LETTERS TO THE EDITOR
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Daratumumab and Eltrombopag for Pure Red Cell Aplasia Post ABO Incompatible Allogeneic Hematopoietic Stem Cell Transplant for Acute Lymphoblastic Leukemia

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Dear Editor,
ABO incompatible Allogeneic stem cell transplantation (ASCT) has been associated with delayed erythrocyte engraftment and pure red cell aplasia (PRCA)(1,2). PRCA is seen in 7.5% to 29% of major blood group incompatible transplants (3,4). There are rare reports of the use of daratumumab and eltrombopag in the treatment of post-transplant PRCA (5,6,7). We describe the first case in the literature where both new agents (Daratumumab and EPAG) were used in the same patient and a response was obtained.
A 29-year-old male with T cell -acute lymphoblastic leukemia underwent ASCT from a HLA A mismatch unrelated male donor. Major blood group mismatch was present (patient 0 Rh positive and donor A Rh positive). He received conditioning with Fludarabine Cyclophosphamide and Total Body Irradiation (TBI) (myeloablative regimen). The GVHD prophylaxis was post-transplantation Cyclophosphamide, Cyclosporin and Mycophenolate mofetil. Due to high level of Anti A isohemagglutinin titer (1/512)before SCT, we applied plasmapheresis to the patient with fresh frozen plasma. After plasmapheresis anti-A titer was 1/16. He continued to require red blood cell transfusion support post engraftment once or twice every two weeks. Anti-A titer was detected as 1/128 during follow-up. The bone marrow aspiration and biopsy performed on D+45 did not show any erythroblasts, but cells belonging to other series were present. (Figure 1 A/B). During this time, the corrected reticulocyte count was a persistently low count (0.8%-1.5%).
Direct coombs test was negative, and the lactate dehydrogenase level was elevated at 370 U/L. (upper limit of normal,120-246 U/L).
The level of erythropoietin was >750 U/L (4.3-29IU/L). In the first month, he had 100% donor chimerism. IVIG was given at 400 mg/kg/day for 5 days D+46-50 for PRCA. He did not have any evidence of GVHD, hence mycophenolate mofetil was stopped on the 35th day and the cyclosporine taper was initiated on D +60 . The anti-A antibody titer and reticulocyte value remained unaltered on day +90 (subsequent to the cessation of immunosuppressive treatment, rituximab and IVIG therapy).
He was given 16 mg/kg of Daratumumab (Dara) by intravenous infusion once a week for eight weeks from D+175 to D+252 of HSCT. During Dara treatment, 14 units of erythrocyte replacement were required. Following Dara therapy, the corrected reticulocyte count was 1.48%, the anti-A titer was 1/16 and the haptoglobin was 2.03. (Figure 2,3). Post-transplant Anti-A titer decreased after the 8th weekly dose of Daratumumab. EPAG treatment(50mg/day) started because of transfusion dependence. During the course of EPAG therapy, the patient requires 3 units of erythrocyte suspension. On day 12 of treatment, the patient had anti-A negative, haptoglobin 2.06 and a corrected reticulocyte count of 1.74%. After 12th day of therapy, he did not need erythrocyte suspension and hemoglobin levels increased. On the 18th day of treatment, reticulocytosis was detected and bone marrow aspiration and biopsy showed hyperplasia in erythroblasts. The decrease in anti-

A titer under Dara treatment and The subsequent transfusion independence observed following the switch to EPAG treatment may be indicative of an additive effect exerted by both agents.

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