, from antigen-negative chronic transfusion support to apheresis, intensified immune suppressant therapy and off-label daratumumab in rare instances.

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France

Question 1

In 2019, the Besancon University Hospital transplantation unit performed 32 autologous and 55 allogeneic hematopoietic cells transplantation, figures similar to previous years regarding allogeneic transplantation but number of auto HSCT is slightly decreasing.

Question 2

Up to 3 months (1 year in case of total body irradiation) after autologous HSCT and 1 year after allogeneic HSCT, with the exception of patients per.

The platelets units are no longer irradiated since they undergo amotosalen plus UVA illumination treatment.

- X-ray.
- As recommended by our National Health Authorities, the energy applied to the unit has to be between 25 and 45 Gy. In our institution, the device is set up for 35 Gy.

Question 3

A complete blood count every day during HSCT along with a white blood cell differential twice a week, and not differently between autologous or allogeneic transplantation.

Question 4

Regarding the red blood cell transfusion protocol:

- The national recommendation for transfusion in stem cell transplantation is to keep a level of haemoglobin superior to 7 g/dl [1]. In fact, 70% of the French centres participating to the survey published in 2019 [1], including ours, use a 8 g/dl threshold for red blood cell transfusion. This cut-off is adapted to the clinical tolerance of anaemia.
- It is recommended to use one rather than 2 RBC for transfusion [1]. In practice, more than 90% of RBC transfusion include 2 units because of the convenient set-up of such a policy (one appointment rather than 2 for outpatients, reduction of nursing care plan. . .)
- Starting the day of transplantation, RBC concentrates are ABO compatible with both the donor and recipient ABO groups. In case of Rh and Kell incompatibility between donor and recipient, donor compatibility is privileged. We provide to the recipient a document containing a personalized 'transfusion policy'. After 3 months, this policy is adapted to the engraftment only for platelet transfusion. If engraftment confirmed, dual (prior) recipient and donor ABO compatibility is no longer required while the recipient remains transfused with donor-compatible platelets units. The engraftment is determined by both forward (cellular) and reverse (plasmatic) group typing.

Question 5

Regarding platelet transfusion protocol:

- We use prophylactic strategy for autologous HSCT.
- Our threshold is 20 G/l. The recent national survey shown that one third of participating centres have a threshold at 10 G/l for platelet transfusion and two-third at 20 G/l. The national recommendation for platelet transfusion [2] determines different thresholds considering risks factor for bleeding: 10 G/l for patients without risk factors and 20 G/l for patients with fever, infection, mucositis, arterial hypertension or fast decrease of platelet level in the last 72 h. Most of the patients with hematopoietic cell transplantation are in the second group, explaining our policy.
- Approximately two thirds of platelets units transfused are random platelets. The platelets are suspended in additive solution.
- In case of minor ABO-incompatible platelets transfusion, we transfuse platelets with low titre A/B Ab.
- We rarely monitor the efficacy of platelets transfusions immediately after transfusion. However, platelet counts are verified the day after (daily CBC count). Earlier monitoring (60 min) may occur in cases of (anti-HLA or anti-HPA) alloimmunization and after transfusion of compatible platelets units.
- We verify HLA or HPA alloimmunization, if so compatible units are selected for further transfusions. In the absence of haemorrhagic features, we change our policy from 'prophylactic' to 'curative'.

Question 6

In case of ABO mismatch transplantation, isoagglutinin titre is systematically measured before transplantation and one month after transplantation. After this delay, isoagglutinin titre is measured only in case of transfusion dependency (pure red cell aplasia). In other cases (ABO compatibility), isoagglutinin titre is not routinely assessed.

Question 7

We do not perform direct antiglobulin test after ABO-incompatible HSCT. We do, however, undertake graft

plasma depletion or RBC depletion (in case of minor or major ABO mismatch, respectively).

Question 8

The incidence of pure red cell aplasia (PRCA) after allogeneic HSCT in our centre is around 5%. If PRCA persists for more than 6 months, we consider the use of rituximab or more recently daratumumab. Otherwise, we wait for spontaneous improvement.

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Brazil

Question 1

The Sírio-Libanês Hospital performs an average of 24 autologous HSCT and 32 allogeneic HSCT per year.

Question 2

All patients undergoing autologous or allogeneic HSCT receive irradiated blood components from the time of initiation of conditioning chemotherapy and we continue to provide this special care throughout the life of these patients.

To red blood cell concentrate (RBC), the source of irradiation is caesium-137 and the dose is of at least 2500 cGy into the centre of the component.

To platelet components and fresh frozen plasma, since March 2017, all of these components are treated to pathogen inactivation by INTERCEPT® (from CERUS) and we considered that the UV irradiation of this procedure is an effective prophylaxis for Transfusion-Associated Graft-vs-Host Disease (TA-GVHD) too.

