Abstract Title: Mitigating Daratumumab Interference in the Laboratory

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Multiple Myeloma is an incurable haematological cancer characterised by abnormal plasma cells in the bone marrow. Daratumumab (DARA) is a monoclonal antibody directed against CD38, a cell surface protein that functions as a receptor and as an enzyme and is weakly expressed on haematological and solid tissues. The expression of CD38 is uniformly increased on malignant cells in MM. However, low levels of CD38 are also expressed on red cells, which becomes problematic in pre-transfusion serological testing. DARA in the patient's plasma causes pan-reactivity with reagent red cells by the indirect antiglobulin test. This interference can prevent blood compatibility testing being performed.

Three different methods were evaluated to mitigate the effects of DARA: allo-adsorption studies, DTT treatment of reagent red cells and cord cells as reagent cells.

The optimum adsorption technique was found to be the LISS addition method using a ratio of 4:1:1 with untreated cells. This removed DARA spiked plasma (conc. of 1µg/ml) following four adsorptions but not at a concentration of 35µg/ml which was equivalent to that found in patient samples. DTT treatment was successful at mitigating DARA interference and allowing for the presence of underlying antibodies to be identified. Underlying antibodies could be detected using reagent DTT treated red cells or phenotyped cord cells.

Of the three methods tested, DTT treatment of reagent red cells proved the most robust method for identification of underlying alloantibodies. However, the DTT treatment process is labour intensive taking approximately 4 hours and DTT treatment of red cells removes some red cell antigens including Kell system, Lutheran, Dombrock and YT antigens (and therefore antibodies to these antigens will not be detected using this method).