

Mezagitamab Interference in Serological Testing can be eliminated with anti-CD38 Fab Fragments

Background

Administration of anti-CD38 antibodies is a state-of-the-art therapy for patients diagnosed with multiple myeloma. However, treatment with the currently approved anti-CD38 antibodies regularly results in widespread agglutination of red blood cells in indirect antiglobulin tests (IAT), making the determination of irregular antibodies and timely transfusion of compatible blood a challenge.¹

Mezagitamab (TAK-079), a novel monoclonal anti-CD38 antibody, is currently under clinical investigation, not only for the treatment of multiple myeloma but also for other indications such as generalized myasthenia gravis.

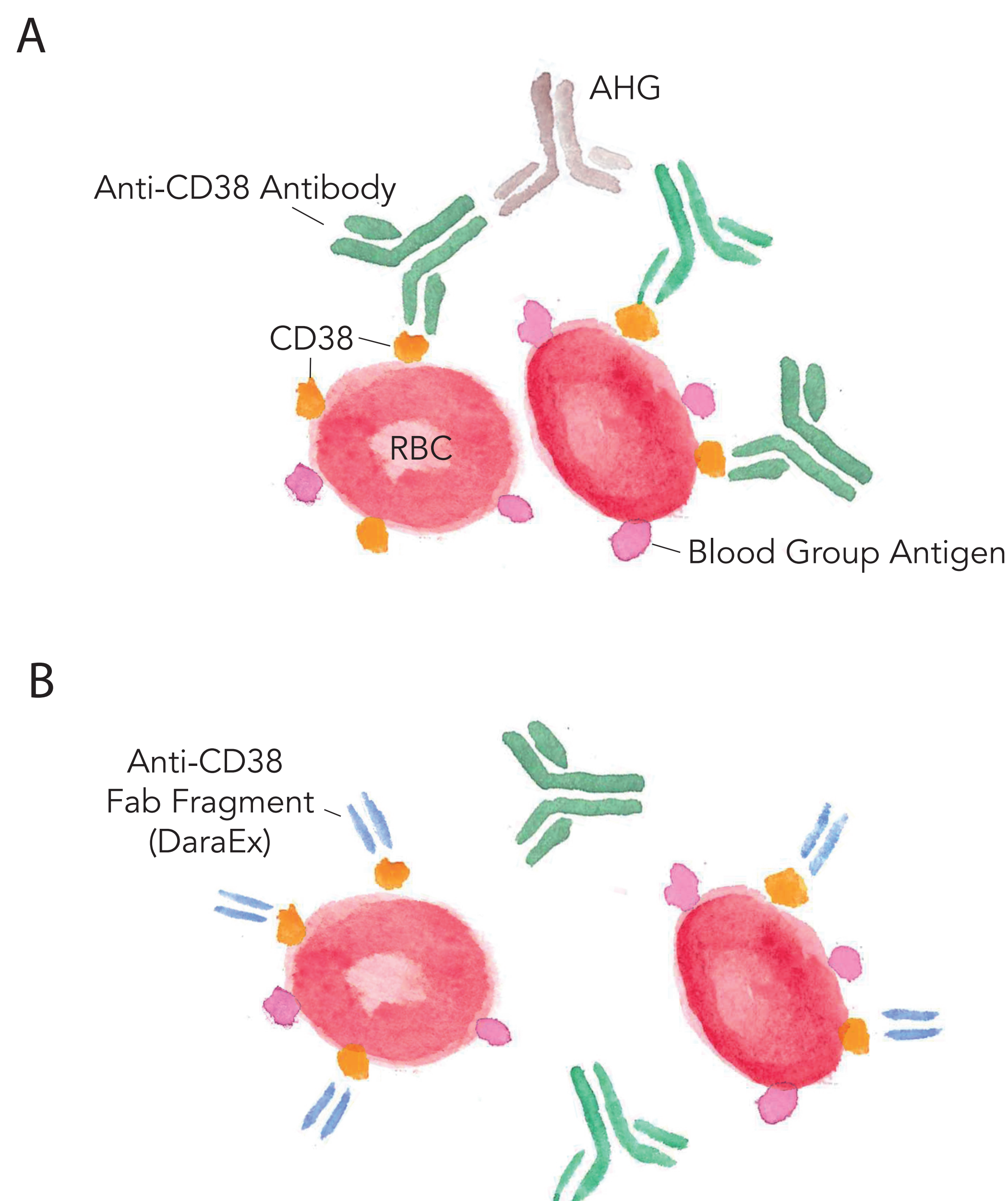


Figure 1. Principle of the Antigen Masking Indirect Antiglobulin Test (AMIAT)

(A) When an anti-CD38 antibody (green) is present in a patient sample, it binds to CD38 (yellow) on the surface of red blood cells (RBC). The cells are then agglutinated by anti-human globulin (AHG, brown) in the IAT. (B) In the AMIAT, a specific antigen on the surface of the red blood cells is masked before AHG is added. In the case of DaraEx (blue), the Fab fragment of an anti-CD38 antibody, CD38 is masked, thereby preventing anti-CD38 antibodies from binding.

Methods

We tested mezagitamab (MedChemExpress) against a test cell panel in the IAT and compared its interference to daratumumab. Additionally, we titrated mezagitamab to see if interference was likely to occur at the expected serum levels. Finally, we tested if DaraEx (imusyn), a reagent containing Fab fragments of an anti-CD38 antibody, was able to eliminate the interference in the antigen masking indirect antiglobulin test (AMIAT, see Figure 1).²

References

- 1 Oostendorp et al. When blood transfusion medicine becomes complicated due to interference by monoclonal antibody therapy. *Transfusion*. 2015;55(6 Pt 2):1555-1562.
- 2 Habicht et al. Mitigation of therapeutic anti-CD38 antibody interference with fab fragments: How well does it perform? *Transfusion*. 2023 Apr;63(4):808-816.

Conflict of Interest

CPH and CS are employees of imusyn GmbH & Co. KG. CS is a designated inventor of the technology presented here.

