Abstract: S119

Title: COMBINATION OF MINI-HYPER-CVD AND INOTUZUMAB (INO) FOLLOWED BY BLINATUMOMAB (BLINA) CONSOLIDATION IN PATIENTS WITH RELAPSED/REFRACTORY (R/R) ACUTE LYMPHOBLASTIC LEUKEMIA (ALL): A PHASE II TRIAL

Abstract Type: Oral Presentation

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Background:

The prognosis of patients (pts) with R/R ALL is poor. InO and blina as single agents improved the outcomes of pts with R/R disease. Encouraging results were seen with the combination of low intensity mini-Hyper-CVD (mini-HCVD) chemotherapy and InO in this setting. The addition of blina may further improve outcomes.

Aims:

The aim of this study is to assess the safety and efficacy of mini-HCVD in combination with InO, with or without blina, in R/R ALL.

Methods:

Pts with R/R Philadelphia chromosome-negative B-ALL were eligible. Odd cycles of mini-HCVD (Cycles 1, 3, 5, 7) consisted of cyclophosphamide (150 mg/m^2 every 12 h on Days(D) 1-3), vincristine (2 mg flat dose on D1 and 8), and dexamethasone (20 mg on D1-4 and D11-14) without anthracyclines. Even cycles (Cycles 2, 4, 6, 8) consisted of cytarabine (0.5 g/m^2 given every 12 h on D2 and 3) and methotrexate (250 mg/m^2 on Day1). During the first 4 courses, rituximab was given for CD20+ as intrathecal chemotherapy. Initially, InO was administered on D3 of the first 4 cycles at the dose of 1.3-1.8 mg/m^2 in Cycle 1, followed by 1.0-1.3 mg/m^2 in subsequent cycles. Pts received maintenance therapy with POMP, consisting of 1 year (yr) of monthly prednisone 50 mg/d for 5 days and vincristine at 2 mg every month, along with 3 yrs of 6-mercaptopurine 50 mg twice daily and weekly oral methotrexate 10 mg/m^2. An amendment to the protocol was made after the inclusion of 67 pts to add 4 cycles of blina after 4 cycles of the combination mini-HCVD + InO. InO was given on D2 and 8 at the dose of 0.6 and 0.3 mg/m^2 in Cycle 1, respectively, followed by D2 and 8 at the dose of 0.3 and 0.3 mg/m^2 in subsequent cycles; blina was continuously infused over 28 days every 42-day cycle for 4 cycles. Maintenance therapy was reduced to 12 cycles of POMP with 1 cycle of blina after each 3 cycles of POMP for a total of 4 cycles. The decision to undergo ASCT was based on the discretion of the treating physician after discussion with the patient.

Results:

Between 2/2013 and 7/2021, 110 pts were treated. Patient characteristics are shown in **Figure 1**. 79 (72%) pts were treated in Salvage (S) 1, and 31 (28%) in S2+. 21 (19%) pts had received prior ASCT. 91 (83%) pts responded (complete remission, 63%). The overall response rate was 93% in S1, 59% in S2, and 57% in S3+. The rates of MRD negativity by flow were higher in S1 vs S2+ (89% vs 67%; P=0.047). 53 (48%) pts underwent ASCT.

After a median follow-up of 48 months (mo) (range, 9-115), the median OS and RFS were 17 mo (4-yr, 36%) and 13 mo (4-yr, 37%), respectively. Pts in S1 had better OS compared with S2+ (4-yr OS, 43% vs 18%; P<0.001). The 4-yr RFS was 38% in S1 and 27% in S2+ (P=0.14). In S1, 41 pts were treated before the amendment and 38 after the amendment; their 4-yr OS was 41% and 48% (P=0.99), and their 4-yr RFS was 39% and 36%, respectively (P=0.95).

A landmark analysis of pts who achieved remission showed no survival difference between pts who did or did not undergo ASCT, with 4-yr OS of 49% and 48% (P=0.98), and 4-yr RFS of 46% and 37% (P=0.68), respectively. Sinusoidal obstruction syndrome (SOS) was noted in 10 (9%) pts, and its incidence decreased from 13% with

single dose of InO to 2% with lower and fractionated doses of InO (*P*=0.056).

Summary/Conclusion:

The outcome of pts with R/R ALL improved with the combination of mini-HCVD and reduced-dose InO with the sequential addition of blina. These variations of the treatment schedule reduced the incidence of SOS compared with the original design.

Patient characteristics

Characteristic Median [range] / N (%)	**Category**	**Pre Amendment N=67**	**Post Amendment N=43**
Age (yrs)		34 [17-87]	42 [18-79]
Status	S1 S1, Primary Refractory S1, CRD1 < 12m S1, CRD1 ≥ 12m S2 ≥ S3	38 (57) 5 17 16 29 (43)	42 (93) 10 9 23 3 (7)
Prior ASCT		19 (28)	2 (5)
Karyotype	Diploid KMT2Ar Misc IM/ND	14 (21) 8 (12) 35 (52) 10 (15)	14 (33) 2 (5) 23 (51) 6 (14)
SOS		9 (13)	1 (2)

Keywords: Relapsed acute lymphoblastic leukemia, Survival, Acute lymphoblastic leukemia, Phase II