S115 CONSOLIDATION WITH BLINATUMOMAB IMPROVES OVERALL AND RELAPSE-FREE SURVIVAL IN PATIENTS WITH NEWLY DIAGNOSED B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA: IMPACT OF AGE AND MRD LEVEL IN ECOG-ACRIN E1910

**Topic:** Clinical updates in ALL

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**Background:**

Patients (pts) with newly diagnosed acute lymphoblastic leukemia (ALL) often relapse even with achieving complete remission (CR) and minimal residual disease (MRD) negative (MRD-) status after chemotherapy (chemo). Blinatumomab (blin) is a bi-specific T cell engager molecule approved for relapsed/refractory ALL pts and pts MRD positive (MRD+) (>0.1%) in 1st or 2nd CR. E1910 was a phase III trial randomizing pts age 30-70 yrs to chemo +/- blin to test whether blin improves outcomes in BCR:ABL-negative B-ALL. The study showed that in pts who were MRD- after induction, there was a significant improvement in overall survival (OS) in favor of the blin arm. These subgroup analyses describe outcomes in pts based on age (< or > 55 yr) and depth of MRD (undetectable vs between undetectable-0.01%).

**Aims:**

Primary objective compared OS in MRD- pts who received chemo +/- blin. Subgroup analyses look at outcomes based on age <55 or >=55 yrs, which was a pre-specified stratification factor. Additional subgroup analyses look at depth of MRD below 0.01%, which was not a pre-specified stratification factor.

**Methods:**

Pts received 2.5 mo of combination chemo using a BFM-like regimen adapted from the E2993/UKALLXII clinical trial with extended remission induction, addition of pegaspargase for pts <55 yr of age and addition of rituximab.
for CD20+ pts. Details regarding remission induction (step 1), high dose methotrexate with pegaspargase for CNS prophylaxis (step 2), blin randomization (step 3), and maintenance (step 4) or hematopoietic cell transplant (HCT) were presented previously at ASH 2022. MRD status was determined centrally by 6-color flow cytometry with level of sensitivity of 0.01%. MRD- was defined as <0.01%. With a minimum of 190 MRD- pts, the study had an 80% power to detect a 45% reduction in hazard rate in the blin arm relative to the control chemo arm, using one-sided log rank test at significance level of 0.025 and assuming 2 yrs of follow-up. Estimates of OS were calculated using the Kaplan-Meier method. Comparison of OS between treatment arms was conducted using age, CD20 status, rituximab use, and whether pts were intended to receive HCT or not as stratification factors.

**Results:**

772 pts were screened and 488 were enrolled. Median age was 51 yr. 224 MRD- pts were randomized, 112 pts to each arm. 22 pts in each arm proceeded to allogeneic HCT. The CR/CRi rate after induction was 81%. Among MRD- pts, OS significantly favored the blin arm (median OS: not reached vs. 71.4 mo; Hazard ratio (HR) 0.42, 95% CI: 0.24 - 0.75; two-sided p=0.003).

The RFS in MRD- pts (n=224) favored the blin arm (median RFS: not reached vs. 71.4 mo; HR 0.46, 95% CI: .027-0.78; p=0.004). In MRD+ pts (N=62), the OS for blin vs control arm was (median OS not reached vs vs 22.4 months; HR 0.39, 95% CI: 0.14-1.10; p=0.066).

In MRD- pts < 55 yr (n=132), OS favored the blin arm (median OS not reached vs not reached; HR 0.18, 95% CI: 0.06-0.52; p <0.001). In MRD- pts >55 yr (n=92), the OS for blin vs control arm was (median OS not reached vs. 71.4 mo; HR 0.77, 95% CI: 0.37-1.58; p=0.47).

In pts with undetectable MRD (n=187) at randomization, OS favored the blin arm (median OS not reached vs not reached; HR 0.51, 95% CI: 0.27-0.97; p=0.038). In pts with MRD between undetectable and 0.01% (n=37), the OS for blin vs control arm was (median OS not reached vs. 38.0 mo; HR 0.35, 95% CI 0.06-1.94; p=0.16).

**Summary/Conclusion:**

Adding blin to chemo improves OS and RFS in pts MRD- at randomization. The effect of blin was particularly evident in pts < 55 yr and in patients with undetectable MRD.