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Therapeutic monoclonal antibodies & blood transfusion

Essential information for hospital transfusion laboratories, transfusion practitioners & haematology clinical teams

Caring Expert Quality

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Background

- Targeted therapeutic monoclonal antibodies (TMAbs) are used to treat patients with myeloma and other haematological malignancies.
- It is likely that these patients will need regular transfusion support.
- Depending on the nature of the monoclonal antibody, these drugs may interfere with pre-transfusion testing.
- The use of these targeted monoclonal antibody therapies is increasing, as promising clinical trials lead to their administration in routine clinical practice.

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Which drugs are involved?

- Anti-CD38 (Multiple Myeloma, Light Chain Amyloidosis, AIHA)
  - Daratumumab (Darzalex®)
  - Isatuximab (Sarclisa®)

- Anti-CD47 (esp. acute myeloid leukaemia and myelodysplastic syndrome)
  - Magrolimab (previously known as Hu5F9-G4) (e.g. ENHANCE 2 / ENHANCE 3 Trials)
  - Evorpacept (ALX-148) (trials in advanced solid organ malignancy)

Anti-CD38 TMAbs overview

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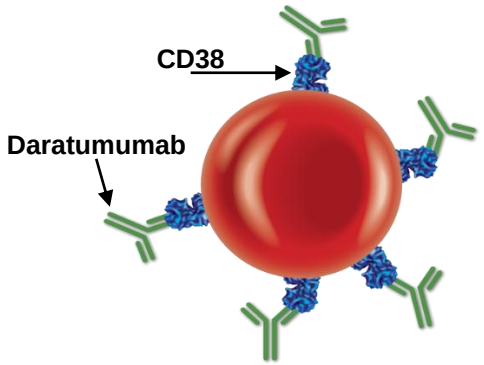
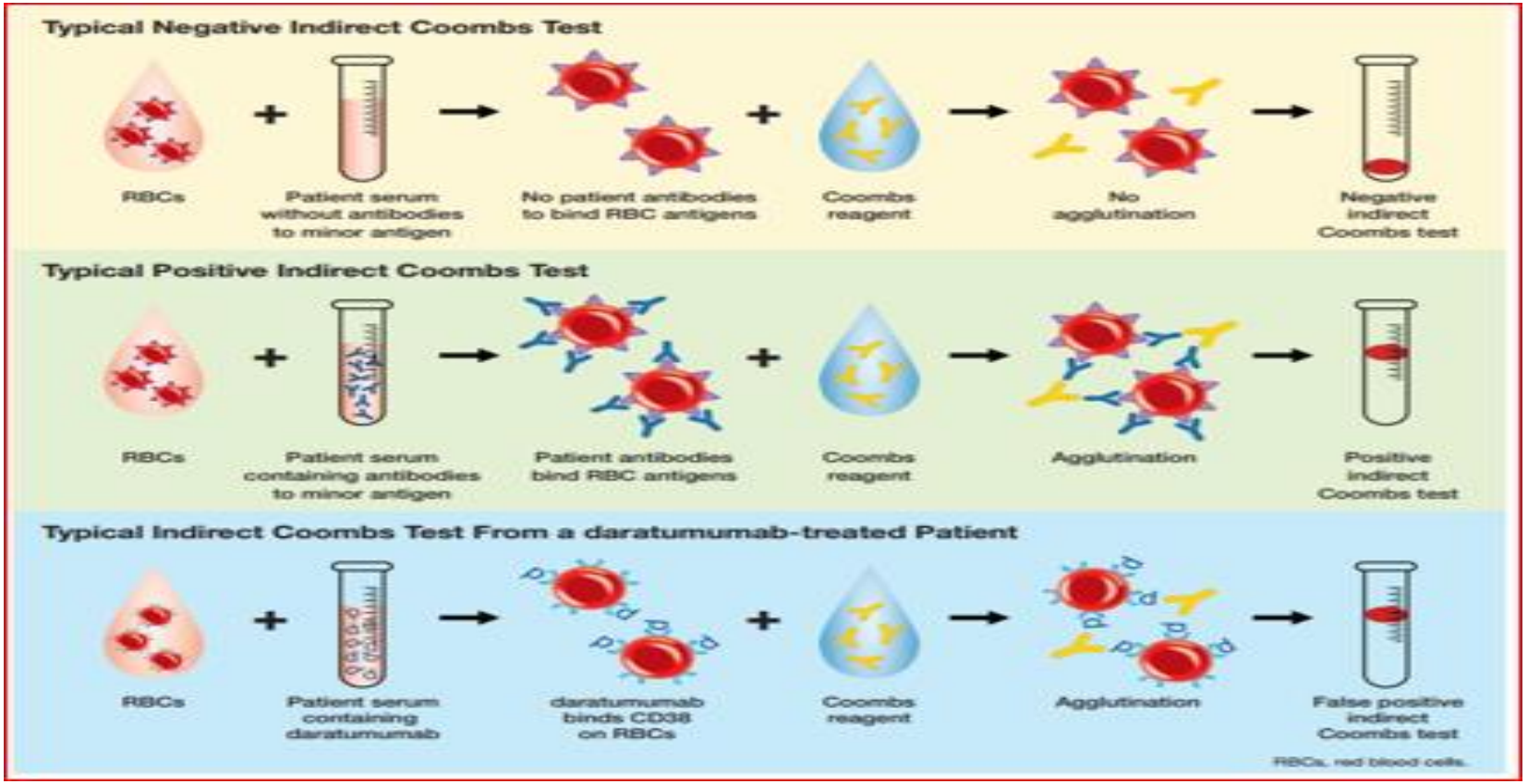
- Anti-CD38 TMAbs, including Daratumumab and Isatuximab are monoclonal antibodies licensed for the treatment of multiple myeloma.
- They bind to CD38, a protein that is ubiquitously expressed on myeloma and lymphoma cells but expressed at low levels on normal lymphoid and myeloid cells.
- CD38 is also expressed at low levels on red blood cells (RBCs).



