Methodology: In this post hoc analysis of the HERCULES (NCT02553317) intent-to-treat population (caplacizumab, $n=72$; placebo, $n=73$), we identified patients with a fast platelet count response (i.e., ≤3 days vs. >3 days) and described the exacerbation rate by treatment group. Time to durable platelet count response (defined as time to last daily TPE during the overall treatment period), time to complete remission (defined as platelet count $>150 \times 10^9$/L and lactate dehydrogenase <1.5 × the upper limit of normal for >30 days after cessation of daily TPE), and recurrence-free survival (absence of exacerbation or relapse during the overall study period) were calculated.

Results: More than half of the patients in the HERCULES trial achieved an initial platelet count normalization within 3 days (caplacizumab, 56/72 [78%]; placebo, 43/73 [59%]). In patients with a fast platelet count response (ie, ≤3 days), the exacerbation rate was 3.6% (2/56) with caplacizumab and 44.2% (19/43) with placebo, suggesting that the rapid platelet count response was sustained with caplacizumab, whereas almost half of the fast responders in the placebo group subsequently exacerbated. In patients with time to platelet count response >3 days, the exacerbation rate was 6.7% (1/15) with caplacizumab and 30.0% (9/30) with placebo, confirming the durable response with caplacizumab. The exacerbation rate among placebo patients with platelet response >3 days remained high but was numerically lower compared with fast responders. Of the patients who experienced exacerbations, 90% (2/3 in the caplacizumab group and 26/28 in the placebo group) switched to open-label caplacizumab, which may have favored the outcomes of placebo patients. Despite this bias, the median (95% CI) time to durable response was 4.5 (4.4–4.6) days with caplacizumab and 10.5 (6.5–14.5) days with placebo; accordingly, the median (95% CI) time to complete remission was shorter in the caplacizumab group (40.0 [37.7–41.1] days) compared with placebo (44.2 [42.0–48.2] days). The analysis of overall recurrence-free survival during the entire study period demonstrated an early and sustained benefit for caplacizumab over placebo, mainly driven by significant reduction in exacerbations during the study drug treatment period. The effect was sustained, despite six relapses in the caplacizumab group in the follow-up period in patients with unresolved underlying autoimmune disease activity.

Conclusion: Caplacizumab demonstrated a faster and sustained platelet count response compared with the placebo group, in which many fast responders subsequently had an exacerbation. Fast platelet count responses with caplacizumab were maintained and translated into clinically relevant improvements in time to complete remission and overall recurrence-free survival. Data first presented at EHA 2020 virtual meeting, June 11–21st. Study sponsored by Sanofi.

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STEM CELL TRANSPLANT

PP 50

Transplant in aplastic anemia using combined G-CSF primed blood and bone marrow stem cells – a retrospective analysis

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Objective: Aplastic anemia is characterized by diminished or absent hematopoietic precursors in the bone marrow, most often due to injury to the pluripotent stem cell. In Pakistan, Aplastic Anemia is not uncommon and allogeneic hematopoietic stem cell transplant remains the only curative option in these patients. We aim to determine the transplant outcome of combined, G-CSF primed blood and bone marrow grafts in adult and pediatric patients with aplastic anemia.

Methodology: We retrospectively collected data of all transplant procedures performed from 2004–2019 at Aga Khan University Karachi, Pakistan. Variables analyzed included type of transplants, age, gender, type of stem cells used, conditioning regimens and overall survival for patients undergoing transplant in aplastic anemia.

Results: A total of 351 transplants were performed during the study period. Out of these, 239 were allogeneic transplants whereas 112 were autologous procedures. There were 254 males and 97 females. The main indications for allogeneic stem cell transplant were aplastic anemia (70), acute leukemia (58) and beta thalassemia major(40). Out of 70 patients with aplastic anemia, 52 were males and 18 were females. 38.6% percent of patients were from pediatric age group. The median age ± SD was 17.5 ± 9.4 years (range: 2–43 years). Cyclophosphamide/ATG was used as a conditioning regimen in 67 patients, while ATG/cyclophosphamide/fludarabine was used in 2. Haploidentical transplant was done in 1 patient. Twenty seven percent of patients underwent sex-mismatched procedures. In 52 patients, a combination of GCSF primed blood and bone marrow stem cells were used. The mean CD34 count was 5.2 × 10/kg. GVHD prophylaxis was done with cyclosporine and methotrexate. All patients received standard infection prophylaxis. Engraftment was achieved in 75% of patients. The median day of myeloid engraftment was 15 (range 10–22 days). Chronic GVHD was present in 3 patients while 4 had acute GVHD. The overall survival was 71.2% (median duration of 80 months). The causes of mortality included gram-negative sepsis (5), graft versus host disease (4), graft failure (4), disseminated fungal infection (2), intracranial bleed (2), bleeding diathesis (2) and transplant associated microangiopathy (1).

Conclusion: Combination of blood and bone marrow stem cells results in early engraftment with decreased frequency of GVHD in aplastic anemia. The overall survival was comparable to international literature.

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