Assessment of Outcomes of Consolidation Therapy by Number of Cycles of Blinatumomab Received in Newly Diagnosed Measurable Residual Disease Negative Patients with B-lineage Acute Lymphoblastic Leukemia: in the ECOG-ACRIN E1910 Randomized Phase III National Clinical Trials Network Trial

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INTRODUCTION

ECOG ACRIN E1910 is a randomized phase III trial that showed adult patients (pts) with newly diagnosed BCR::ABL1 negative acute lymphoblastic leukemia (ALL) who become MRD negative (<0.01%) after induction chemo who receive blinatumomab with conventional chemotherapy have improved survival compared with those who received conventional chemo only.

However, not all pts were able to receive all four planned cycles of blinatumomab in consolidation. In this report we assessed outcomes of pts in the blinatumomab arm of the trial who received all 4 cycles of blinatumomab compared to those who received 1-2 cycles or 2 cycles only.

METHODS

Patients 30–70 years of age with newly diagnosed *BCR::ABL1* negative B-lineage ALL were enrolled and initially received 2.5 months of combination induction chemo utilizing a BFM-like regimen adapted from the E2993/UKALLXII clinical trial with extended remission induction, addition of pegaspargase for pts <55 years of age and addition of rituximab for CD20 positive patients.

After remission induction (step 1) pts in morphologic complete remission (CR/CRi) received high dose methotrexate intensification with pegaspargase for CNS prophylaxis (step 2).

METHODS

At the conclusion of step 2, remission and MRD status were determined centrally by 6-color flow cytometry with MRD negativity defined as <0.01%.

In the primary analysis subset, MRD negative pts were randomized to receive an additional 4 cycles of consolidation chemo or 2 cycles of blinatumomab at 28 mcg/day for 28 days each cycle followed by 3 cycles of consolidation chemo, a 3rd 4-week cycle of blinatumomab followed by an additional cycle of chemo and then a 4th cycle of blinatumomab (step 3).

Following completion of step 3, pts were given 2.5 years of POMP maintenance therapy timed from the start of the intensification cycle (step 4).

OS was calculated using the Kaplan-Meier method.

Landmark analysis was used to compare OS of pts in the blinatumomab arm who received all 4 cycles of blinatumomab to those who received 1-2 cycles or 2 cycles only.

Time 0 was chosen as 9 months post step 3 randomization (the time that pts were supposed to complete 4 cycles of blinatumomab). Four pts who received blinatumomab but died within 9 months post step 3 randomization were therefore excluded from this analysis.

RESULTS

Study Activation: Dec 2013 / Study Termination: Oct 2019

772 pts were screened, 488 were enrolled; Median age 51 years

CR/CRi rate after induction was 81%

224 MRD-negative pts were randomized, 112 in each arm

In the blinatumomab arm, 12 pts received 1 cycle (11%), 32 pts received 2 cycles (29%), 4 pts received 3 cycles (4%) and 63 pts received 4 cycles (57%) of blinatumomab.

The OS of pts who received 1-2 cycles of blinatumomab compared to control (Figure 1) was not significantly different (hazard ratio 0.62, 95% CI 0.28 to 1.34, p=0.22).

Fig 2 compares the survival of those who received 1-2 cycles to those who received 4 cycles (HR: 0.39, 95% CI 0.12 to 1.16, p=0.076).

Figure 1

1 - 2 Cycles Vs. Control

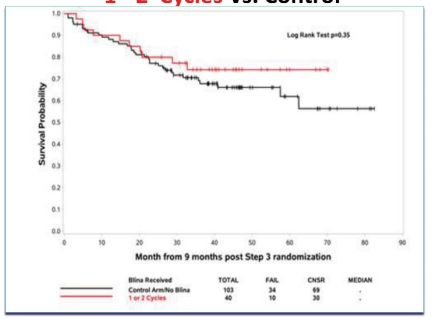
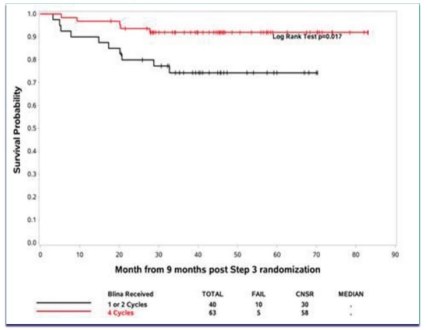


Figure 2

4 Cycles Vs. 1 – 2 Cycles



Landmark analysis was used, where time 0 is 9 months post step 3 randomization (the time that patients were supposed to complete 4 cycles of blinatumomab).

CONCLUSIONS

The addition of blinatumomab to consolidation chemo resulted in a significantly better overall survival in pts with diagnosed B-lineage ALL who were MRD negative after intensification chemo.

The optimal dose and number of cycles is however unknown.

In this unplanned subgroup analysis, we demonstrate that a survival benefit can only be confirmed in patients who receive the intended 4 cycles of blinatumomab during consolidation.

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REFERENCES

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