PA2177 ANTITHYMOCYTE GLOBULIN AS TREATMENT OF ACUTE GRAFT VERSUS HOST DISEASE - 10 YEARS OF EXPERIENCE AT A SINGLE-CENTER

Topic: 22. Stem cell transplantation - Clinical

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Background: Acute graft versus host disease (aGVHD) is the leading cause of morbidity and non-relapse mortality, following allogeneic hematopoietic stem cell transplant (AHSCT). It affects particularly the skin, liver, and gastrointestinal tract (GI). The recommended first-line treatment is glucocorticoid therapy. However, 35-50% of patients (pts) become refractory to steroid therapy (SR-aGVHD). There is still no consensus regarding subsequent treatment, and outcomes remain poor. Antithymocyte globulin (ATG) is an alternative therapy. Although leading to an initial response, especially in pts with skin-only GVHD, studies have suggested that it may not be an effective option since it does not prolong OS (5.5 months) and it is associated with high mortality rates due to infection.

Aims: To characterize pts with SR-aGVHD treated with ATG 2mg/kg or thymoglobulin 1.5mg/kg in alternate days for 5 administrations.

Methods: Forty-three pts were treated between August 2010 and April 2021. Diagnosis and classification were based on clinical, laboratory and histological data. Response criteria was defined as: complete response (CR); Very Good Partial Response (VGPR); Partial Response (PR); No Response (NR). Endpoints were overall survival (OS) and response after 28 days of treatment.

Results: Patient characteristics are shown in table 1. Median time of follow-up was 4 months (1-129). aGVHD was diagnosed at a median of 23 days (7-228) and immunosuppressive therapy was started immediately in all cases except for 11pts with grade < II. Before any treatment, median clinical stage score was II (range II–IV). Initial organ involvement was skin only (n=22), GI only (n=5) or multiorgan (n=16). Median time from steroid treatment to ATG was 23 days (5–213) and from AHSCT to ATG was 57 days (28-249). At day one of ATG, more than 50% had multiorgan involvement (n=24), followed by GI only (n=10), skin only (n=8) and liver only (n=1). ATG was second-line therapy in 40pts and third line in 3pts, with a median of 5 doses (1-5). Response to ATG was assessed on a weekly basis, but for the purpose of the study, we considered the assessment after 28 days of the first dose. 26pts had NR; 8 VGPR; 7 achieved PR and 2 CR. Most of the pts that were refractory to ATG had multiorgan involvement (n=17), followed by GI only (n=6), liver only (n=1) and skin only (n=1). Of those who achieved at least a PR, 7pts only had the skin affected, 6 had multiorgan and 4 had GI only. Adverse events included virus reactivation in 16pts (62.5% had cytomegalovirus) and bacterial infection in 8pts. A total of 33pts died: 23 from infection, 10 from other complications directly related to aGVHD. The NR group had more deaths (25 vs 9 pts). Median OS was of 5 months (3.6–6.3). Those who responded to ATG had a significantly better OS (12 vs 4 months, p=2.8x10⁻⁵). There is a correlation between the organs affected and the response to ATG ($\chi^{2}$, p=0.011): when the skin is the only organ affected, pts are more likely to respond than when compared to multiorgan involvement.

Image:
Summary/Conclusion:

Except for ruxolitinib, no treatment has shown superiority over other treatments and no new drugs have been approved either as first-line or second-line treatment for aGVHD in the past 30 years. Our study showed that ATG can be a good alternative in pts with less extensive GHVD limited to single organs, particularly the skin alone, and that in more extensive disease it led to infrequently sustained responses and consequently poorer survival. A high rate of major complications, mainly infectious, was observed after treatment with ATG.