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722.ALLOGENEIC TRANSPLANTATION: ACUTE AND CHRONIC GVHD, IMMUNE RECONSTITUTION

Safety and Efficacy of Extracorporeal Photopheresis for Acute and Chronic Graft-Versus-Host-Disease

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Introduction

Graft-versus-host disease(GVHD) is a severe complication of allogeneic hematopoietic cell transplantation(alloHCT), directly linked to increased morbidity and mortality. Despite novel biologic agents under study or commercial use in this field, corticosteroids and conventional intensified immunosuppressive therapy remain the cornerstone of treatment. Extracorporeal photopheresis (ECP) has been used as an alternative treatment. We studied the safety and efficacy of ECP in a large real-world cohort of GVHD patients.

Methods

We enrolled consecutive patients, of our JACIE-accredited center, that received ECP post alloHCT over the last 2 decades for cGVHD and over the last decade for steroid-dependent or refractory grade II-IV aGVHD. All patients with unrelated or haploidentical donors received thymoglobulin (ATG) 5mg/kg as prophylaxis. GVHD prophylaxis included cyclosporine-methotrexate in myeloablative and cyclosporine-MMF in reduced toxicity/intensity regimens. Before ruxolitinib or ibrutinib availability, MMF, cyclosporine or ATG were commenced as second line treatment in steroid-refractory patients, depending on previous prophylaxis. ECP was mostly administered as third line treatment for cGVHD and after assessment of response of 5 days of steroid treatment according to our protocol: 1 session/week for the 1 st month for cGVHD and 2sessions/week for aGVHD, 1 session/2 weeks for 3 months, evaluation of response and 1 session/month for 6 months. Before Ruxolitinib's availability, ATG was commenced simultaneously with ECP initiation in steroid-refractory aGVHD patients.

Results

We studied 112 patients with moderate or severe cGVHD. Only 13 received 4 or less ECP sessions because of severe GVHD-related morbidity and were excluded from further analysis. Median ECP sessions were 17(6-49). There were no ECP-related adverse events. 67 patients presented with cutaneous sclerosis manifestations, 73 mucocutaneous disease, 36 liver, 42 visceral and 27 lung involvement. ECP was commenced as second line in 35 patients. Ruxolitinib was administered in combination with ECP in 19 patients, while ibrutinib in 2. Bacterial infections were observed in 43 patients, viral in 38 and fungal in 11 patients.

Only 19 patients did not show response. Significantly lower rates of response presented in patients with visceral involvement($p=0.037$) and earlier post-transplant GVHD diagnosis ($p=0.001$). With a follow-up of 45.2 (5.6-345.1) months, 5-year CI of cGVHD-related mortality was 21.2% and was significantly reduced in patients with ECP response ($p<0.001$). 5-year OS was 65.3% and was independently associated with HLA matching ($p=0.011$), higher number of ECP sessions($p<0.001$), later initiation of ECP ($p=0.002$), response to ECP ($p=0.036$) and no relapse($p=0.001$).

Regarding aGVHD, we studied 28 patients, aged 45 (18-67), with myeloablative (16), reduced toxicity (8) and intensity (4) conditioning, from sibling (4), matched (11) or one locus mismatched (12) volunteer unrelated and haploidentical (1) donors. Disease risk index was very high (1), high (11), intermediate (14) and low (2). aGVHD was observed at day +17(8-50). Skin, intestine and liver involvement was evident in 9 patients, skin and intestine in 13 and skin only in 6 patients. 13 patients were steroid-dependent and 15 steroid-refractory.

ECP was commenced at day +18 (8-56) for 15 (4-20) sessions. The majority of patients (19/27) presented partial (7), very good (11) or complete (1) response. With 9.9 (1.7-113) months of follow-up, immunosuppression was reduced in 12/27 and ceased in 1 patient. Clinically significant bacterial infections were found in 19 patients, fungal in 3, CMV and EBV reactivation in 19 and 12 respectively and other viral in 6 patients.

Cumulative incidence of aGVHD was 56.4 at 1-year.Five-year overall survival (OS) was 34%. Reduction of immunosuppression($p=0.026$) and number of ECP sessions($p<0.001$) were associated with improved OS, irrespectively of other factors. In particular, optimal OS was observed in patients that received more than 19 ECP sessions (Figure).

Conclusion

Our data confirm that ECP is safe and effective for GVHD. Even in the era of novel biologics, ECP should be considered early in the course of GVHD, before irreversible end organ damage has been established. Combination with other treatments and individualized treatment algorithms remain important unanswered questions.

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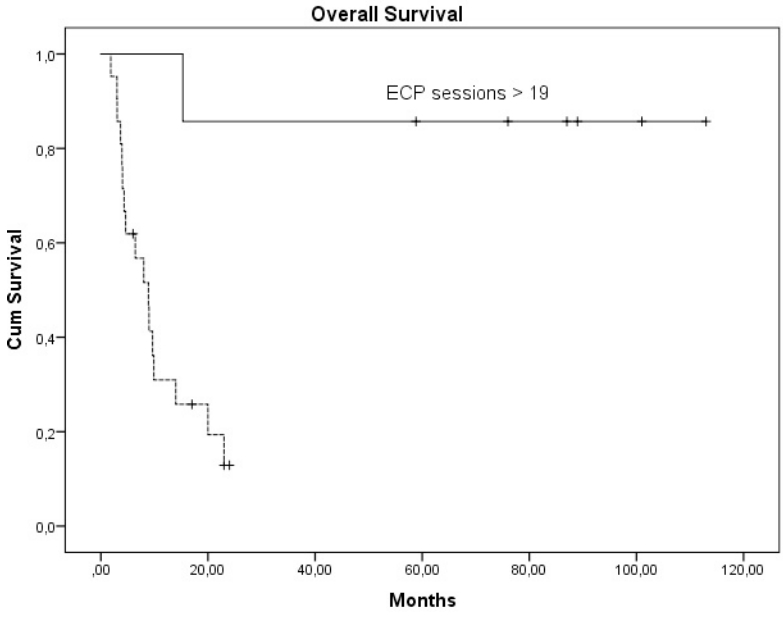

Figure 1

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