# A Blood Center's Experience Negating the Serological Interference of Daratumumab

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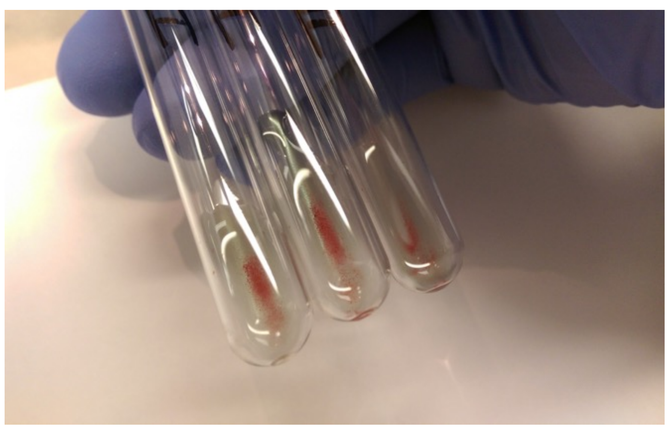
## Background

Daratumumab is an anti-CD38 monoclonal antibody approved by the FDA in November 2015 to treat relapsed or refractory multiple myeloma. CD38 is a type II transmembrane glycoprotein whose primary functions include receptor-mediated adhesion and ectoenzymatic activity in the catabolism of extracellular nucleotides. CD38 is overexpressed on multiple myeloma cells and has a large extracellular domain, making it an ideal target for daratumumab. CD38 is also expressed on other cells including red blood cells. Patients undergoing treatment with daratumumab will exhibit panreactivity on antibody screen and crossmatch compatibility testing. This interference creates a complication in providing safe and timely blood products for patients requiring transfusion support while receiving daratumumab treatment. Our reference laboratory saw its first patient receiving daratumumab therapy in December 2015.



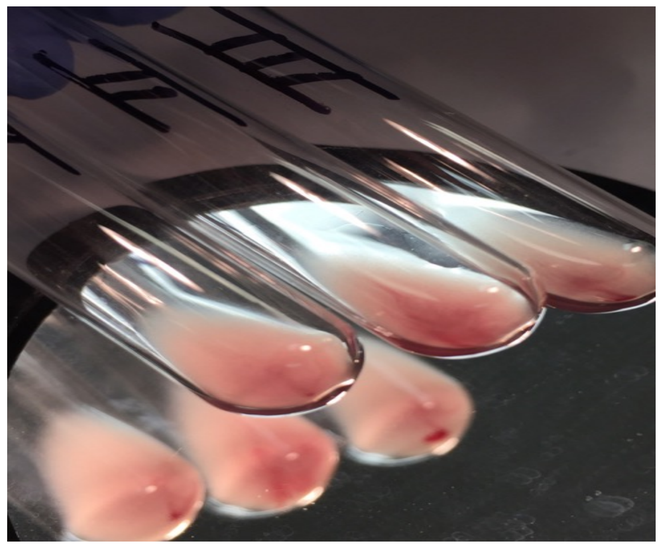
1+ reactive antibody screening cells of patient receiving daratumumab therapy.

## Methods

If testing was requested prior to the patient starting daratumumab we performed an ABO/Rh type, baseline antibody screen, and offered to perform a red blood cell serological phenotype or molecular genotype at the preference of the referring facility. If testing was requested after treatment was started, we performed an ABO/Rh type, antibody screen with dithiothreitol ( DTT) treated reagent red blood cells (RBCs). If the antibody screen was negative with the DTT treated RBCs, we issued ABO compatible, KEL1 negative red cell units. If a genotype had been performed, phenotypically matched red cell units would be issued and testing with DTT treated RBCs would not be performed. In March 2016, we also started testing two samples of cord blood (confirmed positive for the KEL2 and KEL4 antigens) with the patient's plasma in parallel with the DTT treated RBCs to exclude high frequency antibodies from the Kell system if the genotype had not been performed. All red cell units were negative for the KEL1 antigen and issued as crossmatch incompatible due to interference caused by daratumumab.

## Results

To date we have performed a total of 54 workups on 21 patients referred for pretransfusion testing. On each workup every patient had panreactive antibody screens with all cells tested but negative antibody screens after DTT treating the RBCs; and no reactivity seen when testing the patient's plasma with cord cells. No adverse reactions were reported for any of the transfusions.



Negative antibody screen following DTT treatment of reagent red blood cells.

## Conclusions

By testing the plasma of patients receiving daratumumab with DTT treated RBCs and cord blood cells, it is possible to exclude clinically significant antibodies with the exception of KEL1. However, the DTT treatment of the reagent red cells takes approximately one hour to complete. If the patient has been previously phenotyped or genotyped, and requires urgent transfusion, phenotypically matched red blood cells would be a better option.