Daratumumab interference with blood compatibility testing

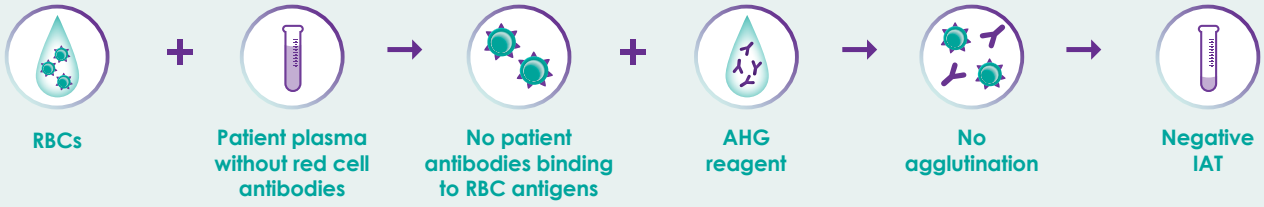
GUIDELINES FOR THE MANAGEMENT OF DARATUMUMAB INTERFERENCE WITH BLOOD COMPATIBILITY TESTING

DARZALEX® daratumumab concentrate for solution for infusion

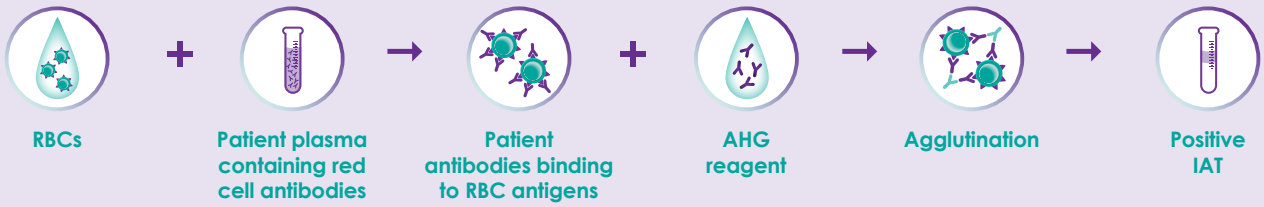
DARZALEX® SC daratumumab subcutaneous

DARATUMUMAB MAY RESULT IN POSITIVE INDIRECT ANTIGLOBULIN TESTS[1-3]

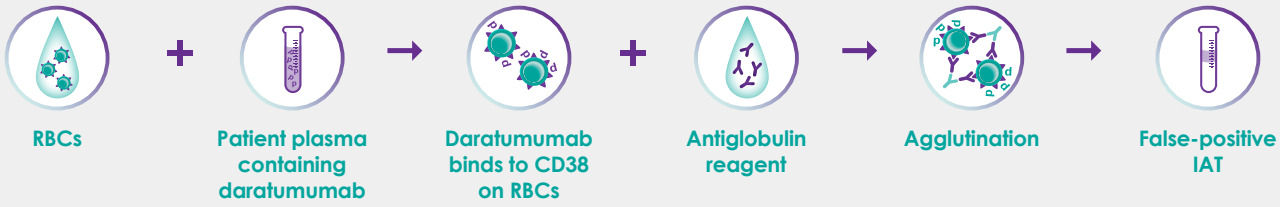
Negative indirect antiglobulin test



Positive indirect antiglobulin test



Indirect antiglobulin test from daratumumab-treated patient



Adapted from Chari *et al.* 2018.[5]

- Daratumumab is a human monoclonal antibody for the treatment of multiple myeloma or AL amyloidosis that binds to CD38, a protein that is highly expressed on multiple myeloma cells.[1,2]*
- CD38 is also expressed at low levels on RBCs, causing daratumumab to bind to some RBCs.[1,2]
- Daratumumab binding to RBCs may mask the detection of antibodies to minor antigens in the patient's serum. This interferes with blood bank compatibility tests, including antibody screening and crossmatching (both indirect Coombs tests) that are part of the routine pre-transfusion work up.[6]

Daratumumab-mediated positive IATs may persist for up to 6 months after the last daratumumab infusion.[7]

