S184 SAFETY AND OUTCOMES FOLLOWING IMMUNOSUPPRESSIVE THERAPY WITH ATG/CYCLOSPORIN +/- ELTROMBOPAG FOR OLDER PATIENTS WITH SEVERE APLASTIC ANEMIA

Topic: BMF and PNH novel clinical data

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Background:
Immunosuppressive therapy (IST) with anti-thymocyte globulin (ATG), cyclosporin (CSA) +/- eltrombopag (EPAG) is the now established 1st line non transplant therapy for severe aplastic anemia (SAA), but there are concerns regarding its safety in older patients. We evaluated toxicity of horse or rabbit ATG/CSA +/- EPAG therapy and long-term outcomes in our SAA cohort.

Aims:
1. Compare type and frequency of post IST toxicities in an older (≥60 years) versus younger (<60 years of age) cohort of SAA patients
2. Evaluate clinical baseline predictors of toxicity to IST
3. Describe disease outcomes for older patients following IST

Methods:
This was a single center, retrospective analysis evaluating data collected as part of the following clinical trials for treatment naive SAA: NCT00260689 (randomized trial of horse versus rabbit ATG), and NCT01623167 (single arm trial of horse ATG/CSA + EPAG). Data were derived from logged AEs or SAEs or were retrospectively collected from clinical records. All patients gave written informed consent. Univariate logistic regression was used to assess predictors of toxicity. Overall survival probabilities were evaluated using Kaplan-Meier estimates.

Results:
SAA (n=321) patients were evaluated; 54 (17%) were ≥60 years old (range 60-82). The median age of the older cohort was 68 compared to 25 (range 2-59) in the younger. Older patients had significantly more baseline comorbidities than did younger patients (p <0.001); cardiovascular disease history or risk factors were identified in 25 (46%) of the older cohort compared to 21 (8%) in younger patients. There was no significant difference in baseline disease characteristics including blood counts, time to diagnosis, or disease severity between older and younger patients.

Complications including serum sickness, hypertension, anaphylaxis, and cardiac, liver or renal toxicity within the 1st 30 days were individually compared between cohorts, as typical in IST. The numbers of these IST specific toxicities were not significantly different between cohorts. Older patients had a lower frequency of SAEs within 30 days post treatment compared to younger patients (30% versus 62%) but a similar frequency of SAEs recorded at

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3 and 6 months. Commonest SAEs by 30 days were infection (n=8), respiratory issues (n=2) and serum sickness (n=1) in older patients, and infection (n=35), fever without identified organism (n=36), serum sickness (n=12), and bleeding (n=4) in younger. Ten (4%) younger patients and 5 (9%) older patients required transfer to an intensive care unit during their admission for IST.

Age, sex, time from diagnosis to treatment as a continuous variable, history of cancer, or the presence of baseline cardiac, autoimmune, or infectious comorbidities did not predict for IST related toxicity in the 1st 30 days.

While older patients and younger patients had similar overall response to therapy (72% versus 69% p=0.7), older patients had poorer survival, with a median of 977 versus 1346 days in younger patients (p=0.002) (Figure 1A). However, survival up to 2 years was equivalent. Poorer survival in older patients associated with higher rates of relapse (Figure 1B) and clonal evolution compared to younger patients (Figure 1C). Overall, this is suggestive that poorer outcomes in older patient relate to underlying disease rather than toxicity.

Summary/Conclusion:

1. Older SAA patients have a similar tolerance to IST as younger patients.
2. There were no pre-treatment predictors of IST toxicity identified.
3. Relapse and clonal evolution are higher in older SAA patients and may contribute to poorer survival. Pursuit of novel therapies for older patients with AA is required.