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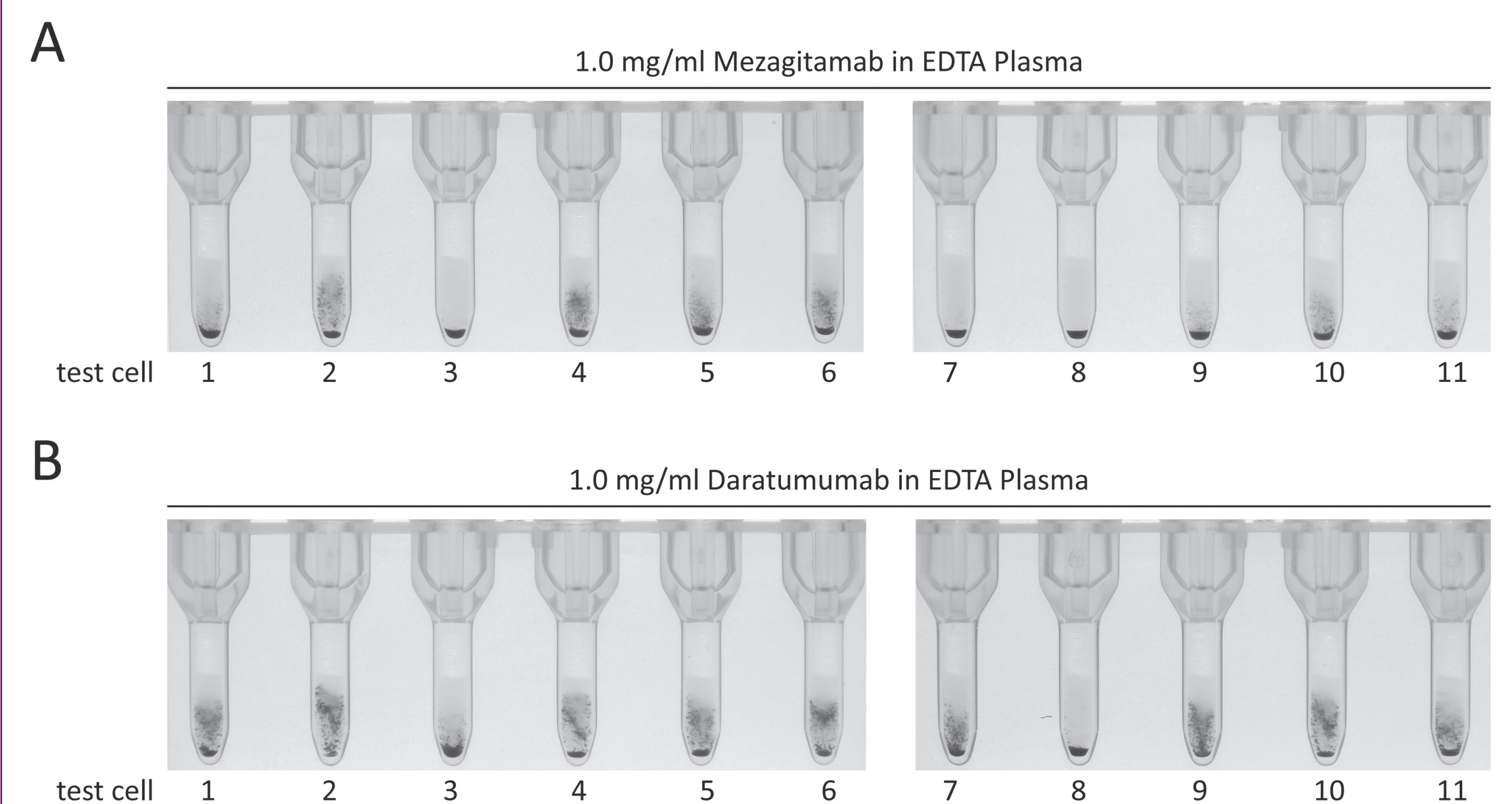


Figure 2. Mezagitamab interferes with serological testing in the column agglutination technique showing weaker agglutination strength than the first-in-class anti-CD38 antibody daratumumab. A test cell panel was tested with EDTA plasma spiked with either (A) 1 mg/ml mezagitamab or (B) 1 mg/ml daratumumab.

