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Allogeneic transplantation for peripheral and cutaneous T-cell lymphomas

Few studies have evaluated the role of allogeneic stem cell transplantation (SCT) in peripheral T-cell lymphomas (PTCL). Recent reports have evaluated allogeneic SCT exclusively in relapsed setting and showed an evidence for a graft-versus-lymphoma effect (GVL). In this report we extended our previous observations to 38 patients. All patients received several courses of debulkying chemotherapy followed by allogeneic SCT with a reduced intensity conditioning (RIC) regimen. Patients' median age was 45 years (range, 15-64). Histologic PTCL subtypes included: unspecified (n=15), ALCL (n=9), AILD (n=5), intestinal (n=3), other subtypes (n=6). Twenty-eight pts (74%) received transplant from HLA-identical sibling donors, 5 from haploidentical donors (13%) and 5 from unrelated donors (13%). The median time from diagnosis to allogeneic SCT was 16.4 months. Twenty-one patients (55%) had failed a previous autologous SCT. Twenty-eight (73%) had chemosensitive disease (n=13 in CR, n=15 in PR). Ten patients received low dose alemtuzumab in the conditioning regimen for GVHD prophylaxis.

At median follow-up of 50 months, 21 (55%) were alive (n=19 in CR, n=2 with disease) and 17 died (n=12 disease, n=5 toxicity). Patients allografted in complete remission had the better outcome (66% *vs.* 52% versus 25% for patients allografted in CR, PR and progressive disease, respectively). The incidence of acute and chronic GVHD were 47% and 42%, respectively. The estimated 5 year OS and PFS projections were 53% (95%CI, 36%-67%) and 52% (95%CI, 35%-67%), respectively. The median time to relapse was 140 days (range, 38-603 days). Eight patients received DLI for progressive disease: we observed 3 complete remissions, 1 partial remission, and 4 progressive disease. The response was associated to occurrence of GVHD.

Our results showed that allogeneic SCT is a potential curative treatment for PTCL. In addition, our results are comparable to those reported recently by Le Gouill et al in 2008 (5 year OS anf EFS were 57% and 53%, respectively).

Major issues remain open: i) when allogeneic SCT should be performed; ii) PTCL included several different subtypes; actually we did not know if the graft-versus-lymphoma effect is stronger in some particular entity.

Among cutaneous T-cell lymphomas (CTCL), advanced-stage mycosis fungoides (MF) and Sezary syndrome (SS) have an aggressive clinical course, eventually leading to a very short sur-

vival. Even though novel compounds with promising activity are currently under investigation, there is no effective standard of care for patients with advanced-stage CTCL. Therefore, alternative strategies based on autologous and allogeneic HSCT are being increasingly explored. Indeed, significant rates of CR have been occasionally reported by approaches based on high-dose chemotherapy followed by autologous HSCT, with or without purging by means of T-cell depletion. However, long-term results of such treatment strategies were disappointing, with short-term disease relapses being the most frequently observed outcome.

By preventing tumour contamination of the graft and possibly providing the additional GVL effect, allogeneic HSCT may represent a more effective strategy of cure in this setting. However, a higher morbidity and mortality may offset the potential benefit of the procedure, especially when standard myeloablative conditioning (MAC) are employed. In this regard, because the majority of patients with CTCL are often elderly and with poor performance status, the introduction of RIC regimens allowed to expand the eligibility of such patients in experimental trials of allogeneic HSCT. In several phase II studies, RIC regimens have been demonstrated to significantly decrease TRM, allowing gradual establishment of full donor chimerism and possible GVL effect. So far, only few experiences of allogeneic HSCT in CTCL have been published, both with MAC and RIC regimens. With regard to this latter strategy, the largest series of patients has been treated at the University of Milan (Italy) between 09/2000 and 12/2007. In this trial, 13 patients with refractory stage III/IV MF (n=9) or SS (n=4) underwent allo-HSCT from a HLA-identical sibling following a conditioning regimen including fludarabine/cyclophosphamide/TBI200 or pentostatin/TBI200. Source of stem cells was peripheral blood in all patients. Clinical CR was obtained in 11 patients; 2 patients died of TRM. After a median follow-up of 43 months (range 2-99), 9 patients are alive and CR is sustained in 8 of them.

Although highly encouraging, further studies in larger patient populations are warranted to confirm the curative potential of this treatment strategy.