sCD38: an alternative to resolve Daratumumab-induced interference with blood compatibility testing

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Background: Anti-CD38 IgG monoclonal antibody therapy, Daratumumab (DARA), interferes with blood compatibility testing by causing panagglutination in the Indirect Antiglobulin Test (IAT). Different laboratory techniques are in use to mitigate interference including extended RBC geno-/phenotype matching, reagent RBC dithiothretol (DTT) treatment, or blocking CD38 epitopes with DARA-Fab fragments (DaraEx®). Grifols sCD38® (Medion Grifols Diagnostics, Switzerland) is a new DARA-neutralizing CE-marked reagent for the pre-treatment of plasma, and is planned to be launched by the end of 2023.

Methods: Seventy-seven plasma samples from patients treated with DARA were tested using the current routine method, namely an in-house 0.02 mol/L DTT treated ab-screening panel, with subsequent crossmatching using DaraEx®. Plasma aliquots were frozen to be re-tested in larger batches with the sCD38 reagent, which is a high-affinity proprietary molecule that binds DARA.

Neutralization of the plasma was performed by adding sCD38 to the plasma in the upper-chamber of the DG gel card. After incubation reagent RBCs were added. The protocol was modified to include mixing the sCD38 reagent and the plasma before the addition of reagent RBCs, starting with sample 34. Standard serological methods were applied for ab-screen for 8 patient samples spiked with known alloantibodies.

Results: In 10 of the first 33 samples, anti-CD38 activity could not be neutralized completely according to the original protocol even with the highest permitted dose of 6 ul. Anti-CD38 activity of 67 samples were completely neutralized; 17 with 2µl sCD38, 24 with 4µl and 26 with 6µl of sCD38.

The 10 non-inhibited samples were tested post-study with another panel of RBCs in an external laboratory. Nine were this time inhibited with the 6µl dose and one continued to show a doubtful reaction with one cell of the panel.

8 aliquots from 8 different samples were spiked with low-titer anti-E, anti-K, anti-Kp^a, anti-Lu^a, anti-Jk^a, anti-S, anti-Fy^a or anti-Fy^b. With the exception of two anti-Fy^a and one anti-Fy^b, 2µl sCD38 was sufficient to neutralize anti-CD38 and yet detected the alloantibodies.

Conclusions: Incubating plasma with sCD38 eliminated or markedly reduced panreactivity in all tested laboratory approaches. Identification of underlying clinically significant alloantibodies was achieved in alloantibody-spiked samples. An interference with low-titer ab of the FY-system was observed. Nevertheless, the Swiss recommendation of pre-typing in KEL-, FY-, JK- and MNS- systems before DARA treatment would make it simple to select FY-compatible blood. The level of CD38 expression on the surface of RBCs panels is variable and is a factor that can modulate the strength of panagglutination. Soluble CD38 is an alternative and straightforward technique that can be applied in standard transfusion laboratories.