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Original Research

Comparable results of autologous and allogeneic haematopoietic stem cell transplantation for adults with Philadelphia-positive acute lymphoblastic leukaemia in first complete molecular remission: An analysis by the Acute Leukemia Working Party of the EBMT☆

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Abstract ***Background:*** Allogeneic haematopoietic stem cell transplantation (alloHSCT) is considered a standard treatment for patients with Philadelphia chromosome–positive acute lymphoblastic leukaemia (Ph+ ALL) achieving complete remission after induction containing tyrosine kinase inhibitors (TKIs).
Methods: We retrospectively compared results of myeloablative alloHSCT from either matched sibling donor (MSD) or unrelated donor (URD) with autologous (auto) HSCT for adults with Ph+ ALL in molecular remission, treated between 2007 and 2014.
Results: In univariate analysis, the incidence of relapse at 2 years was 47% after autoHSCT, 28% after MSD-HSCT and 19% after URD-HSCT ($P = 0.0002$). Respective rates of non-relapse mortality were 2%, 18%, and 22% ($P = 0.001$). The probabilities of leukaemia-free survival were 52%, 55% and 60% ($P = 0.69$), while overall survival rates were 70%, 70% and 69% ($P = 0.58$), respectively. In multivariate analysis, there was a trend towards increased risk of overall mortality after MSD-HSCT (hazard ratio [HR], 1.5, $P = 0.12$) and URD-HSCT (HR, 1.6, $P = 0.08$) when referred to autoHSCT. The use of total body irradiation (TBI)–based regimens was associated with reduced risk of relapse (HR, 0.65, $P = 0.02$) and overall mortality (HR, 0.67, $P = 0.01$).
Conclusion: In the era of TKIs, outcomes of myeloablative autoHSCT and alloHSCT for patients with Ph+ ALL in first molecular remission are comparable. Therefore, autoHSCT appears to be an attractive treatment option potentially allowing for circumvention of alloHSCT sequelae. Irrespective of the type of donor, TBI-based regimens should be considered the preferable type of conditioning for Ph+ ALL.

1. Introduction

The Philadelphia chromosome (Ph) translocation (9; 22) is the most common chromosomal abnormality seen in adult patients with acute lymphoblastic leukaemia (ALL), detected in 25–40% of cases [1,2]. Historically, Ph-positive ALL (Ph+ ALL) was considered a very high-risk subtype with inferior attainment of complete remission (CR) and subsequent high risk of relapse [3]. Hence, allogeneic haematopoietic stem cell transplantation (alloHSCT) was considered the standard of care for all eligible patients resulting in 30–35% of patients achieving long-term survival compared with only 10% of patients treated with chemotherapy exclusive approaches [4,5].

The outcome of patients with Ph+ ALL had substantially improved with the introduction of tyrosine kinase inhibitors (TKIs) [6,7]. The combination of imatinib with either steroids or multiagent chemotherapy has resulted in a 90–100% rate of CR [8–12]. Unfortunately, without alloHSCT most of these patients ultimately experience relapse [12]. The use of up-front second-generation TKIs such as dasatinib or nilotinib is associated with more rapid disease debulking and increased rate of molecular remissions [13,14]. Still, long-term disease control remains challenging, mainly because of the presence of BCR-ABL kinase domain mutations, in particular T315I [15]. The clinical horizon may change with the use of the third-generation TKI, ponatinib, which may overcome resistance to first- or second-generation TKIs [16]. It has been successfully used both as salvage therapy and upfront in combination with intensive chemotherapy [17]. Taken together, the role of front-line alloHSCT for patients with Ph-positive ALL, especially those achieving molecular CR becomes questionable, and therefore alternative, less toxic treatment options started to be considered [18,19].

In recent years, several study groups reported encouraging results of autologous (auto) HSCT for patients with Ph+ ALL [12,20,21]. According to a retrospective analysis by the Acute Leukemia Working Party (ALWP) of the European Society for Blood and Marrow Transplantation (EBMT), results of autoHSCT in this subgroup of patients improved substantially over time with a 52% leukaemia-free survival (LFS) rate reported at 3 years in the era of TKIs compared with 11% for historical controls [20]. Chalandon *et al.* reported comparable results after autoHSCT and alloHSCT for patients initially treated with imatinib in combination with chemotherapy [12]. Although a similar observation had been previously presented by Wetzler *et al.* [21], in both studies, the number of patients treated with autoHSCT was relatively small (n = 28 and n = 19, respectively). Furthermore, in the French trial, only patients with major or complete molecular response were candidates for autoHSCT which may have affected results of the comparative analysis [12].

The aim of the present study was to compare results of autoHSCT and alloHSCT in a large, registry-based, retrospective analysis. To reduce the risk of a pre-