BC CANCER
Provincial Health Services Authority

Pharmacy FAQ

Daratumumab & Isatuximab Pre-Treatment Blood Screening

BC Cancer protocols containing daratumumab or isatuximab require pre-treatment blood screening. In particular, "Red Blood Cell (RBC) phenotype & Group and Screen" are required at baseline. What are these tests and why is it important they are drawn prior to starting treatment?

What are these tests?

Pre-transfusion testing is done to ensure compatibility between the patient and the blood components intended for future transfusion.[1] Pre-transfusion testing ensures the most compatible blood can be given if transfusion is required. This minimizes the risk of hemolytic transfusion reactions.[2]

Compatibility testing can include blood antigen typing and antibody screening, and further "cross-matching" to confirm compatibility with available transfusion blood as required. A cross-match order is generally done when a transfusion is definitely required. If a transfusion is possible but not certain, a "Type and Screen" (also called "Group and Screen") is ordered. This ensures blood will be available for patients who may require a transfusion in a surgical or medical setting. [1]

The *Group and Screen* test includes ABO and Rh typing of the patient's RBC antigens and an antibody screen of the patient's blood components (i.e., "Blood Type and Indirect Ab Screen" in CareConnect). [1]

- The ABO test shows if patients have one of four blood types: A, B, AB, or O. This is determined based on the type of antigens present on the patient's RBCs: A antigen, B antigen, neither antigen (O) or both antigens (AB). Compatible blood for transfusion should have the same antigens in order to prevent transfusion reactions.[3]
- The Rh grouping result (+/-) is also included (i.e., "ABO & Rh Group" in CareConnect).

- The blood group antibody (Ab) screen determines if the patient's plasma/serum contains additional antibodies (non-ABO/Rh) that could react with antigens on transfused RBCs as there are other known blood group systems (e.g., Kell).[4,10] Antibodies may develop in patients who have been exposed to RBC antigens different from their own, through pregnancy or prior transfusion. [1] The Coombs tests is used to detect the presence of antibodies against circulating red blood cells. The presence of antibodies can potentially cause hemolysis of RBCs.[4]
    - The direct Coombs test, also known as the direct antiglobulin test (DAT), utilizes a reagent on the patient's own RBCs that will cause RBC clumping if there are in vivo antibodies attached to them.
    - The indirect Coombs test, also known as the indirect antiglobulin test (IAT), utilizes two reagents on the patient's serum (not RBCs):
        - lab supplied reagent RBCs expressing clinically significant antigens that can attach to antibodies in the patient's serum,
        - and a reagent that will cause RBC clumping if the antibodies are present.[4]

An extended *RBC antigen phenotype* test (i.e., "Blood Group Ag" in CareConnect) can be requested for patients who have not received a transfusion in the prior three months. The extended phenotype test will further establish a patient's baseline blood phenotype beyond ABO/Rh and assist in providing more closely matched blood. The test can look for RBC antigens such as C, K, Fy(a), Fy(b), Ss etc.

Why is it important for these blood compatibility tests to be done prior to starting daratumumab or isatuximab treatment?

Blood transfusions are an important part of the supportive care of patients with myeloma given the frequency of developing anemia.[5] Daratumumab and isatuximab interfere with IAT antibody screen results.[9]

Daratumumab and isatuximab bind to CD38, a protein which is also expressed in low levels on RBCs. When plasma from patients on the anti-CD38 monoclonal antibody is used in the IAT antibody screen, positive results (agglutination) can occur.[6] Additional testing is then required to identify if clinically significant antibodies to foreign RBC antigens (alloantibodies) are actually present, which can lead to delays in providing RBCs to patients in routine transfusion.[4] This effect can persist for up to 6 months after treatment.[7]

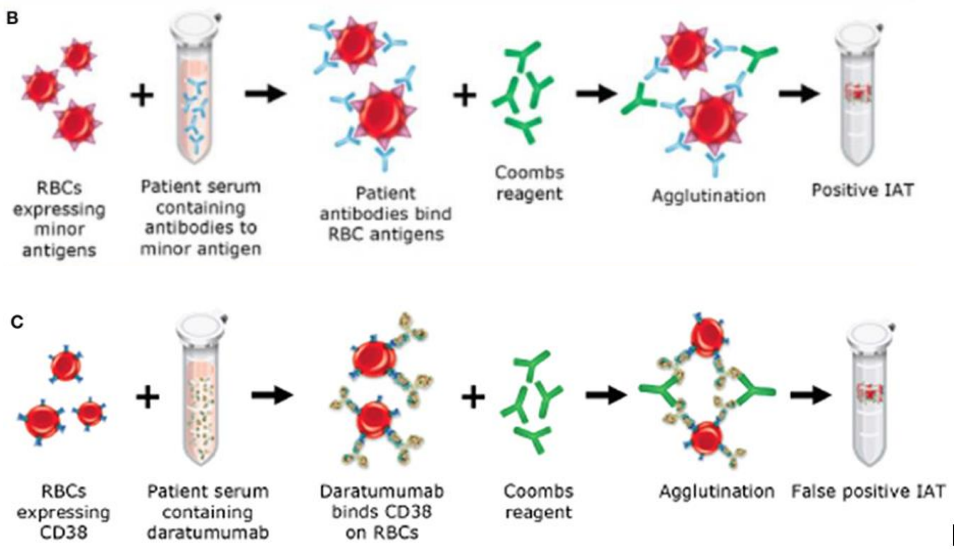

Figure 1. Mechanism of daratumumab interference with the indirect antiglobulin test (IAT)[4]

Masking the detection of antibodies in the patient's serum and subsequent interference with blood bank testing can lead to compromised transfusion safety, redundant testing, increased laboratory costs, and may cause significant delays in transfusions posing a serious threat to patient safety.[6,8] It is important to ensure pre-transfusion testing is complete prior to patients starting treatment with daratumumab or isatuximab.

At times it can be difficult to determine if RBC phenotype testing is in process, depending on how the lab results are reported. Transfusion Medicine, at the relevant laboratory, can be contacted with any patient-related queries.

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