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P352 PROPHYLACTIC AND PREEMPTIVE USE OF DLI COMPARE FAVOURABLY TO THEIR THERAPEUTIC USE IN ADULT ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) – RESULTS OF A MULTICENTRE RETROSPECTIVE STUDY

Topic: 2. Acute lymphoblastic leukemia - Clinical

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Background:

Relapsed ALL after allogeneic stem cell transplantation (SCT) is associated with a poor prognosis. The therapeutic use of donor lymphocyte infusion (DLI) upon clinical relapse is established, but its efficacy is limited. Preemptive (based on MRD positivity or mixed chimerism after SCT) and prophylactic (in MRD-negative pts with complete donor chimerism but high-risk of relapse) DLI may be more effective. However, comparative data on effectiveness and toxicity are lacking.

Aims:

The aim of the study was to evaluate the toxicity and efficacy of DLI with respect to the indication. Primary endpoints were overall survival (OS) and progression-free survival (PFS). The main secondary endpoints were response and incidences of acute (aGvHD) and chronic GvHD (cGvHD).

Methods:

Adult ALL pts undergoing SCT between 01/2005 – 12/2017 and subsequently receiving at least one DLI according to national registry data (Deutsches Register für Stammzelltransplantation, DRST) were included. Detailed evaluation on indication of DLI and toxicity was performed for those pts (indication subset) treated within prospective trials or registry of the German Multicentre Study Group for Adult ALL (GMALL) at participating centres by a pseudonymised CRF. Study was supported by AMGEN.

Results:

For the total cohort 243 pts were identified. Median age at SCT was 33 years, 152 (63%) pts were male and in 180 (74%) B-ALL was diagnosed. BCR-ABL positivity was seen in 50 (21%) pts. SCT was performed in first complete remission (CR) in 173 (71%) pts. Myeloablative conditioning was applied in 221 (91%) pts and immunosuppressive therapy after SCT was calcineurin based in 213 (88%) pts. Application of antithymocyte globulin (ATG) was

reported in 120 (49%) pts. Indication for DLI was high-risk disease in 92 (38%), relapsed ALL in 45 (19%), and molecular failure in 14 (6%) pts. Median number of DLI given was 1 (range 1-9). Median OS and PFS after SCT were 33.1 and 24.8 months and incidences of aGvHD III-IV and extensive cGvHD were 14% and 13% respectively.

Disease, patient and SCT characteristics for the indication-subgroups were similar. As expected, a combination of ALL directed drug treatment and DLI was reported in 21 (33%) and 10 (15%) pts with therapeutic and preemptive DLI respectively. For the prophylactic, preemptive and therapeutic subgroup median number of DLI given was 3 (range 1-4), 2 (1-7), and 2 (1-9) and incidence of aGvHD III-IV° after DLI was 5%, 14% and 13% in the respective groups. Extensive cGVHD was lower after therapeutic DLI with 8% compared to 22% in preemptive use. Response after therapeutic DLI was seen in 44%. In the preemptive setting 25% became MRD negative after DLI. Median DLI-number and dose was equal in responding and non-responding pts. A clear difference in OS (Fig. 1) and PFS was observed for the different indications: median OS and PFS was not reached in the prophylactic-DLI group and was 44.9 and 17.4 months respectively in the preemptive-DLI and 18.1 and 14.4 months in the therapeutic-DLI group. In multivariate analysis, lack of complete remission before SCT, therapeutic indication for DLI but also lack of chronic GVHD after DLI were independent negative predictors of shorter OS and PFS.

Summary/Conclusion:

Our data indicate that the use of DLI in ALL is established. However, a prophylactic or pre-emptive application may be more effective than therapeutic DLI without inferring an increased risk of toxicity. The therapeutic use of DLIs only leads to dismal results and should be considered cautiously, especially in light of new therapeutic options (e.g. CART).

Figure 1: OS from first DLI according to subgroups of indication for DLI (n=147)