Question 3

The routine is to perform a complete blood count every day during HSCT until the platelet and neutrophil engraftments are established. No differentiation is made in monitoring patients undergoing autologous or allogeneic HSCT.

The platelet engraftment is considered when the patient's count is at least 20 000/μl after three consecutive days without platelet transfusion, and the neutrophil engraftment is defined when the patient presents an absolute neutrophil count of more than 500/μl across three consecutive days too.

Question 4

Regarding the red blood cell transfusion protocol:

- For stable and hospitalized patients, the red blood cell transfusion has been considered to a haemoglobin threshold of 7.0–8.0 g/dl, unless the patient is symptomatically anaemic or has other comorbidities.
- We are adhering to a restrictive strategy and our policy is to transfuse one red blood cell unit and evaluate the clinical and laboratory response of the patient, as long as he is stable, before indicating the second unit.
- The transfusion strategy in ABO-mismatched cases must consider both the blood group systems of the recipient and the donor.

In case of major or bidirectional ABO-mismatched transplants, transfusion of blood group O RBCs is necessary until anti-donor isohemagglutinins (IHA) are undetectable in two consecutive blood samples of the recipients.

At our institution, if a patient is independent of RBC transfusion for 90 days and no incompatible isohemagglutinins against the new RBC phenotype are detected in two consecutive blood samples, then the patient's native blood type is switched to the donor type for future transfusion.

Question 5

Our institutional protocol recommends prophylactic platelet transfusion at a platelet count of 10×10^9 cells/l or less in a nonbleeding patient.

The recommendation of a 50×10^9 cells/l platelet transfusion threshold is considered for a major invasive procedure and 30×10^9cells/l for patients having elective central venous catheter placement.

In the presence of active bleeding, the platelet count is evaluated in conjunction with clinical signs, and the transfusion is considered therapeutic.

We transfuse pools of random platelets and single donor platelets by apheresis devices with no distinction, unless to patients with specific antibodies identified. Both of them are doses of around 3×10^{11} cells suspended in plasma.

ABO-compatible platelet transfusions are always preferred. When it is not available and the patient needs to receive ABO-incompatible plasma via platelet transfusion, the product with a titre of anti-A and/or Anti-B isohemagglutinins less than 100 is selected. Furthermore, when only products with high titres are available, a plasma volume reduction is performed.

The efficacy of platelet transfusions by a post-transfusion platelet count at 15–60 min are not systematically monitor. This procedure is adopted when the patient shows clinical signs or a 24-h platelet count suggestive of low transfusion increment.

Initially, the non-immune conditions, such as consumptive coagulopathy, sepsis and splenomegaly are evaluated.

The investigation of alloimmune refractoriness in a patient with thrombocytopenia due to bone marrow failure is considered when a 1-h increment is less than 7.5×10^9 cells/l on two consecutive occasions, using ABO-identical platelets and the absence of predominantly non-immunological factors.

To manage these situations, we perform different methods to screening (the indirect Platelet Immunofluorescence Test – PIFT) and identification (Monoclonal Antibody Immobilization of Platelet Antigen – MAIPA) of platelet antibodies.

The patients who are refractory to platelet transfusion and have class I HLA antibodies and/or HPA antibodies identified, have been transfused preferably with class I HLA and/or HPA-selected platelet components.

In our Institution, approximately 2000 donors are already typed by class I HLA and HPA 1, HPA 5. And, additionally, 500 donors are typed to all other HPAs.

Question 6

In cases of major ABO incompatibilities, our centre monitor post-transplantation anti-A and anti-B isohemagglutinins IgG and IgM titres weekly, especially when pre-transplant levels are high.

After transplantation, the intention is to achieve titres below 1:16.

We believe that this is particularly important to allow detection of an increase in titre when this coincides with the appearance of donor-derived RBCs.

Hemagglutinin titre quantification is followed until it is undetectable for two consecutive weeks, except in patients with persistent RBC transfusion requirements.

Question 7

In the case of minor ABO incompatibility, we perform a direct antiglobulin test (DAT) and antibody screening test periodically, at least once a week, until negative results are obtained.

Question 8

Unfortunately, we do not have this data. The clinical management of these patients is done by the physician directly responsible for the indication of the transplant.

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Question 1

In 2019, 116 allogeneic HSCT (16 sibling donor, 3 haploidentical, 95 unrelated and 2 umbilical cord) were performed at University Hospitals Birmingham across two inpatient facilities. 22 patients had myeloablative conditioning. 158 autologous HSCT were performed.

