Abstract: S112

Title: BLINATUMOMAB AS CONSOLIDATION IN A PAEDIATRIC PROTOCOL LEADS TO HIGH RATES OF END-CONSOLIDATION MRD NEGATIVITY AND EXCELLENT OUTCOMES IN AYA ALL – FINAL RESULTS OF THE ALLG ALL09 "SUBLIME" STUDY

Abstract Type: Oral Presentation

Session Title: Acute lymphoblastic leukemia - Clinical 1: Immunotherapy: antibodies and CAR-T cells

Background:

Paediatric inspired regimens have improved outcomes in AYA ALL, but results remain inferior versus children due to poorer treatment tolerance and the unique biology of AYA ALL. Our previous ALL06 study demonstrated that a BFM based protocol could be administered to pts aged 15-39 years, in a similar timeframe to children with estimated 3 yr DFS 72.8% and 3 yr OS 74.9%. In ALL06, only day 79 (end-consolidation) MRD and BMI ≥30kg/m2 were associated with DFS and OS. Blinatumomab, a bispecific T cell engager, is effective in relapsed/refractory and MRD-positive CD19+ pre-B ALL. In this phase II study, Australasian Lymphoma and Leukaemia Group (ALLG) ALL09 "SUBLIME", cytotoxic therapy in consolidation and reconsolidation was replaced with blinatumomab to improve end-consolidation (day 79) MRD response and outcomes in AYA ALL. Herein we report the final results from ALL09.

Aims:

The primary objective of ALL09 was to determine whether substituting blinatumomab for standard consolidation in the ALL06 protocol leads to improved day 79 MRDneg rates compared to the ALL06 cohort.

Methods:

De novo CD19+ Ph-negative ALL pts aged 15-39 years were eligible. ALL09 replaced standard cyclophosphamide, cytarabine and 6MP with 1 x 28 day cycles of blinatumomab in consolidation and reconsolidation but was similar to ALL06 in all other phases of therapy. MRD using RQ-PCR (sensitivity ≥10-4) at day 33 and day 79 of protocol I was reported using EuroMRD criteria. Stratification to high-risk therapy was based on diagnostic and treatment response criteria prior to allogeneic transplant (SCT) if a suitable donor was available or remaining on protocol if no donor. Genomic studies were performed but did not alter treatment intervention. Adverse (AR) vs standard (SR) genomic risk was based on contemporary classifiers. The primary objective was tested using a Simon's 2-stage design on a modified intention to treat (mITT) population consisting of all ITT patients who 1. commenced blinatumomab at day 36 and 2. had informative MRD at day 79.

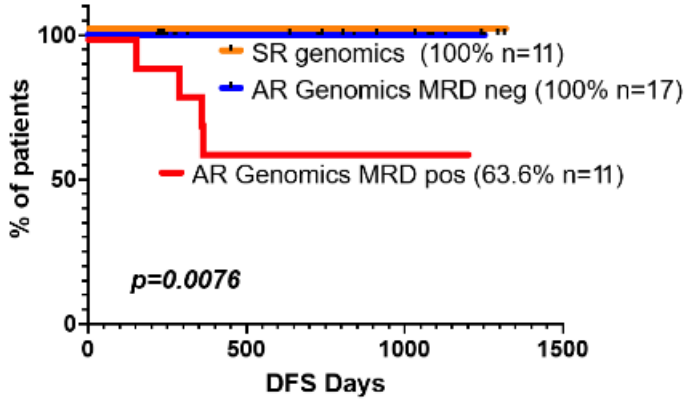
Results:

55 pts were enrolled from 04/19 to 04/22 with median follow up 739 (638-932) days. Median age was 25 (16-39) yrs. 54.5% were male. At presentation, WCC was <100 x 109/L in 91%, 7.3% had evidence of extramedullary disease with CNS disease in 5.5%. N=4 had t(4;11). Morphological CR was achieved in 100% of n=52 pts evaluable at day 79. Median time to protocol M/HR1 was 84 (77-134) days with 82.7% commencing by day 94 in ALL09 vs 96 (78-139) days and 45% in ALL06 (HR 2.19 [95%CI:1.47-3.27], p<0.001 and p<0.001 respectively]. Genomic results were available in 45 pts (39/45 with an MRD marker) - 73% were AR. There have been 5 relapses and 4 deaths (n=1 treatment related) with 2 yr DFS 86.2% (95%CI,71.5-93.6) and OS 90% (95%CI,75-96) in the ITT cohort. 34.6% proceeded to HR therapy with n=11 proceeding to SCT. The mITT cohort constituted 48 pts at day 79. Day 79 MRDneg improved from 60% in ALL06 to 70.8% in the ALL09 mITT cohort (p=0.025). 2yr DFS and OS was 100% in the day 79 MRDneg cohort. 5/5 relapses came from the AR cohort, including 3/3 *TCF3*r pts 1/5 hypodiploid and 1/7 *PAX5*alt (Fig 1).

Summary/Conclusion:

Substituting blinatumomab in consolidation of a BFM based protocol was associated with a significantly higher rate of day 79 MRDneg remission and more rapid progression to next protocol phase than our previous ALL06 protocol together with excellent 2 yr DFS and OS with no events recorded to date in the day 79 MRDneg cohort. We plan to take this platform forward in a larger study while introducing novel therapies in HR blocks to improve MRDneg rates in those already exposed to blinatumomab prior to SCT.

Fig 1.



Keywords: Acute lymphoblastic leukemia, Clinical trial, Young adult, Adolescents