The prognostic significance of minimal residual disease monitoring by WT1 gene expression in peripheral blood before and after allogeneic transplantation in AML patients


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Background & Aims

The high risk AML patients may benefit from the allogeneic stem cell transplantation (allo-SCT) as a consolidation of complete remission (CR). In the absence of an universal marker for minimal residual disease (MRD), little information is still about the importance of MRD prior to allo-SCT. The aim was to confirm our previous experience with prognostic relevance of WT1- MRD status before allo-SCT in AML patients in CR. Another aspect was to assess the significance of WT1- MRD monitoring in these patients after allo-SCT.

Methods

The expression of WT1 gene was measured by real-time polymerase chain reaction in peripheral blood according the European Leukemia Net recommendations. Between 2005-2019, we have analyzed 147 consecutive AML pts with high WT1 expression at diagnosis, transplanted in CR1 or CR2. Median age was 46 years (range; 21-66), men 76, good risk 21, intermediate risk 91, high risk 35. A total of 116 pts were transplanted in CR1 and 31 pts in CR2. In 128 pts PBPC were used, in 19 pts bone marrow. The donors were identical siblings in 30 pts, 9 haploidentical, matched unrelated donors in 73 pts and mismatched UDs in 35 pts. Conditioning was myeloablative in 117 pts, RIC in 30 pts. At the time of allo-SCT 107 pts were WT1-negative (WT1< 50 copies) and 40 pts were WT1-positive.

RESULTS AND CONCLUSION

Median follow-up was 21 months. Estimated 5-years OS and EFS (Fig.1) was significantly better in WT1 neg cohort (65% and 57% vs 37% and 25% resp, p= 0.0003 and <0.0001), as well as 5-years RI was significantly lower in WT1 neg group (25% vs 60%, p<0.0001). 5-years NRM was not significantly different (24% and 27%). Multivariate analysis revealed WT1-MRD positivity and aGVHD grade 3-4 as a significantly negative prognostic factors for OS. Higher ELN risk groups, aGVHD grade 3-4 and WT1 positivity were negative predictors for EFS (Table 2). Overall 50 pts developed WT1-MRD positivity in post-transplant period, in forty cases the therapeutic intervention was performed. Haematological relapse occurred in 42 pts, in all relapsed patients where WT1-MRD was monitored (38 pts) we detected the positivity, in median of 28 days (0-485) before haematological relapse. 3-years OS in pts with molecular relapse only (12 pts) was 56% vs 74% in non-relapsed group (p=ns). (Table 3). The results of the analysis confirmed our previous experience that WT1 status before allo-SCT is a strong prognostic factor for both OS and relapse risk. WT1-positive patients should be considered for more intensive pre-transplantation therapy or earlier immunomodulatory intervention after allo-SCT (pre-emptive DLI).

Our experience suggests that this marker is also useful for monitoring MRD after allo-SCT. Well-defined clinical studies will be needed to assess the importance of therapeutic intervention based on WT1-MRD positivity.