P805 ALEMTUZUMAB IN RELAPSED SEVERE APLASTIC ANEMIA: LONG-TERM RESULTS OF A PHASE II STUDY

Topic: 12. Bone marrow failure syndromes incl. PNH - Clinical

Nidhi Aggarwal1, Ash Lee Manley1, Jibran Durrani1, Ruba Shalhoub2, Olga Rios1, Jennifer Lotter1, Bhavisha Patel1, Colin Wu2, Neal Young1, Emma Groarke1

1 Hematology Branch, National Heart, Lung, and Blood Institute, Bethesda, United States; 2 Office of Biostatistics Research, National Heart, Lung, and Blood Institute, Bethesda, United States

Background: Aplastic anemia (AA) is characterized by pancytopenia and a hypocellular bone marrow from immune-mediated bone marrow destruction. Immunosuppressive therapy (IST) is a good alternative to hematopoietic stem cell transplantation (HSCT), but relapse occurs in about 30% of cases, necessitating further therapy. We investigated alemtuzumab, a humanized IgG1 monoclonal antibody targeting CD52. We initially reported on 25 relapsed patients with 56% response. Here, we present long-term results of a total 42 patients.

Aims: Assess the efficacy and long-term outcomes in patients with relapsed severe AA (SAA) who received alemtuzumab.

Methods: Participants met Camitta criteria for SAA, had received at least one course of antithymocyte globulin (ATG)-based IST, and had relapsed. Alemtuzumab was administered intravenously (IV) (n=28) or subcutaneously (SC) (n=14). The primary endpoint was hematologic response at 6 months, with blood counts no longer meeting SAA criteria. Secondary endpoints included robust response (platelet or absolute reticulocyte count >50x10^9/L at 6 months), relapse, clonal evolution to myelodysplasia and leukemia, response to therapy after relapse, and survival. Patients were assessed annually, and additional AA therapy and transfusion dependence was also recorded. Cumulative incidence curves were used to estimate the probability of relapse among responders and clonal evolution, with death as a competing risk. Overall survival probabilities were evaluated using Kaplan-Meier curves. This trial is registered at clinicaltrials.gov (NCT00195624).

Results: Patients were enrolled over 9 years with a median follow-up of 6 years. Median age was 32 years and 57% were female. Five patients (12%) had neutrophil count <0.2x10^9/L prior to receiving alemtuzumab. At 6 months, 18 (42%) patients had achieved a response, and 12 (29%) attained a robust response. Response was achieved in 15 (54%) of those who received alemtuzumab IV, versus 3 (21%) who received SC. Of non-responders or those off study at 6 months (n=24), 2 achieved a late response by 1 year.

Another relapse occurred in 8 patients, and cumulative incidence at median follow-up was 39%. Of those who were refractory to or relapsed (n=28) after alemtuzumab, 4 (15%) proceeded to HSCT, 12 (43%) to other medical AA therapies, and 10 (37%) to both. Subsequent treatments included eltrombopag (n=13), r-ATG (n=8) CSA (n=6), androgen (n=3) or other (n=4); response to further treatment occurred in 2 (29%) of relapsed and 5 (38%) of refractory patients, with response unknown in 7.

Clonal evolution occurred in 9 patients; cumulative incidence at median follow-up was 23%. Of these, 4 were non-responders. Evolution was high risk (morphological MDS, AML, or chromosome 7 abnormality) in 7 patients.

Overall survival was 67% at median follow-up (Figure 1). At last follow-up, 10 of the 18 responders (56%) had durable response and were both transfusion- and AA therapy-independent. Patients had prolonged immunosuppression after alemtuzumab, with CD4+ T cell counts <200 in 81% of assessed patients at 6 months, 67% at 1 year, and 42% at 2 years.

Image:
Summary/Conclusion: Alemtuzumab is effective for relapsed SAA. The rate of hematologic response was greater with IV rather than SC administration. Most responders achieved durable long-term hematologic improvement, and the rate of clonal evolution was similar to that seen in our SAA patients treated with rabbit ATG. Immunosuppression can persist for years following alemtuzumab therapy, requiring long-term monitoring and antimicrobial prophylaxis.