Abstract: P381

Title: FULL PEDIATRIC INDUCTION IN ADULTS AGED UP TO 55 YEARS WITH PHILADELPHIA-NEGATIVE ACUTE LYMPHOBLASTIC LEUKEMIA IS WELL TOLERATED AND RESULTS IN VERY HIGH CURE RATE

Abstract Type: Poster Presentation

Session Title: Acute lymphoblastic leukemia - Clinical

Background:

Historically, treatment of acute lymphoblastic leukemia (ALL) in adults showed unsatisfactory outcomes, if compared to the outstanding results obtained in pediatric patients. Pediatric protocols rely on increased drug intensity, and on a tighter evaluation of minimal residual disease (MRD) for early intensification. Nowadays, pediatric-inspired protocols have been established as the standard of care for adolescents and young adult patients (AYA), leading to improved results, but the feasibility of such intensive therapies and in particular of high doses PEG-asparaginase (PEGASP) administration for older patients is still matter of debate.

Recently, the NOPHO group reported that a full-pediatric protocol was feasible and highly effective in younger adults patients, up to 45 years.

Aims:

The aim of our study was to evaluate the feasibility and efficacy of the entire full pediatric AIEOP-BFM LAL 2009 protocol in an older cohort of adult patients up to 55 years.

Methods:

Since May 2013, 28 consecutive adults diagnosed with Ph-neg ALL received first line therapy according to AIEOP-BFM-ALL 2009 protocol, which includes high PEG-asparaginase (PEGASP) doses.

Median age in our study was 45 years (range 17-55), equal to the maximum age allowed in the NOPHO study.

Fifteen patients had B-ALL, 13 T-ALL/T including 5 Early-T phenotype. Dose intensification and stem cell transplantation (SCT) were scheduled according to baseline and MRD-driven risk assessment. MRD was evaluated by multicolor-flow cytometry (MFC), with a threshold for positivity of 0.025%, and molecular PCR for JH rearrangement (MOL), with a sensitivity greater or equal to 10^{-4} in all patients. Patients with MOL MRD $>10^{-4}$ but $<10^{-3}$ were defined as low level positive. MRD time points were day 33 and day 78 (MFC and MOL).

Results:

All patients achieved complete hematological remission after first Induction course (100%). One patient died during induction due to infection by multidrug resistant P. *aeruginosa*.

In general, therapy was well tolerated. Remarkably, patients in this study received high dose of PEGASP (median 10000 UI/sqm, equal to 4 administrations at 2500 UI/sqm each) without experimenting life threatening toxicities, which mostly consisted in asymptomatic elevation of transaminase (7 patients G3, 1 G4) and/or bilirubin (9 patients G3, 1 G4) only requiring supportive therapy. No major bleeding or thrombotic events o other >G2 toxicities were observed.

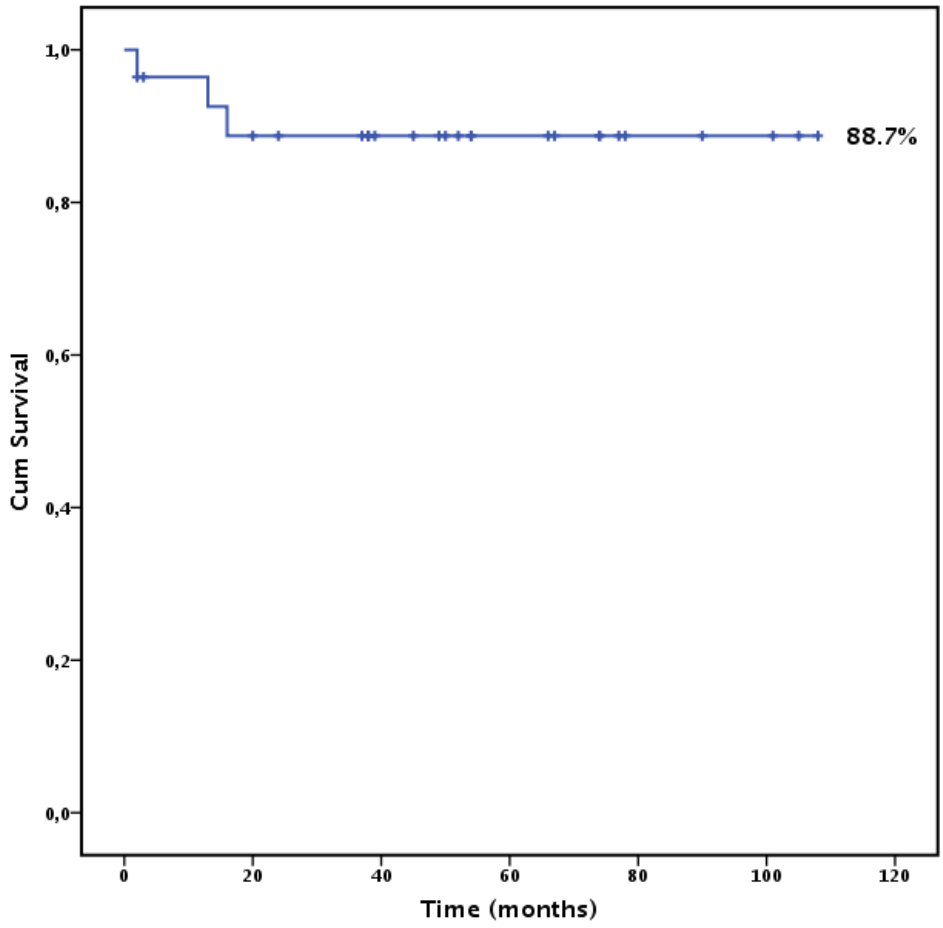
All but 1 patient achieved CR at day 33 and all patients achieved CR at day 78. MFC MRD evaluation at day 33 resulted negative in 24/25 evaluable patients (95%). Day 33 MOL-MRD was evaluated in 22 patients, and resulted negative, low level positive or positive in 14, 5 and 3 patients, respectively. MRD assessment at day 78 showed both MFC and MOL negativity achieved in all 25 and 22 evaluated patients, respectively. Four very high-risk patients underwent SCT in negative MRD status.

After a median follow up of 54 months (CI 95% 33.85-74.15), median survival was not reached, 5-years OS was 88.7%. One patient died due to progressive transverse myelitis after isolated CNS relapse and 1 patient died due to sudden cardiac arrest while in complete MRD negative remission, 6 months after completion of therapy. All other 25 patients are alive and in complete MRD negative remission.

Summary/Conclusion:

The application of a full pediatric induction regimen in a cohort of adult ALL patients with a median age of 45 years proved to be feasible, with mild toxicities. Specifically, we didn't observe major toxicities during the intensified PEGASP administration, and all patients were able to receive the planned PEGASP doses. This translated in very high MRD negativity rate and promising OS survival.

Fig. 1 Overall Survival in all patients



Keywords: ALL, Minimal residual disease (MRD), Pediatric, Adult