Daratumumab binds to CD38 on RBCs

Anti-CD38 TMAbs result in a false positive antibody screen



- Anti-CD38 TMAbs may mask the detection of antibodies in the patient's serum. This interferes with compatibility tests, including the antibody screening and crossmatching that are part of a routine pre-transfusion work up.

Management of interference with blood compatibility testing by Anti-CD38 TMAbs

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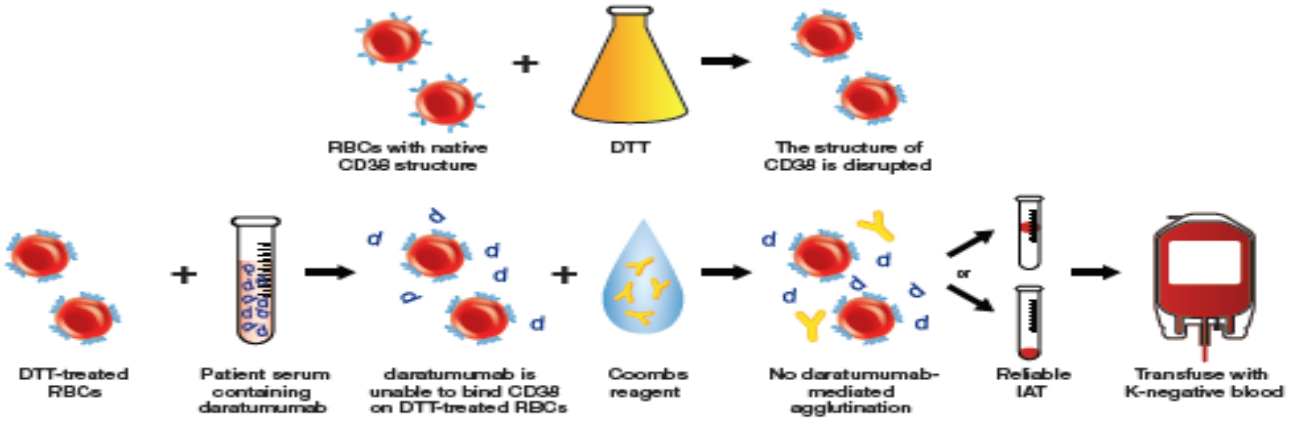
Treat reagent RBCs with DTT or locally validated methods

- Treat reagent RBCs with 0.2M dithiothreitol (DTT) to disrupt anti-CD38 TMAb binding, thus allowing antibody screening or cross-matching to be performed; (Chapuy *et al.* 2015*).* Alternative locally validated methods can also be used.
- Blood components for transfusion are identified for anti-CD38-treated patients, after using DTT-treated reagent RBCs for antibody screening.
- Since the Kell blood group antigens are also sensitive to DTT treatment, units should be supplied which are matched for K- or k- patients, based on their phenotype or genotype, after ruling out or identifying alloantibodies using DTT-treated RBCs.