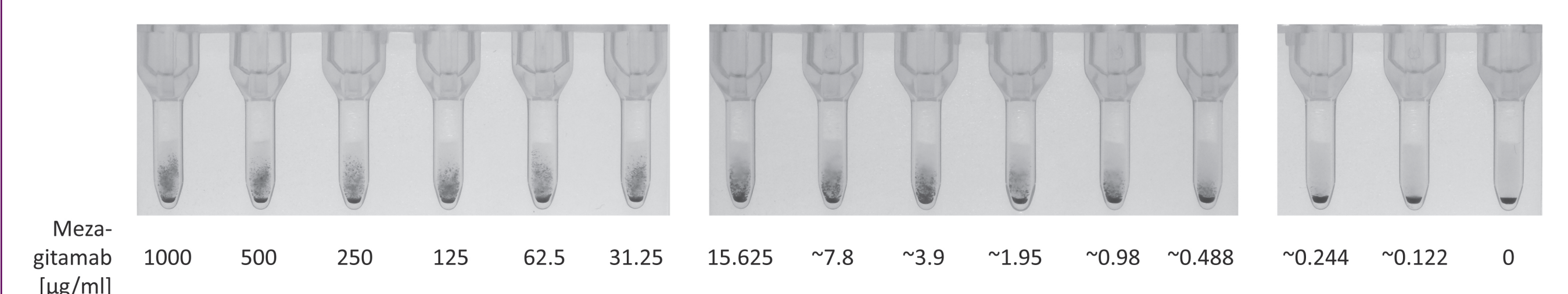


Figure 3. Mezagitamab induces agglutination at concentrations as low as 122 ng/ml (agglutination strength rating 0.5 on a scale of 0 to 4). EDTA plasma was spiked with mezagitamab as indicated and tested on a test cell with intermediate CD38 expression level (test cell number 4, see also Figure 2).

