35th Regional Congress of the ISBT, 2025, Milan, Italy

Comparison of Methods to Mitigate Anti-CD38-Induced Interference in Pretransfusion Testing

Young-Lan Song[1,5], Antigoni Zorbas[1], Clemens Schneeweiß[2], Laziza Amniai[3], Arnaud Reggiani[4], Charlotte Engström[1]

[1] Department of Immunohematology, Blood Transfusion Service Zurich, Swiss Red Cross, Switzerland
[2] imusyn
[3] Grifols
[4] Scientific Affairs, Bio-Rad Laboratories, DiaMed GmbH, Cressier, Switzerland
[5] Department of Internal Medicine, Clinic of Medical Oncology and Hematology, Municipal Hospital Zurich Triemli, Zurich

Background

The anti-CD38 IgG monoclonal antibody therapy (anti-CD38) induces panagglutination in the indirect antiglobulin test (IAT) and therefore poses a challenge in the accurate detection of clinically relevant alloantibodies (ab), which may lead to delays in the provision of compatible blood. To date, anti-CD38 interference has primarily been mitigated through the treatment of test cells with DTT. However, this approach is impractical for various laboratories due to reasons well-documented. To address this issue our reference laboratory has evaluated different alternative techniques, including the use of DaraEx/Plus® (imusyn, DE), sCD38® Grifols, CH) and Anti-Daratumumab (Bio-Rad, CH).

Aim

The objective of this comparative compilation was to evaluate the mode of action, analytical safety and handling of the reagents mentioned above, as well as to elucidate possible limitations.

Methods

For each method we evaluated a minimum of 16 samples from patients undergoing anti-CD38 therapy, with and without underlying ab. Ab detection and compatibility testing were performed for each individual method using IAT, employing either pre-treated test cells or serum, as outlined below.

- DaraEx Plus® is a CE-IVD-labelled Fab fragment of an anti-CD38-antibody which selectively blocks CD38 epitopes on erythrocytes. There is no need for pre-incubation of the test cells and can be used in company-independent ID-/Gelcards.
- sCD38, a CE-IVD-marked reagent, is a soluble recombinant protein designed to inhibit anti-CD38 ab interference in plasma/serum. After mixing of sCD38 and sera/plasma a pre-incubation time of 15 minutes is required before adding the red blood cells.
- Anti-Daratumumab ab is an anti-idiotypic ab specific to Daratumumab. The in-use solution is stable between 2-8°C over a week and for 24 months frozen. The product is added to sera/plasma and no pre-incubation is required prior to testing. To date this product has a Research Use Only (RUO) status.

Results

DaraEx Plus® consistently demonstrated reliable performance in IAT testing since the application period in 2019, with all underlying alloantibodies successfully detected and

represents a robust alternative in the context of mitigating Anti-CD38 interference. Initially in rare cases the standard dose of DaraEx Plus® was not sufficient to mitigate samples with high-titer anti-CD38.
During our evaluation of sCD38® full neutralization was attained with the lowest dose in most samples and almost all underlying ab specificities were identified. Interference with low-titer ab of the FY-system was confirmed, a caution mentioned in the reagent leaflet. This limitation of the reagent, however, can be readily resolved by selecting FY-compatible blood products.
In our assessment all samples treated with Anti-Daratumumab achieved complete neutralization. For all samples, the lowest dose was sufficient to neutralize anti-CD38 interference and all underlying ab were successfully detected.

Conclusion
In conclusion, all three methods present reliable and highly effective approaches, also user-oriented to suite smaller laboratories. Each method has its specific advantages, which can be leveraged depending on the number of samples and the laboratory preferences. The price, still partly undetermined, will certainly be a decision criterion.