Allogeneic stem cell transplantation effective after pathway inhibitor treatments in CLL.

Allogeneic Stem Cell Transplantation for Chronic Lymphocytic Leukemia after Multiple Pathway Inhibitors – an Analysis of the Chronic Malignancy Working Party of EBMT.

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Introduction

With the introduction of targeted therapies such as covalent BTK, BCL2 and PI3K inhibitors (here referred to as pathway inhibitors), the use of allogeneic stem cell transplantation (alloSCT) has significantly decraesed, though not entirely (Tournilhac et al., BMT 2022). A likely reason for the continued use of alloSCT is disease progression due to resistance or intolerance in the absence of available alternative options. Data on the efficacy of alloSCT in CLL patients previously exposed to multiple pathway inhibitors are limited but crucial for patient counseling. To address this, we analyzed the outcome of alloSCT in CLL patients in the era of pathway inhibitors, as recorded in the EBMT database.

Methods

We selected 127 CLL socalled 'double or triple exposed' patients from the EBMT database who underwent alloSCT between 2015 and 2020, excluding those with Richter's transformation. We further categorized these patients based on whether or not they had received prior CLL-specific chemotherapy. These groups were then subcategorized according to whether they had been treated with two or three types of pathway inhibitors, and subsequently to disease status (responsive or refractory) at the time of alloSCT. Kaplan-Meier curves were generated to assess progression-free survival (PFS) for each group.

Results

Of the 127 identified double or triple exposed CLL patients, 103 had received chemotherapy prior to pathway inhibitor treatment, while 24 had not. The 2-year PFS for patients with responsive disease

after two (n=74) or three (n=34) pathway inhibitors was 58%, regardless of prior chemotherapy. For patients pretreated with chemotherapy who had refractory disease after their second pathway inhibitor, the 2-year PFS was 42% (n=21). Five of the six patients with refractory disease after a third pathway inhibitor died within a few months following alloSCT. The number of chemotherapy-naive patients with either responsive disease to three pathway inhibitors or refractory disease after two or three pathway inhibitors was too small to draw any meaningful conclusions. Data on the cumulative incidence of non-relapse mortality, relapse, and TP53 abnormality status are currently being analyzed and will be presented at the conference.

Conclusion

The administration of two pathway inhibitors in CLL patients, regardless of prior chemotherapy, did not impact outcomes after alloSCT, as the 2-year PFS was comparable to results from the pre-pathway inhibitor era (Schetelig et al., Risk Factor Analysis for Treatment Failure after alloSCT in CLL, EBMT, BMT 2017, p. 552). This also holds true for chemotherapy-pretreated patients with responsive disease on a third pathway inhibitor before alloSCT. These results are better than with the non-covalent BTK-inhibitor pirtobrutinib in ‘double-exposed’ CLL patients (Zuber et al., Cancer Medicine 2024, e70258).