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Anti-CD47 overview

- Anti-CD47 is a monoclonal antibody mainly used to treat acute myeloid leukaemia and myelodysplastic syndrome.
- The Anti-CD47 TMAb, Magrolimab (previously known as Hu5F9-G4) is being used in clinical trials (CAMELLIA / ENHANCE-2 / ENHANCE-3)
- CD47 is widely expressed on human tissues and red cells.
- CD47 acts as a marker of self, a "Do not eat me" signal for healthy tissue.
- Blocking of CD47 on the surface of the RBC with the use of targeted monoclonal antibodies decreases the protective signal and increases the phagocytosis of circulating RBCs by macrophages in the spleen.
- Increased phagocytosis by splenic macrophages is clinically manifested with indices of extravascular haemolysis.

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Anti-CD47 overview

- RBCs express high levels of CD47
- Treatment with anti-CD47 is likely to cause anomalous grouping results
- If after treatment, the ABO group cannot be concluded, group O red cells may be required for transfusion
- Alloadsorption studies with papain treated cells may allow satisfactory antibody detection / identification in some cases, however the number of adsorptions required to remove the anti-CD47 is likely to vary between patients.
- The use of a different monoclonal anti-IgG may assist in the indirect antiglobulin testing of these patients.

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Recommendations for serological testing - 1

- **Prior to commencing any monoclonal antibody therapy**
- It is recommended to undertake the following testing:
  - Baseline ABO and D group and antibody screen, and antibody identification if required
  - Direct antiglobulin test (DAT)
  - Undertake phenotype/genotype Rh CcDEe, MNSs, Kk, Jk^a, Jk^b, Fy^a and Fy^b groups.

Recommendations for serological testing - 2

- **Once anti-CD38 therapy commenced**
  - ABO and D type by normal methods
  - DAT may be positive (or negative)
  - The antibody screen / identification will be positive due to interference by the drug
  - The effect can persist for up to 6 months after treatment.

Recommendations for serological testing - 2

- **Once anti-CD47 therapy commenced**
  - ABO and D type as per normal method. If the ABO group cannot be concluded, group O red cells may be required for transfusion.
  - In patients who are DAT positive, alloadsorption studies may allow satisfactory antibody detection / identification in some cases.
  - Extended phenotype / genotype matched RBC may be provided if the serology is unresolvable, and the extended phenotype or genotype is known.
  - The use of a different monoclonal anti-IgG may assist in the indirect antiglobulin testing of these patients
  - Onward referral to an NHSBT RCI laboratory for investigation by Capture methodology may be necessary if extended phenotype / genotype matched cells are not available, or if an extended phenotype / genotype is not known. Contact your local NHSBT RCI laboratory for advice before referral.

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Provision of blood

- Elective and non urgent transfusion - Provide ABO / Extended Rh and K compatible, antigen matched (for any alloantibody/ies) units after ruling out or identifying alloantibodies using a panel of DTT-treated reagent RBCs or alloadsorptions, as indicated.
- Irradiated blood components should be provided, where required.
- If blood is needed urgently, provide ABO / Extended Rh and K compatible units pending the results of further serological testing.
- In an absolute emergency - Uncrossmatched, ABO and D compatible RBC units should be administered as per local hospital transfusion laboratory practice.