Daratumumab does not interfere with determination of the patient's ABO and Rh blood type.[4]

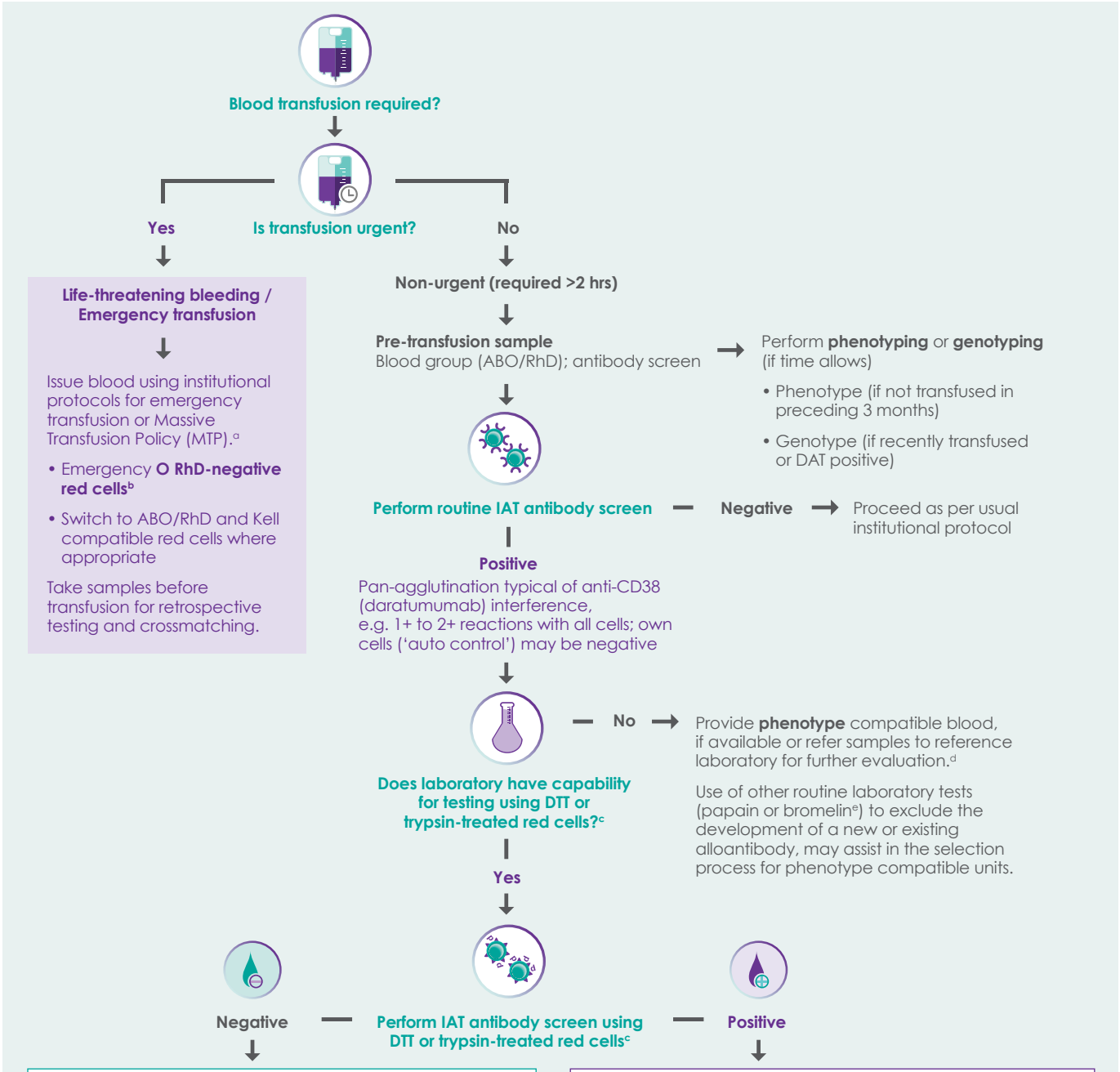
Pan-agglutination may persist once treatment with daratumumab is discontinued. The duration of this effect varies from patient to patient, but may persist for up to 6 months after the last daratumumab infusion. Therefore, patient should carry their Patient ID Card for 6 months after the treatment has ended.[6]

*Clinical significance has not been established.

