



## The 65th ASH Annual Meeting Abstracts

## ORAL ABSTRACTS

**614.ACUTE LYMPHOBLASTIC LEUKEMIAS: THERAPIES, EXCLUDING TRANSPLANTATION AND CELLULAR IMMUNOTHERAPIES****Dose Reduced Chemotherapy in Sequence with Blinatumomab for Newly Diagnosed Older Patients with Ph/BCR::ABL Negative B-Precursor Adult Lymphoblastic Leukemia (ALL): Preliminary Results of the GMALL Bold Trial**

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Older patients (pts) with newly diagnosed ALL are ineligible for unmodified pediatric-based therapies. Although results are improved with age-adapted, dose-reduced regimens including MRD-based treatment modification, there is much space for further improvement. Therefore, the GMALL study group developed a trial to evaluate Blinatumomab, a CD19 directed bi-specific T-cell engager, in sequence with chemotherapy in this patient population with high medical need (NCT 03480438). Importantly, Blinatumomab replaced three cycles of standard consolidation chemotherapy. Pts aged 56 - 76 years (yrs) with CD19-positive, Ph-neg B-precursor ALL were eligible. The primary endpoint was complete hematologic remission (CR) after induction (1 cycle chemo, 1 cycle Blinatumomab) and the key secondary endpoint was molecular response (table 1). The efficacy population included pts treated with dose reduced and shortened induction I (IP1) and Blinatumomab 1 or early death (ED). Induction was followed by 3 further Blinatumomab cycles alternating with age adapted consolidation cycles (HDMTX/ASP, HDAC, reinduction and maintenance) according to GMALL protocols for older pts (Goekbuget et al, ASH 2021).

The median age was 66 (56-76) yrs. 21% had pro-B-ALL and 79% c/preB subtype. 40% had comorbidities according to the Charlson Score; most frequent were diabetes (13%) myocardial infarction (10%) or vascular diseases (10%).

50 pts were evaluable for IP1: 76% achieved CR/CRu and 2 pts (4%) died due to infections. 33% (N=11) had a molecular response and 18% MoICR (table 1). 47 pts were evaluable for the primary endpoint after Blinatumomab 1: CR/CRu was observed in 85%; 2 experienced ED (4%; those mentioned above; no additional ED). 88% of the CR pts had a molecular response (82% MoICR).

The median follow-up is 757 (61-1584) days. Overall Survival (OS) after 1 and 3 yrs was 80% and 67% for the efficacy population (figure 1). The resp results for the total population were 82% and 65%. The 3y OS was 69% for c/pre-B-ALL and 58% for pro-

B-ALL ( $p > .05$ ). 3y OS was 81% for pts aged 55-65 yrs and 53% for those older than 65 yrs ( $p = .025$ ). Only three pts received an allogeneic stem cell transplantation in CR1. 6 pts relapsed, 2 pt developed a secondary malignancy (Colon Ca, MDS) and 3 pts died in CR (1 HLH, 1 arterial disease, 1 Covid19). EFS was 60% at 3 yrs.

We compared the results with those of the current GMALL standard therapy for older pts with B-precursor ALL (N=186) (Gökbuget et al, ASH 2022). Patient characteristics were similar. CR rates after induction were 85% vs 78% for BOLD vs standard ( $p > .05$ ). Molecular CR rates in pts with hematologic CR were 82% vs 55% ( $p = .006$ ). OS at 3 yrs was 67% and 49% ( $p = 0.08$ ) and Remission Duration (RD) was 83% vs 58% ( $p = 0.055$ ).

Overall tolerability and efficacy of the regimen was very promising with a high hematologic and molecular response rate; mortality in induction and consolidation was low. In comparison with the current standard therapy the MRD response rates were significantly better. OS and RD was superior despite the omission of several chemotherapy cycles in contrast to other trials with unmodified chemotherapy but additional cycles of Blinatumomab. An ongoing randomized trial (NCT04994717) compares an even more dose reduced combination of Blina and chemotherapy with standard of care.

*This is an independent academic trial initiated by the GMALL Study Group which received free supply of Blinatumomab and financial support by Amgen.*

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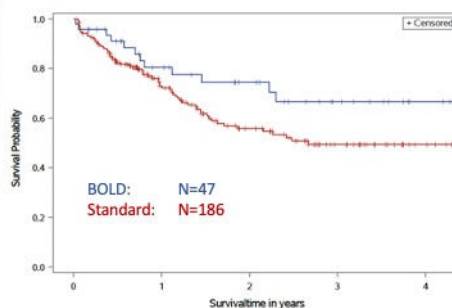
**OffLabel Disclosure:** Blinatumomab in first line

**Table 1: Results of Remission Induction**

	Induction I	Blna I
<b>N Hematologic Response*</b>	50	47
<b>Hematologic CR</b>	38 (76%)	40 (85%)
<b>Early death</b>	2 (4%)	2 (4%)
<b>Failure/PR/Relapse</b>	10 (20%)	5 (11%)
<b>N Molecular Response**</b>	34	37
<b>Molecular CR</b>	6 (18%)	28 (82%)
<b>Molecular IMR</b>	5 (15%)	2 (6%)
<b>Molecular Failure</b>	23 (68%)	4 (12%)

\* Evaluable pts with remission control after the respective cycles  
 \*\* Pts with evaluable MRD test after the respective cycle; calculated in relation to CR pts: **Molecular CR (MolCR):** MRD negative with sensitivity of 0.01%; **Molecular Failure (MolFail):** MRD positive above 0.01%; **Intermediate Risk (IMR):** MRD below 0.01% or not quantifiable; **Molecular not evaluable:** Negative with sensitivity above 0.01%, lack of marker or material

**Figure 1: Overall Survival BOLD vs GMALL Standard of Care**



**Figure 1**

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