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Blood transfusion management in the new era of immune therapy: experience from the Belgian Red Cross Blood Services

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Background: Daratumumab (anti-CD38), already in use as monotherapy for adult patients with relapsed and refractory multiple myeloma, recently received the extended approval as a second line therapy in EU. This medication, however, interferes with routine blood bank tests by direct binding to CD38 expressed on reagent red blood cells (RBCs) or on cross-matched RBCs. A number of different methods exists to eliminate or bypass the anti-CD38 effects: dithiothreitol- or trypsin-treated reagent RBCs, cord RBCs, antigen-matched RBC transfusions guided by patient phenotyping or genotyping, and anti-CD38 neutralization. Unfortunately, there is no consensus on the best method or combination of methods to be used. The following transfusion policy was implemented by the Belgian Red Cross in Flanders region: RBC genotyping for clinically significant antigens was provided to patients before starting anti-CD38. Afterwards, on demand, blood was selected on the basis of extended donor phenotype and patient's genetically predicted phenotype.

Aims: We aimed to analyze one year after implementation if our transfusion policy was efficient, safe and adequate to the increasing demand of transfusions in immune therapy settings.

Methods: The study period was from November 2016 till November 2017. Patient molecular RBC typings were performed by RBC-FluoGene vERYfy PCR-SSP kit (Inno-Train). In the Rh system, C, c, E, e and Cw alleles are detected. Furthermore, blood groups Kell (KEL1/KEL2), Kidd (JK1/JK2), Duffy with the alleles FY1(A), FY2(B), FYX and Fynull (GATA-box mutation), MNS with the alleles MNS1(M), MNS2(N), MNS3(S), MNS4(s), U+var (P2) and U+var (NY) are tested. Regular blood group O and A donors are continuously phenotyped in Kell (K, k), Duffy (Fya, Fyb); Kidd (Jka, Jkb); MNS (S,s) systems.

Results: A total of 425 patient RBC molecular typings were performed. Over 130 patients enrolled in anti-CD38 treatment were genotyped (32,8% of all RBC genotypings). With an average of 24% of phenotyped active donors, resulting in 25.640 phenotyped blood group O RBCs and 13.653 phenotyped blood group A RBCs available for distribution, we were able to address the actual blood transfusion need for these patients. A total of 195 antigen-matched units were selected at our blood bank laboratories and were transfused to a total of 27 patients. No adverse transfusion events were reported. One of the patient presented a rare blood group antigen combination (O positive ccEE, K-k+ Fya- Fyb+ Jka+ Jkb+ M- N+ S+ s- Doa- Dob+) resulting in a complete phenotype with combined incidence of 0,009%. A total of 22 pheno-identical donations were successfully transfused to this patient for a 3 month-period.

Summary/conclusions: The selection of antigen-matched RBCs to support transfusion decisions is already common practice in complex clinical situations with panreactivity (e.g. auto-immune hemolytic anemia). Patients receiving Daratumumab could be successfully managed in the same manner. This approach avoids time and labor consuming pre-transfusion serologic techniques for CD38 elimination. Delay in issuing of RBC units is prevented too. If in the future Daratumumab becomes more widely used, the availability of convenient laboratory tests to cross match RBCs may become critical for adequate blood supply.