Question 2

Use of irradiated cellular blood components is in keeping with British Society for Haematology (BSH) guideline [1] which states that irradiated cellular blood components should be given to recipients of autologous HSCT from initiation of conditioning chemo/radiotherapy until

3 months post-transplant (6 months if total body irradiation was used in conditioning). After allogeneic stem cell transplant, irradiated components should be given from the time of initiation of conditioning chemoradiotherapy and continued for the duration of graft-versus-host disease (GvHD) prophylaxis, that is usually for 6 months post-transplant, or until lymphocytes are $>1 \times 10^9$/l. If chronic GvHD is present or if continued immunosuppressive treatment is required, irradiated blood components should be given indefinitely.

In practice, patients are identified as requiring irradiated components and we do not proactively remove this requirement. Few autologous recipients go on to have significant transfusion requirements, and many allogeneic SCT recipients have other indications to need lifelong irradiated components, for example anti-thymocyte globulin, alemtuzumab or fludarabine given during conditioning.

Irradiation is undertaken by NHS Blood and Transplant usually using a gamma irradiator or on occasion an x-ray irradiator, if the component is irradiated at a site other than our regional blood centre. These meet the specification defined by the Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee, that is a minimum of 25 Gy, but with no part receiving more than 50 Gy [2].

Question 3

Platelet counts are performed daily for inpatients. Patients remain in hospital until they demonstrate marrow engraftment. Following engraftment, counts are done at least weekly until the 100th day post transplant, or on every patient contact, if required more frequently for clinical reasons.

Autologous transplants may be performed as an outpatient but all patients are admitted at the onset of neutropenia until neutrophil recovery at which stage neutrophile and platelet counts are measured until neutrophil engraftment documented according to EBMT criteria. Following discharge from hospital, blood counts are done at every clinical review, many of which are performed at referring centres, the frequency of which is guided by clinical circumstances.

Question 4

The haemoglobin threshold is 70 g/l for stable patients during the period of aplasia, in the absence of significant cardiac disease. Single unit transfusions are used for inpatients unless they are scheduled for imminent discharge in which case two units may be transfused. For outpatients, two units may be given depending on the trajectory of the count, frequency of visits and comorbidities of the patient.

Donor group red cells are transfused following full conversion to the donor group. This is established by the

(1) Disappearance of any dual population on forward and reverse ABO grouping by indirect antiglobulin testing
(2) Negative direct antiglobulin test (DAT) with polyspecific anti-human globulin

As an additional measure, at one of the hospital sites, donor group components are not transfused for the first year after transplant, and until full or near full chimerism is confirmed.

Question 5

A prophylactic treatment strategy for both autologous and allogeneic HSCT is used, with a threshold of 10×10^9/l in the absence of fever, bleeding or planned procedures. Thresholds are in keeping with BSH guidelines for platelet transfusion [3]. Single donor apheresis platelets and pooled platelets are used interchangeably. Apheresis platelets are collected solely from male donors, or female donors who have been tested and are negative for human leucocyte antigen (HLA) and human platelet antigen (HPA) antibodies. Apheresis platelets are suspended in plasma. Pooled platelets are suspended in 60–65% additive solution and 30–35% plasma (from a male donor) [4].

For minor ABO-incompatible platelet transfusions, 'high titre negative' units are given (high titre is defined as >1/128) [4]. Pooled platelets are given in this scenario where possible due to their lower plasma volume.

Post transfusion increments are only undertaken if there is a concern regarding poor increments, or after transfusion of HLA-selected platelets in order to guide further donor selection. Platelet counts are routinely taken within 24 h of most transfusions by virtue of the patient being in hospital during the hypoplastic phase. When increments are checked, these are performed within 15–60 min of the end of the transfusion.

Platelet refractoriness is managed by first demonstrating true refractoriness, investigating and then providing appropriate support. In the first instance, refractoriness is demonstrated with increments taken within 24 h of a single unit of ABO identical platelet transfusion on two occasions. If the rise in platelet count is $<10 \times 10^9$/l on both occasions, the patient is considered refractory. Causes of platelet refractoriness (including immune and non-immune) are considered and addressed where possible. Patients with no reversible cause and clinical suspicion of immune refractoriness are tested for HLA antibodies. If no HLA antibodies are detected, HPA antibodies are tested for.

If alloantibodies are detected, apheresis platelets from donors negative for the corresponding antigen are selected, and post-transfusion increments are taken with every bag to guide further donor selection. If no HLA or HPA antibodies are detected but there is strong clinical suspicion of alloantibody destruction of transfused patients, apheresis platelets are selected based on the HLA type, to closely match the patient as much as possible and avoiding potential sensitisation to high frequency antigens.

Question 6

Isoagglutinin titres are not routinely measured following HSCT.