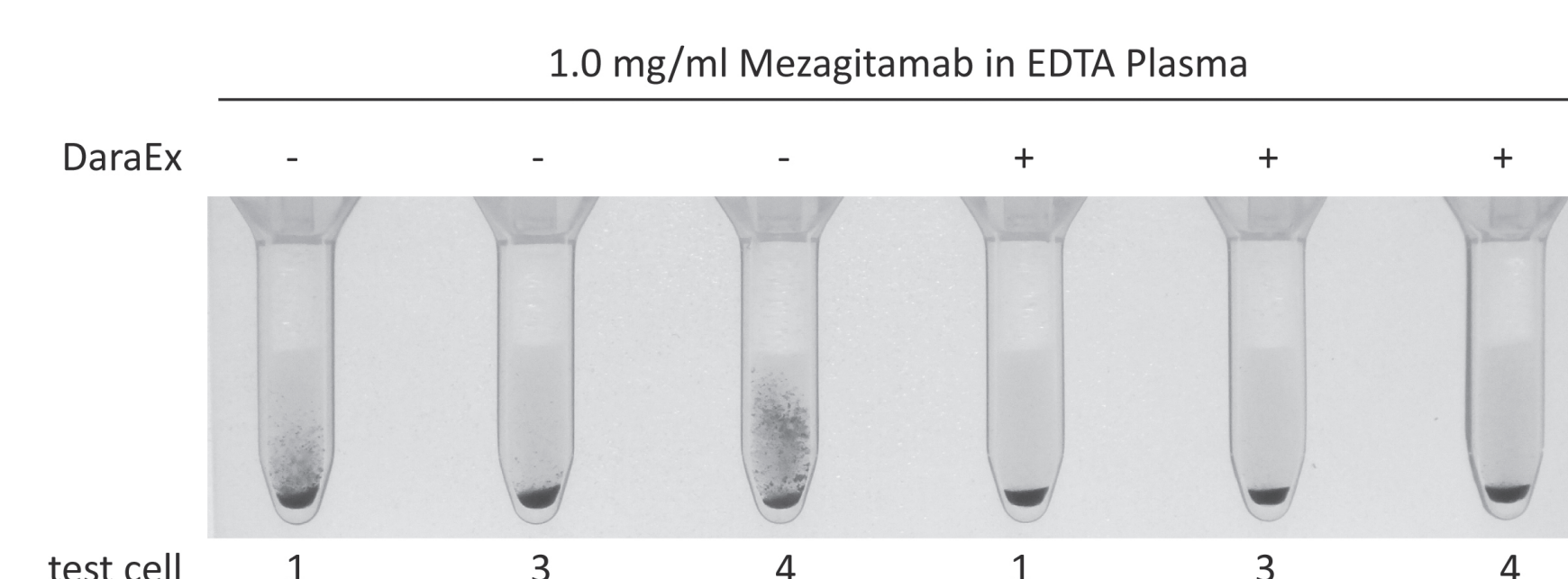


Figure 4. DaraEx completely mitigates the interference of mezagitamab in the AMIAT. Three different test cells were treated or not with 10 µl of DaraEx prior to the addition of EDTA plasma spiked with 1 mg/ml mezagitamab.

Results

Mezagitamab also interferes with the IAT, with comparable titers but weaker reaction strengths than daratumumab (Figure 2 and 3). DaraEx is able to completely overcome this interference in the AMIAT (Figure 4).

Conclusion

Once approved by the medical authorities, mezagitamab is likely to become a challenge for diagnostic laboratories. DaraEx treatment remains a simple and effective way to mitigate the interference of anti-CD38 antibodies.