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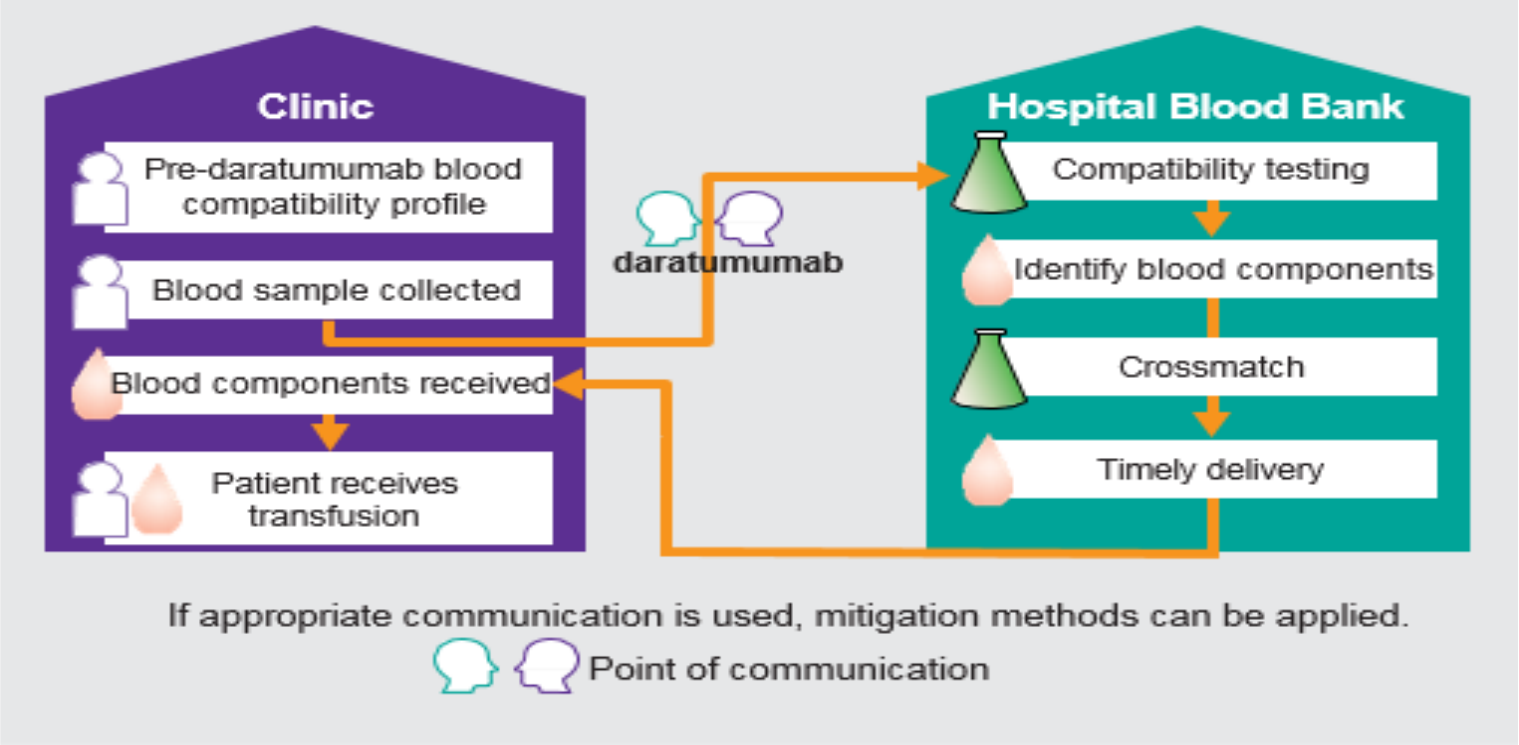
How to prevent blood transfusion delays – communication cascade



Cascade the following key messages to hospital clinical teams

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- To ensure that your patient receives a timely transfusion, send a group and screen sample prior to starting monoclonal antibody therapy and inform the blood bank that the patient is to commence monoclonal therapy.
- Inform any shared care hospitals
- Extended phenotyping/genotyping is recommended prior to starting any monoclonal antibody therapy that is likely to interfere with routine blood bank testing.
- If patients have already commenced monoclonal antibody therapy it is essential to inform the blood bank.
- Specific techniques will be required for blood compatibility testing and blood component selection with likely referral to the NHSBT Red Cell Immunohaematology (RCI) reference lab.
- This communication is essential to avoid delays in transfusion.

Inform the patient - provide a Patient Card

- Advise patients that they should carry their Patient ID Card for 6 months after the treatment has ended.
- Patient ID Card information includes
  - The name of the patient
  - Name of the TMAb
  - If they are no longer taking TMAb, the date they stopped treatment
  - Their blood type (A, B, AB, O, RhD+, RhD-) before starting TMAb
  - Their antibody screen results before starting TMAb

Daratumumab PATIENTS: Provide this card to healthcare providers BEFORE blood transfusion and carry it for 6 months after treatment has ended. For further information, please refer to the Patient Information Leaflet

Patient ID Card for DARATUMUMAB

Name: _____

I am taking the following medication:

Daratumumab antibody product for the treatment of Multiple Myeloma

I stopped taking this medication on ____ / ____ / _____
DD MM YYYY

Before starting daratumumab my blood test results collected on

_____ / _____ / _____ were:
DD MM YYYY

Blood type: □ A □ B □ AB □ O □ RhD+ □ RhD-

Antibody screen was:

□ Negative □ Positive for the following antibodies:

_____

Other: _____

Contact details of institution where the blood tests were performed:

_____

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Action needed – effective communication

- Effective communication is essential between the following to ensure appropriate care and to avoid delays in transfusion:
  - Patients
  - Hospital consultants, trainees and nurses treating patients or covering on call
  - Hospital transfusion laboratories
  - Shared care hospitals
  - NHS Blood and Transplant Red Cell Immunohaematology (RCI) laboratories.
- Complete the contact details of the institution where the blood tests were performed on the patient card, it is especially useful in emergency situations.

References

- British Society for Haematology: Addendum to the Pre-Transfusion Compatibility Procedures in Blood Transfusion Laboratories, (2017) https://b-s-h.org.uk/guidelines/
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- Tan, M *et al*. (2022) *Internal Medicine Journal*, 52(12), pp.2165-2171.