Understanding Daratumumab Interference with Blood Compatibility Testing

Objectives:
- The mechanism of action of daratumumab
- Daratumumab interference with indirect antiglobulin test
- Protocols for mitigating daratumumab interference with blood compatibility testing
- Information important to communicate for the patient on daratumumab

Daratumumab Indication

- Daratumumab is indicated for the treatment of patients with multiple myeloma (MM) who have received at least three prior lines of therapy, including a proteasome inhibitor (PI) and an immunomodulatory agent, or who are double-refractory to a PI and immunomodulatory agent
- This indication is approved under accelerated approval based on response rate
- Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials

Mechanisms of Action of Daratumumab in the Bone Marrow Microenvironment

- Multiple myeloma (MM) plasma cells uniformly overexpress CD38
- Daratumumab is a human anti-CD38 IgG1κ monoclonal antibody

Mechanism of Daratumumab Interference With Blood Compatibility Testing
Daratumumab Binds to CD38 on Red Blood Cells (RBCs)

• CD38 is expressed on RBCs\(^1\)–\(^3\)

• Daratumumab binding to CD38 on the surface of RBCs interferes with blood bank compatibility tests, including the antibody screening and crossmatching\(^1\) (indirect antiglobulin test)

Mechanism of a Typical Indirect Antiglobulin Test

• In an indirect antiglobulin test (IAT) antibodies in patient’s serum to minor antigens on potential donor RBCs are detected by agglutination

Sera Containing Daratumumab Results in a Positive IAT

• In an IAT, daratumumab binds to reagent or donor RBCs, resulting in agglutination and giving a positive panreactive result\(^1,2\)

• Daratumumab interference was identified when 100% of daratumumab-treated patients requiring transfusion were panreactive during RBC panel testing\(^1,2\)

Clinical Impact of Daratumumab Interference with Blood Compatibility Testing

Daratumumab Interference Is Clinically Manageable

• To date, no clinically significant hemolysis has been observed in patients receiving 16 mg/kg daratumumab

• Among a cohort of 46 patients receiving daratumumab at a dose of 16 mg/kg and requiring RBC and whole blood transfusions (135 transfusions received), no transfusion reactions have occurred
Interference With Serological Testing

- Daratumumab bound to CD38 on RBCs masks detection of antibodies to minor antigens in the patient’s serum. The determination of patient’s ABO and Rh blood type are not impacted.
- Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received daratumumab
- Type and screen patients prior to starting daratumumab

Effects of Daratumumab on Laboratory Tests

Interference with Indirect Antiglobulin Tests

- Daratumumab binds to CD38 on RBCs and interferes with compatibility testing, including antibody screening and cross matching
- Daratumumab interference mitigation methods include treating reagent RBCs with dithiothreitol (DTT) to disrupt daratumumab binding or genotyping
- Since the Kell blood group system is also sensitive to DTT treatment, K-negative units should be supplied after ruling out or identifying alloantibodies using DTT-treated RBCs
- If an emergency transfusion is required, non-cross-matched ABO/RhD-compatible RBCs can be given per local blood bank practices

IAT Using DTT-Treated RBCs

- In a single institution study, for patients requiring transfusion, treatment of reagent RBCs with DTT eliminated pan-reactivity in 100% of daratumumab-treated patient samples

<table>
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<tr>
<th>Patient</th>
<th>DARA dose, mg/kg</th>
<th>Results of antibody screen using non-DTT-treated RBCs</th>
<th>Results of antibody screen using DTT-treated RBCs</th>
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</thead>
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<tr>
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<td>Pan reactive</td>
<td>Negative</td>
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<tr>
<td>5</td>
<td>16</td>
<td>Pan reactive</td>
<td>Negative</td>
</tr>
</tbody>
</table>

- Blood products for transfusion were identified for daratumumab-treated patients, after using DTT-treated reagent RBCs for antibody screening

Information to Communicate to the Blood Bank

If a Patient Who Received Daratumumab Requires a Transfusion

- Type and screen patients prior to starting daratumumab and inform the blood bank that your patient has been treated with daratumumab
- Ensure that your patient’s blood sample is identified as treated with daratumumab
- Double-check standing orders for transfusions to determine if your patient received daratumumab within the last year
- Provide your patient’s pre-daratumumab compatibility profile, if available, to the blood bank
- Ask your patient to tell their HCPs that they have received daratumumab, particularly before a transfusion

Information for the Daratumumab-Treated Patient
Ensure That Your Patients Take an Active Role in Their Treatment

- Reassure your patient that compatible blood products for transfusion can still be identified
  - In the event of an emergency, protocols are in place to ensure timely transfusions per local blood bank practices
- For at least 6 months after their last daratumumab treatment, patients should
  - Inform their HCPs that they have received daratumumab treatment, particularly before receiving a transfusion
  - Carry their patient ID card, if applicable, and provide it to their HCPs

Summary

- Daratumumab is a human monoclonal antibody for the treatment of multiple myeloma\(^1\)
- Daratumumab binds to CD38, a protein that is expressed on myeloma cells and on RBCs\(^2\)
- Daratumumab in the patient’s serum binds to reagent or donor RBCs in an IAT, resulting in pan-agglutination, masking the presence of antibodies to minor antigens\(^2\)
  - Daratumumab does not interfere with identification of ABO/RhD antigens\(^2\)

Summary (Cont’d)

- A variety of methods can help to mitigating daratumumab interference\(^1\)-\(^3\):  
  - Treating reagent RBCs with DTT  
  - Use of Kell-negative RBCs  
  - Genotyping  
  - Referring to a patient’s pre-daratumumab blood compatibility profile

Additional Resources

- For additional information, please contact Janssen Medical Information by:
  - Phone: 1-800-JANSSEN (1-800-526-7736)
  - Email: Submit questions via the askjanssenmedinfo.com site
  - Search: www.janssenmd.com
  - Contact your local MSL: http://www.janssen-mls.com/
- Additional resources can be found at
  - www.darzalex.com
- To report suspected adverse reactions, contact Janssen at 1-800-JANSSEN or the FDA at 1-800-FDA-1088, or visit www.fda.gov/medwatch

Other Resources