[a]Refer to ANZSBT Guidelines for Transfusion and Immunohaematology Laboratory Practice [b]O-negative blood is not without risk and may not be suitable in all circumstances, e.g. patient has anti-c or anti-e antibodies [c]Tests using DTT or trypsin-treated red cells are published methods for resolving anti-CD38 (daratumumab) interference, however, testing may not be available in all laboratories and/or subject to regulatory restrictions [d]Extended phenotype/genotype, including, as a minimum: **Rh** (C, c, D, E, e), **K**, **Jk**[a], **Jk**[b], **Fy**[a], **Fy**[b] and **Ss** [e]Papain and bromelin are not IAT methods for crossmatching purposes

PRE-INFUSION TESTING RECOMMENDATIONS[6]

Use of daratumumab by the patient needs to be appropriately communicated for mitigation methods to be applied. Samples may need to be referred to a reference laboratory for additional specialist investigations. Ideally blood compatibility should be determined prior to commencing daratumumab therapy.



Adapted from Quach *et al.* 2018.[6]

Johnson & Johnson (J&J) provided the funding for this independent authorship group to meet and develop these guidelines. J&J reproduced this flow chart to provide a quick reference guide to management of blood compatibility testing when patients may be treated with CD-38 monoclonal antibody medication.[6]

INTERFERENCE MITIGATION METHODS[1,2,4,6,7]

REMEMBER: daratumumab-treated patients may show pan-reactivity in Indirect Antiglobulin Testing

Prior to starting daratumumab

Blood group and antibody screen

After starting daratumumab

Genotyping

or

Treating reagent RBCs with DTT or trypsin

or

Use other enzymatic method (papain or bromelin)

ID card

if available, refer the patient's ID card for their blood type and antibody screen results conducted prior to initiation of daratumumab treatment

REMEMBER - False-positive indirect Coombs test results may persist for up to 6 months after the last dose of daratumumab

Table 1: Antigens denatured or weakened by treatment with DTT or proteolytic enzymes[6]

DTT	Trypsin	Papain/Bromelin
Kell (K, k, Kp^a, Kp^b, Js^a, Js^b, Ku)	Cartwright (Yt^a)	Duffy
Cartwright (Yt^a)	Indian	MNSs, 'N'
Indian	JMH	Indian
JMH	Ge2, Ge3, Ge4	JMH
Scianna	Dombrock	Bp^a
LW	Bp^a	Ch/Rg
Lutheran	Ch/Rg	Xg^a
Mer2	Xg^a	En^{a}FS En^{a}TS
Ge3	MN	Ge2, Ge4
Dombrock	En^{a}TS	Fy^a, Fy^b, Fy6
Some Diego	Lutheran	Yt^a
Cromer	Mer2	
	Knops	

Adapted from Quach *et al.* 2018.[6]

Abbreviations: IAT: indirect antiglobulin test; RBC: red blood cell; AHG: anti-human globulin; Rh: Rhesus; 2-ME: 2-mercaptoethanol; DAT: direct antiglobulin test; DTT: dithiothreitol; eXM: electronic crossmatch; IS: immediate-spin tube technique; ID: identification; ANZSBT: Australian & New Zealand Society of Blood Transfusion.

References: 1. DARZALEX® Product Information, available at innovativemedicine.jnj.com/australia/download/darzalex-pi.pdf 2. DARZALEX® SC Product Information, available at innovativemedicine.jnj.com/australia/download/darzalexsc-pi.pdf 3. Medscape. Direct Antiglobulin Testing Accessed May 2025 at: http://emedicine.medscape.com/article/1731264-overview 4. Chapuy C *et al. Transfusion* 2015;55:1545–1554. 5. Chari A *et al. Clin Lymphoma Myeloma Leuk* 2018;18:44-51. 6. Quach H *et al. IMJ* 2018;48:210–20. 7. Oostendorp M *et al. Transfusion* 2015;55:1555–1562.

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