THE IMPACT OF NGS-BASED MINIMAL RESIDUAL DISEASE LEVEL ON CLINICAL OUTCOME IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Introduction: Accurate evaluation of MRD is the most informative tool for treatment decisions in childhood ALL. Using next generation sequencing we studied if extent of MRD, not only its qualitative assessment, would have impact on clinical outcome.

Material and methods: Overall, 50 patients (43 with B-ALL, 7 with T-ALL) were analysed. Patient-specific gene rearrangements in IGH-FR3/TCRG regions were detected at diagnosis and tracked at two timepoints from therapy onset: end of induction (EOI, d33) and before consolidation (d78). DNA was extracted from bone marrow mononuclear cells. The median follow-up was 39 months.

Results: Based on the MRD level, we divided the patients in three groups: MRD<1E-4, 1E-3≥MRD≥1E-4 and MRD>1E-3. Only 40% of the patients showed early MRD clearance at EOI with MRD level <1E-4 or not detectable (ND). This percent nearly doubled before consolidation (78% had ND MRD). Conversely, 60% of the patients had MRD≥1E-4 on d33, whereas 22% remained MRD positive at d78. High MRD level >1E-3 was observed in 34% of the patients (17/50) on d33 and 5 out of 6 relapses occurred in patients from this group. None of the patients with MRD<1E-4 or ND on d33 relapsed. All relapses occurred regardless of the MRD level on d78: one patient had MRD>1E-3, two patients 1E-3≥MRD≥1E-4 and three had MRD<1E-4 or ND.

Conclusions: High MRD level >1E-3 on d33 is associated with increased relapse risk and should be assigned for treatment intensification. Moreover, for patients with MRD<1E-4 on d33, treatment deintensification should be considered. However, standardisation of this method is needed for routine clinical application.