XIX CONGRESSO NAZIONALE SIES2026
Firenze | 4-6 marzo 2026
Palazzo degli Affari

XIX Congress of the Italian Society of Experimental Hematology ABSTRACT N. P061

Acute Leukemias

CLINICAL OUTCOMES OF YOUNGER ADULT PATIENTS WITH PHILADELPHIA-NEGATIVE ACUTE LYMPHOBLASTIC LEUKEMIA, TREATED IN THE REAL-LIFE WITH A PEDIATRIC-LIKE REGIMEN BASED ON GIMEMA LAL1308 PROTOCOL: AN OBSERVATIONAL RETROSPECTIVE CAMPUS ALL STUDY

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There is currently no definitive evidence that adolescents and young adults (AYA) with Philadelphia-negative acute lymphoblastic leukemia (Ph- ALL) have poorer survival outcomes when receiving modern pediatric-inspired regimens (PIRs) compared with unmodified pediatric protocols. Moreover, major issues related to the application of full pediatric strategies to patients (pts) aged 18-40 years are the compliance to treatment and drug-related toxicity.

We retrospectively recorded clinical data of 36 younger pts (median age 21 years, range 18-38) affected with Ph- ALL (28) or lymphoblastic lymphoma (LL) (8), who received a treatment inspired by the GIMEMA LAL1308 pediatric protocol (Testi et al, Am J Hematol 2021) in a multicenter real-life setting, across Italian centers partecipating to the Campus ALL network between 2014 and 2023, mainly investigating feasibility and efficacy of this intensive chemotherapeutic program.

B- and T-cell immunophenotypes were observed in 23 (63.9%) and 13 (36.1%) ALL/LL cases, respectively. According to GIMEMA prognostic risk stratification based on laboratory and genetic features at diagnosis, 15 (53.6%), 6 (21.4%) and 7 (25%) ALL pts were classified as standard, high or very high risk, respectively. CNS localization at onset was detected in only 2 (5.6%) cases. Following induction course Ia, a morphologic CR was achieved in 24/28 (85.7%) ALL cases, while either a morphologic or radiologic/metabolic CR was eventually documented in 31/36 (86.1%) globally considered ALL/LL pts after phase Ib. Measurable residual disease (MRD) negativity by either molecular or flow-cytometry assays was reached in 17/23 (73.9%) evaluable ALL pts at the prognostic timepoint at the end of Ib induction cycle (TP2). Seven of 25 (28%) ALL pts in CR subsequently experienced either a morphologic or a MRD relapse, with 7 pts receiving blinatumomab, with or without previous salvage chemotherapy. Consolidation/maintenance approaches followed risk-adapted indications without dose-limiting complications, with 20 (55.6%) ALL/LL pts collectively receiving an allogeneic HSCT, due to either adverse prognostic factors, resistance to induction courses, morphologic relapse or MRD positivity at TP2 or subsequent determinations. At a median follow-up of 49 months (IQR 23-77), the median OS and DFS for the entire cohort were not reached, with 5-year OS and DFS of 76.4% and 69.1%, respectively. No significant differences in outcomes were recorded according to the ALL/LL diagnosis, B/T lineage, risk at diagnosis or, surprisingly, MRD status at TP2, probably due to the limited sample size or to optimal risk-adapted and MRD-driven intensification strategies, including prompt allocation to allogeneic HSCT. Unmodified pediatric regimens may be safely administered to AYA ALL pts in a real-life setting, with results that compare favorably to those of the LAL1308 trial or other intensive PIRs not yet incorporating modern frontline immunotherapeutic approaches.