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POSTER ABSTRACTS

723.ALLOGENEIC TRANSPLANTATION: LONG-TERM FOLLOW-UP AND DISEASE RECURRENCE

A Phase IB/II Study of Blinatumomab in Patients with B-Cell Acute Lymphoblastic Leukemia (ALL) and B-Cell Non-Hodgkin Lymphoma (NHL) As Post-Allogeneic Blood or Marrow Transplant (alloBMT) Remission Maintenance

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Background: AlloBMT can be curative as consolidation for high risk B ALL and NHL. However, transplant-related toxicity and disease relapse limit survival. Post-transplantation cyclophosphamide (PTCy) as graft-versus-host disease (GVHD) prophylaxis limits GVHD and facilitates alternative allograft sources. Following PTCy, cellular immune reconstitution is favorable for strategies to augment anti-tumor immunity. Blinatumomab (blina) is effective in the treatment of CD19+ ALL and NHL. Blina leads to T cell activation that may enhance post-transplant tumor-specific T cell responses, leading to a more potent graft-versus-tumor effect. A study of 21 B ALL pts demonstrated the feasibility of post-transplant blina but did not improve survival when pts universally remained on immunosuppression for at least 1 cycle of treatment (Gaballa. Blood. 2022). We present results of a phase Ib/II trial to assess the tolerability and preliminary efficacy of blina as post-alloBMT remission maintenance in B-cell ALL and NHL in pts off immunosuppression.
Methods: Pts ≥1 month-old with high risk CD19+ B ALL or ≥18 years-old with NHL who underwent alloBMT with PTCy were eligible. Pts had to be 60-180 days post-transplant with count recovery and in remission. Pts had to be off immunosuppression for ≥4 weeks prior to treatment, and without a history of grade ≥3 acute GVHD or severe chronic GVHD. Pts could receive 2 cycles of blina if they had evidence of disease (including MRD) at their pre- and/or post-transplant evaluations but otherwise received 1 cycle. Blina was given as a continuous infusion at 9 mcg/day on C1D1-7 and 28 mcg/day on C1D8-28 and C2D1-28.
Results: The study closed to accrual on January 31, 2023 following enrollment of 42 pts (26 male/16 female) with a median age of 54 (Range 30-73). Among enrolled pts, 19 had Ph-negative B ALL and 23 had B-cell NHL. All pts underwent reduced-intensity conditioning alloBMT using a regimen of fludarabine, cyclophosphamide, and total body irradiation. Median prior lines of therapy were 2 (range 1-6). Additional transplant details are presented in Table 1. All B ALL pts were in an MRD-negative CR by flow cytometry at a sensitivity of 0.01% at alloBMT. All pts received a single cycle of therapy. Pts started blina a median of 137 days post-transplant (range, 90-182). Four pts failed to complete a full cycle due to G4 transaminitis (1), G4 neutropenia (1), relapse (1), and patient preference in the setting of tremors (1). Grade 3 or 4 adverse events felt to be at least possibly related to the study drug included G3 neutropenia (7%), G4 neutropenia (19%), anemia (5%), G3 ALT (5%), G4 AST (2%), G3 AST (2%), and neurotoxicity (7%). Two pts (5%) developed chronic GVHD following blina requiring the resumption of immunosuppression. At a median follow-up of 40 months post-alloBMT, the 3-year relapse-free survival is 73% (95% CI 54-85%) due to a 24% (95% CI 12-39%) incidence of relapse and a 4% (95% CI 0-17%) incidence of non-relapse mortality, as shown in Figure 2. All 3 (100%) relapsed B ALL pts and 2/6 (33%) relapsed B NHL pts presented with CNS involvement. Four pts with CNS relapse (80%) had CNS involvement prior to alloBMT. Among 2 pts who died without relapse, 1 was unrelated to alloBMT,

while the other died of therapy-related myeloid neoplasm. Data on biomarkers including changes in T cell subpopulations in both BM and PB, and co-signaling molecule expression will be presented.
Conclusions: Post-alloBMT maintenance therapy with blina is feasible with minimal toxicity in pts off immunosuppression. Initial survival outcomes are promising with the majority of relapses involving the CNS. A randomized trial of maintenance with blina after alloBMT with PTCy is needed to confirm efficacy in this high-risk population.

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OffLabel Disclosure: Blinatumomab as post-alloBMT maintenance for patients in remission

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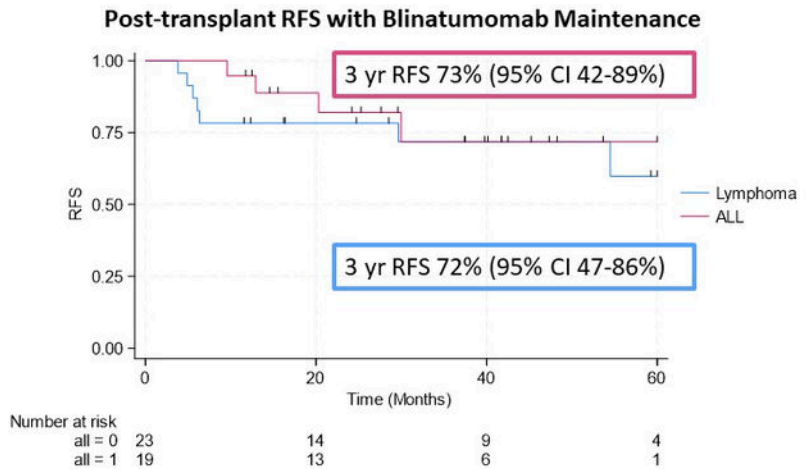
Table 1

Demographic	# of Patients (%) N=42 Total
Median Age at Transplant (Range)	54 (30-73)
Female Gender	16 (38%)
Diagnosis	
Ph-negative B ALL	**19 (45%)**
B Cell Lymphoma	**23 (55%)**
DLBCL	8 (19%)
Transformed DLBCL	7 (17%)
Mantle Cell Lymphoma (MCL)	6 (14%)
PCNSL	1 (2%)
Follicular Lymphoma	1 (2%)
Donor Type	
Haploidentical	30 (71%)
Matched Unrelated Donor	8 (19%)
Matched Related Donor	2 (5%)
Mismatched Unrelated Donor	2 (5%)
Graft Source	
Bone Marrow	24 (57%)
PBSCT	18 (42%)
Median Time from Transplant to Blina Start (Range)	137 Days (90-182)

Figure 1



Patients	3-yr OS (95% CI)	3-yr RFS (95% CI)	3-yr CIR (95% CI)	3-yr NRM (95% CI)
B ALL + NHL	**85% (67-94%)**	**73% (54-85%)**	**24% (12-39%)**	**4% (0-17%)**
B ALL	**78% (46-93%)**	**73% (42-89%)**	**18% (4-39%)**	**10% (0-36%)**
NHL	**90% (67-98%)**	**72% (47-86%)**	**28% (11-48%)**	**-**

Figure 1