Anti-Idiotypic Anti-Daratumumab to Mitigate the Interference of Daratumumab in Pre-Transfusion Testing

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Introduction

Daratumumab (DARA) is an anti-CD38 immunoglobulin monoclonal antibody used in multiple myeloma treatment. This treatment complicates pre-transfusion testing by binding to reagent red cells and causing false positive reactions on all antibody identification and crossmatching tests (1), potentially masking underlying clinically significant antibodies.

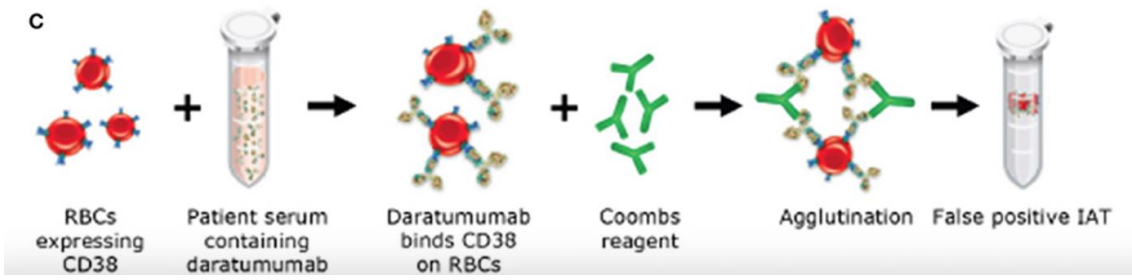

Figure 1. Mechanism of daratumumab interference with the indirect antiglobulin test (IAT) (2)

Traditional solutions, such as treatment of reagent red cells with dithiothreitol (DTT), can be used to mitigate this interference, however this process is time consuming and requires referral to specialist laboratories (3) , resulting in significant delays to blood provision. Additionally, DTT denatures certain red cell antigens, including the clinically significant Kell antigen, which can compromise antibody detection (4).

Objectives

- Evaluate the efficacy of a novel candidate; anti-idiotypic anti-daratumumab (AIAD), in neutralising daratumumab interference.
- Assess AIAD's ability to preserve red cell antigens and detect underlying alloantibodies.
- Determine feasibility for hospital transfusion laboratory implementation.
- Analyse potential benefits, including reduced turnaround times and improved patient care.

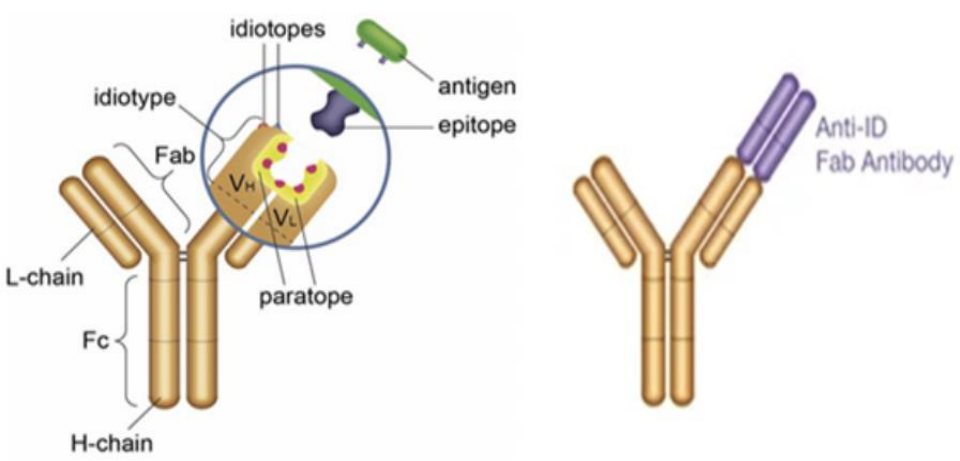

Figure 2. Mechanism of Action of Anti-Idiotypic Anti-Daratumumab Antibody (5)

References and Acknowledgements:

Methods

- Plasma samples from 40 DARA-treated patients were divided into three groups: control, Anti-D-spiked, and Anti-K-spiked.
- Antibody screening was performed using BioRad I-II-III cells (manual technique).
- Pan-reactive samples underwent neutralisation with anti-idiotypic anti-Daratumumab at 10% dilution, followed by repeat screening.
- If 10% was insufficient, neutralisation was repeated at 20%.
- Descriptive analysis assessed neutralisation success and alloantibody detection.
- Costs and turnaround times were compared to evaluate patient benefits.

Results

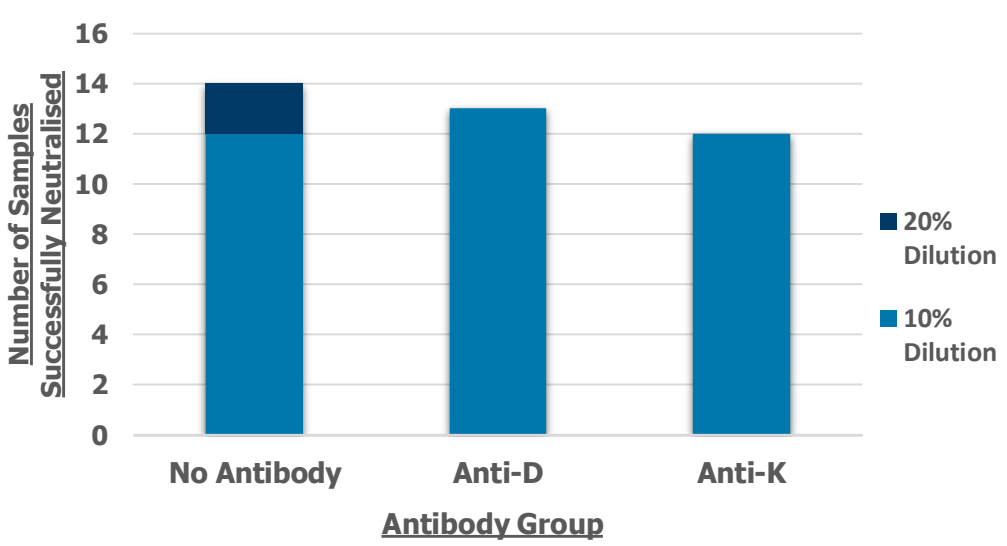

Figure 3. A bar-chart illustrating the number of samples successfully neutralised at 10% and 20%.

- Of 39 samples, 37 (95%) were successfully neutralised with a 10% anti-daratumumab concentration, the further two samples were neutralised at 20%. All underlying alloantibodies (titre 1:1 and 1:2) remained detectable.
- Cost-benefit and turnaround time analysis indicated a significant reduction in expenditure and transfusion delays – cutting turnaround time from 24-48 hours to 1-3 hours.

Conclusion

This novel reagent provides a rapid, reliable, and clinically safe solution for mitigating DARA interference in pre-transfusion testing. With clear advantages over current methods, the current findings support adoption of AIAD as a forward-thinking advancement to improve efficiency and patient centred care.