Question 7

Direct antiglobulin tests are not performed routinely following ABO-incompatible HSCT, except when the forward and reverse groups cease to demonstrate a dual population as described in question 4.

Question 8

Pure red cell aplasia is only rarely observed after allogeneic HSCT. Its incidence is not monitored routinely in our institution. There are some patients with major ABO incompatibility who have a significant red cell requirement for a prolonged period; we investigate in order to exclude PRCA and parvovirus infection, and to confirm trilineage engraftment, and then treat with erythropoietin. Patients with evidence of immune haemolytic anaemia are treated with steroids and rituximab.

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Poland

Question 1

At the Institute of Hematology and Transfusion Medicine (Institute), approximately 60–65 autologous and 65–70 allogeneic transplants are performed per year.

Question 2

At the Institute, every patient who requires multiple transfusions, every potential transplant recipient as well as transplant recipient is transfused with irradiated blood components until transfusions are required. In the case of HSCT patients, cellular blood components are irradiated for at least 12 months after autologous donation and indefinitely following allogeneic transplantations.

Currently, caesium (Cs) is used as source of irradiation.

The dose delivered to the blood component is no less than 25 Gy at each site of the component, but does not exceed 40 Gy. Once in 3 years, the distribution of the delivered dose is mapped. Mapping shows that the central dose is 32 Gy.

For microbiological safety and prophylaxis against graft-versus-host disease, most platelet concentrates are pathogen reduced instead of being subjected to irradiation. If FFP is indicated, it is also administered after pathogen reduction or after quarantine.

Question 3

Yes, complete blood count (CBC) is performed during pancytopenic phase in all transplant patients. During the regeneration phase – when regular transfusion support is not required and the patients are clinically stable – CBC is performed every other day.

Question 4

Red blood cell transfusion protocol:

- The threshold is 8 g/dl.
- We use 2 RBC unit transfusion policy.
- At the Institute, the red blood cell group of RBC concentrates is changed to donor cell group usually within 6 months following transplantation, providing no transfusions were performed and no relapse occurred. At the same time, chimerism is tested and additional immunohematology tests are performed (including – among others – DAT, IAT, blood grouping) for assessment of engraftment.

Question 5

Regarding platelet transfusion protocol:

- At the Institute, we use the prophylactic platelet transfusion strategy for autologous transplantations.
- The threshold is 20 G/l in patients with grade III mucositis, petecchiae or fever ≥38°C. In asymptomatic patients, the threshold is 10–15 G/l.
- Preferably, single donor platelet transfusions are used. If unavailable, which does not often happen, random donor platelets are acceptable. Platelets suspended in additive solution and in plasma are in use at the Institute.
- As a general rule, minor ABO platelet incompatibility is not accepted at the Institute. On rare occasions when minor ABO-incompatible platelets must be used, washed platelets suspended in saline or additive solution are transfused.
- There is no systematic monitoring of the efficacy of platelet transfusions by a post-transfusion platelet count. Efficacy of PLT transfusion is monitored at 60 min only if ineffectiveness is suspected, for example in patients who require daily transfusion support.
- In such case, the diagnostic procedure is performed which consists in detection of anti-HPA and anti-HLA antibodies as well as evaluation of symptoms of post-transplant thrombotic microangiopathy. In cases with better potential, it is recommended to discontinue calcineurin inhibitor administration and switch to regime of mycophenolate and steroids for graft-versus-host disease prophylaxis in allogeneic transplants. If antibodies are detected, we limit prophylactic transfusions of platelets and in case of bleeding – in principle, we administer platelets with no antigens to the antibodies detected in patients.

Question 6

Isoagglutinin titre is routinely measured before transplantation; after transplantation – only fort special indications resulting from post-transplant complications.

Chimerism is monitored with measurements performed monthly and as required. If the results are indeterminate, antibody tests and titre measurements are performed, usually 1 month after transplant and then at 3 months following transplant and if required.

Question 7

At the Institute, prior to transplant, we perform direct and indirect antiglobulin test, blood grouping as well as IgG and IgM antibodies. In the post-transplant period, antibody monitoring is performed, as well as direct antiglobulin test, Rh phenotype as well as other phenotypes, as required.

Question 8

We report pure red cell aplasia in 1–2 patients per year and solely after reduced intensity conditioning. If the patient does not require multiple transfusions, whenever possible, we prefer early start of immunosuppression taper to other therapeutic measures.

Our choice of management procedure is justified by the fact that the majority of such patients is in advanced age and have low-risk diseases. Early immunosuppression taper decreases the risk of relapse. If necessary, we perform plasmaphereses and apply/administer rituximab (especially in case of concomitant graft-versus-host disease) and erythropoiesis-stimulating agents.

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