Recent advances in the treatment of aplastic anemia

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Acquired aplastic anemia (AA) is a hematopoietic disorder caused by the immune system attack on hematopoietic stem cells (HSCs). Recent study revealed clonal hematopoiesis by HSCs with genetic alterations, such as *PIGA*, *DNMT3A*, *ASXL1*, *BCOR/BCORL1*, copy-number neutral LOH of chromosome 6p (6pLOH), and HLA class I allele mutations is common in patients with AA. Genomic landscape of AA is distinct from myelodysplastic syndrome and age-related clonal hematopoiesis. These results suggest that escape from the autoimmune attack is strongly associated with clonal hematopoiesis in AA.

Responsiveness to immunosuppressive therapy (IST) is the best evidence for an underlying immune pathophysiology in AA. Eltrompopag (EPAG), a TPO-RA, has been shown to induce hematologic recovery in about 50% of patients with AA refractory to IST. Moreover, EPAG was reported to increase response rates when added to ATG/CsA in treatment-naive SAA patients compared with a historical cohort. A recent clinical trial showed that another TPO-RA, romiplostim (ROMI), was effective in EPAG-naïve refractory AA patients. Our recent retrospective study showed that high-dose ROMI was highly effective in AA patients refractory to EPAG. Further studies are needed to clarify whether TPO-RA induces clonal expansion of these clones.