Managing patients who are being treated with targeted therapeutic monoclonal antibodies

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Increasingly, targeted therapeutic monoclonal antibodies are used to treat conditions such as myeloma and these patients may also require transfusion support. Depending on the nature of the monoclonal antibody (see below) these drugs may interfere with pre-transfusion testing by causing anomalous results with the clinical consequence of delayed transfusion. More rarely some drugs can worsen anaemia by inducing haemolysis.

A patient being treated with targeted monoclonal antibody therapy may be well-known to a specialist unit but could also present requiring transfusion to a local hospital or even a hospice. Effective communication between clinical teams and transfusion laboratories is critical to managing these patients. This includes blood service reference laboratories who may receive onward referrals from hospital transfusion laboratories.

Prior to commencing a drug known to interfere with pre-transfusion testing, it is good practice to establish ABO, Rh CcDeEe, MNSs, Kk, Jk<sup>a</sup>,Jk<sup>b</sup>, Fy<sup>a</sup> and Fy<sup>b</sup> groups and antibody status because it will be difficult to do so afterwards. This will help inform the choice of red cells, although matching for all these antigens may not be desirable or achievable. The information should be documented in the transfusion laboratory, in the patient’s notes and ideally on a patient-held shared-care record.

Following treatment, the effect on pre-transfusion testing can persist for up to 6 months. Inconclusive pre-transfusion tests can compromise safe transfusion unless they are investigated appropriately, and blood selection is carefully considered. Investigation prior to transfusion can become lengthy and complex. Accordingly, planning transfusion for such patients is essential and investigation outside laboratory core hours must be avoided wherever possible.

Targeted monoclonal antibody therapies, and effect on pre-transfusion testing

**Anti-CD38**

e.g. Daratumumab – is used to treat myeloma. Anti-CD38 is unlikely to interfere with grouping tests, but as CD38 is weakly expressed on red cells, antibody screening, identification and crossmatching using an indirect antiglobulin test (IAT) may give anomalous results. Positive results may be encountered with all screening, panel, and donor cells, and in some cases the direct antiglobulin test (DAT) and/or auto control may also be positive, though this is variable.

Prior to commencement of anti-CD38, the following should be carried out:
• Baseline ABO and D group (follow local policy for requirement of confirmatory sample rule for ABO and D group)
• Antibody screen, and antibody identification if required
• DAT
• Extended phenotyping/genotyping for C, c, E, e, K, (k if K+), MNSs, Jk\textsuperscript{a}, Jk\textsuperscript{b}, Fy\textsuperscript{a} and Fy\textsuperscript{b} groups.
• Red cells should be matched for Rh and K as well as for any alloantibodies (*but see note below)

After treatment with anti-CD38 has started:
• ABO and D typing as per normal method
• Antibody screening, and antibody identification if required, using a strategy to avoid the effect of anti-CD38, e.g. reagent cells treated with 0.2M Dithiothreitol (DTT). Other strategies and techniques for overcoming the effect of anti-CD38 on red cells may become available in the future.
• Red cells should be matched for Rh and K as well as for any alloantibodies (*but see note below)

*DTT treatment of reagent cells destroys Kell system antigens, therefore K negative red cells should be provided for patients unless they are known to be K positive; in this case, k negative red cells should be provided on the rare occasion that the patient is KK.

**Anti-CD47**

e.g. CAMELLIA - is used to treat a range of malignancies. CD47 is widely expressed on human tissues and red cells. Treatment with anti-CD47 is likely to cause anomalous grouping results including ABO and D, and may also cause anomalous antibody screening and identification tests including positive DAT and/or auto control.

Prior to commencement of anti-CD47, the following should be carried out:
• Baseline ABO and D group (follow local policy for requirement of confirmatory sample rule for ABO and D group)
• Antibody screen, and antibody identification if required
• DAT
• Extended phenotyping/genotyping for C, c, E, e, K, MNSs, Jk\textsuperscript{a}, Jk\textsuperscript{b}, Fy\textsuperscript{a} and Fy\textsuperscript{b} groups.
• Red cells should be matched for Rh and K as well as for any alloantibodies.

After treatment with anti-CD47 has started:
• ABO and D typing as per normal method. If the ABO group cannot be concluded, group O red cells may be required for transfusion
• In patients who have autoantibodies, adsorption studies can allow satisfactory antibody detection / identification in many cases
• Red cells should be matched for Rh and K as well as for any alloantibodies.

For patients on either treatment, the purpose of establishing an extended type is to allow matching for Rh CcDEe and K, and to provide information for investigating positive antibody screens. It is not necessary to match patients for the remaining antigens without a specific reason for doing so, such as the presence of an alloantibody. Indeed seeking extensively matched blood without good reason may significantly delay a transfusion unnecessarily.

For patients who have inconclusive grouping results, or who have unresolved positive antibody screens (e.g. autoantibodies which fail to adsorb) then it is important to seek the advice of a consultant-level expert in transfusion medicine.

Where the patient's plasma or the reagent red cells have been manipulated as part of the pretransfusion testing process (e.g. DTT treatment or adsorption), blood for transfusion should be reported in a manner which reflects this (e.g. blood should be labelled 'suitable' rather than 'compatible'). This is in line with the guidance for issuing red cells for patients with autoimmune haemolytic anaemia (7.13.3 in the main body of these guidelines).

Any transfusion-related adverse reactions or incidents occurring as a result of monoclonal antibody treatment or its associated laboratory testing should be reported to SHOT.

References:
