DaraEx

Version 19_EN_RUO, 2022-04

RUO	For research use only
Σ	~30 tests
2°C 8°C	2...8°C
	See package printings

1. Introduction

1.1. Overview

This manual describes the protocol for the imusyn

anti-CD38 antibody neutralizing agent (DaraEx)

for the inhibition of the agglutination effect of the anti-CD38 antibodies Daratumumab, Felzartamab, and Isatuximab in indirect antiglobulin tests (IAT).

Anti-CD38 antibodies can interfere with cross-matching and antibody screening in the IAT. This interference can persist up to 6 months after the last anti-CD38 antibody infusion[1].

1.2. Test Principle

DaraEx masks CD38 on the surface of the erythrocyte, thereby preventing the anti-CD38 antibodies Daratumumab, Felzartamab, and Isatuximab from binding and inducing agglutination.

1.3. Statement of Intended Use

For research use only.

2. Materials and Equipment

2.1. Definition of Symbols

DaraEx DaraEx PC process control

2.2. Components

DaraEx DaraEx 450 µl

⚠ WARNING! May cause an allergic skin reaction (H317). Please wear safety gloves (P280). DaraEx must be disposed in compliance with local regulations.

2.3. Storage and Expiry Date

Store at 2...8°C. Expiry Date is given on the immediate container. Conserved with 0.1% ProClin® 300

WARNING! May cause an allergic skin reaction (H317). Harmful to aquatic life with long lasting effects (H412). Wear protective gloves (P280). If skin irritation or rash occurs: Get medical advice/attention (P333+P313). Dispose of contents/container in accordance with local/regional/national/international regulations (P501).

2.4. Materials and Equipment Supplied by the User

2.4.1. Materials

Material	Supplier
LISS/Coombs ID-Cards Test cell reagents for the ID-System	Bio-Rad
Alternatively Cellbind Screen Test cell reagents for the Cellbind Screen system	Sanquin Reagents B.V: other
Alternatively ORTHO MTS Test cell reagents for the ORTHO MTS system	Ortho Clinical Diagnostics
Pipette tips	Multiple suppliers
Optional DaraEx-PC as PC	imusyn

2.4.2. Equipment

Equipment	Supplier
Laboratory shaker or rotator	Multiple suppliers

3. Preparation and Usage

Contaminations have to be avoided during all steps.

3.1. Antibody Screening and Identification

Use this protocol for ready-to-use cells at a concentration of 0.5 or 0.8% (e.g. a test cell panel), depending on the gel card system used.

3.1.1. Test Cell Preparation

Add 0.3 volumes DaraEx to 1 volume of test cells (test cell concentration: 0.5 or 0.8%). Incubate for 30 min at room temperature in such a way that the cells are kept in suspension (e.g. on a laboratory shaker at 600 rpm).

⚠ WARNING! The test cell concentration is critical! Cells that are concentrated above 0.8% need higher volumes of DaraEx added (see also chapter 3.2)!

The cells are now ready for immediate use.

3.1.2. Test Procedure

Use the DaraEx-treated cells in the IAT system. In addition to your regular samples, include a known and otherwise non-reactive, anti-CD38 antibody containing sample or solution as process control PC. For example, 0.1 mg/ml Daratumumab in 0.9% NaCl can serve as PC, or DaraEx-PC from imusyn.

Each DaraEx-treated cell has to be tested at least once with the PC to confirm the complete neutralization of CD38 on the cells.

3.2. Cross-Matching

Use this protocol for cells at a concentration of 1.0 or 1.6% (e.g. a sample from an erythrocyte concentrate), depending on the gel card system used.

3.2.1. Test Cell Preparation

Add 1 volume of DaraEx to 1 volume of cells (cell concentration: 1.0 or 1.6%, resulting concentration 0.5 or 0.8%). Incubate for 30 min at room temperature in such a way that the cells are kept in suspension (e.g. on a laboratory shaker at 600 rpm).

The cells are now ready for immediate use.

3.2.2. Test Procedure

Use the DaraEx-treated cells in the IAT system. In addition to your regular samples, include a process control PC as above (chapter 3.1.2).

Each DaraEx-treated cell has to be tested at least once with the PC to confirm the complete neutralization of CD38 on the cells.

4. Analysis and Troubleshooting

4.1. Analysis

The treatment of the test cells with DaraEx should abolish all agglutination reactions caused by anti-CD38 antibodies in most cases. The IAT results can be analyzed as if no anti-CD38 antibodies were present.

The DaraEx-treated cells incubated with the PC should not agglutinate. If they do, the test result is invalid and cannot be used.

4.2. Troubleshooting

Problem	Possible Cause	Solution
DaraEx-treated cells agglutinate with the PC.	Incomplete inhibition of the anti-CD38 antibody mediated agglutination.	Ensure that the DaraEx treatment was performed according to this manual. Repeat the test if necessary.
Test cells treated with DaraEx according to chapter 3.1 agglutinate though they should not.	Incomplete inhibition of the anti-CD38 antibody mediated agglutination.	Concentrate the test cells to 1.6% and treat the cells according to chapter 3.2. Repeat the test.

5. Limitations

DaraEx has been tested with the standard volumes used in the given gel card systems. Usage of other volumes than described in the manual of the respective gel card system, especially usage of higher sample volumes can lead to incomplete inhibition of anti-CD38 antibodies. The usage of other gel card systems or IAT procedures than listed in 2.4.1 has to be validated by the user.

Samples of patients with high levels of free anti-CD38 antibodies, e.g. patients that have been treated shortly before the sample has been taken, may still agglutinate DaraEx-treated cells.

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Incorrect execution of the instructions given in this manual can lead to false results. Especially, using more cells or a higher concentration of cells than recommended might lead to incomplete inhibition.

The DaraEx-treatment of the test cells according to 3.1 leads to a slight dilution of the sample (usually around 20%) in the test system. This may decrease the reaction strength of low-titer antibodies.

Some gel card systems are more sensitive to anti-CD38 antibodies than others. If problems with incompletely inhibited anti-CD38 antibody reactions persist, a change of the gel card system may help.

Contamination of reagents or samples, usage of reagents over their life-time, and usage of equipment or reagents not included or recommended may lead to false results. It is not recommended to use Grifols DG Coombs, or Ortho BioVue gel cards.

6. References

1. Oostendorp M, Lammerts van Bueren JJ, Doshi P, et al. When blood transfusion medicine becomes complicated due to interference by monoclonal antibody therapy. Transfusion. 2015;55(6 Pt 2):1555-1562.

Patent EP3548898B1.

Changes to the previous version are highlighted.

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