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POSTER ABSTRACTS

612.ACUTE LYMPHOBLASTIC LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Chemotherapy-Free Combination of Blinatumomab and Ponatinib in Adults with Newly Diagnosed Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia: Updates from a Phase II Trial

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Background
Blinatumomab and ponatinib demonstrated efficacy in patients with Philadelphia chromosome (Ph)-positive acute lymphoblastic leukemia (ALL). A chemotherapy-free regimen combining both drugs in the frontline setting may mitigate the risk of toxicities and the need for hematopoietic stem cell transplantation (HSCT).

Methods
In this phase II trial, patients ≥18 years of age with newly diagnosed Ph-positive ALL were eligible. They were required to have a performance status of ≤2, total bilirubin ≤2x the upper limit of normal (ULN), and ALT/AST ≤3x the ULN. Patients with uncontrolled cardiovascular disease or clinically significant central nervous system (CNS) comorbidities (except for CNS leukemia) were excluded. Patients received up to 5 cycles of blinatumomab in combination with ponatinib, followed by ponatinib maintenance for ≥5 years. Ponatinib 30mg daily was given during Cycle 1 and decreased to 15mg daily once a complete molecular response (CMR) was achieved. Patients also received 12 doses of prophylactic intrathecal (IT) chemotherapy with alternating cytarabine and methotrexate. The primary endpoint was the CMR rate. Secondary endpoints included response rates, safety measures, event-free survival (EFS), and overall survival (OS).

Results
Between June 2018 and May 2023, 62 pts with newly diagnosed Ph-positive ALL were treated. Baseline characteristics are shown in **Table 1**. Twenty-two patients were in complete remission (CR) at the start of therapy. Among 40 patients evaluable for hematologic response, 39 (98%) achieved CR/CRi; 1 patient had early death. Among 55 patients evaluable for molecular response, 37 (67%) achieved CMR after 1 cycle, and 46 (84%) achieved CMR at any time. Forty-seven patients were evaluated for measurable residual disease (MRD) by next-generation sequencing at a sensitivity level of 10^{-6}, of whom 43 (91%) were found to have negative MRD. Five of these patients with undetectable MRD by NGS had low-level *BCR:ABL1* transcripts detected by PCR at the same time (ranging from 0.01% to 1.23% IS). Four of them had p190 transcript and one had p210.
The median follow-up was 17 months (range, 2-61 months). Six patients (10%) relapsed after a median of 21 months of remission (range, 8-24 months): two relapsed in the bone marrow (one with acquired E225V mutation), one had an extramedullary-only relapse (Ph-negative and MYC-rearranged relapse), and three had a CNS-only relapse (after 20, 22, and 23 months). Four patients died (one from intracranial hemorrhage, one from post-procedural hemorrhage, one from brain aneurysm, and one following CNS relapse with intracranial edema and septic shock).
One leukemia-related death occurred on study; the estimated 2-year EFS and OS rates were 77% and 89%, respectively **(Figure 1)**. Only one patient underwent HSCT in first CR due to persistently low-level *BCR:ABL1* positivity. Among the 52 patients in ongoing remission without HSCT, the median duration of response was 16 months (range, 2-61). Most adverse events were grade 1-2 and were consistent with the known toxicity profile of the two agents. Ponatinib was discontinued in two patients due to possibly related adverse events (cerebrovascular accident and coronary artery stenosis in one patient each).

Conclusions

The chemotherapy-free combination of blinatumomab and ponatinib is safe and effective in newly diagnosed Ph-positive ALL, with high rates of MRD negativity. Encouraging duration of remission and OS has been observed without the need for HSCT.

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Table 1. Patient characteristics

Characteristic N (%) / median [range]	N = 62
Age (years) >60 years	56 [20 - 83] 25 (40)
WBC (x10^9/L) at start	4.65 [0.4 - 23.7]
Performance Status 0-1 2	 52 (84) 10 (16)
CNS involvement	3 (5)
CD19 expression	99.8 [74.9 - 100]
>1 cardiovascular risk factor(s)	36 (58)
BCR:ABL1 transcript type *p190* *p210*	 47/61 (77) 14/61 (23)

Figure 1. Event-free survival (EFS) and overall survival (OS)

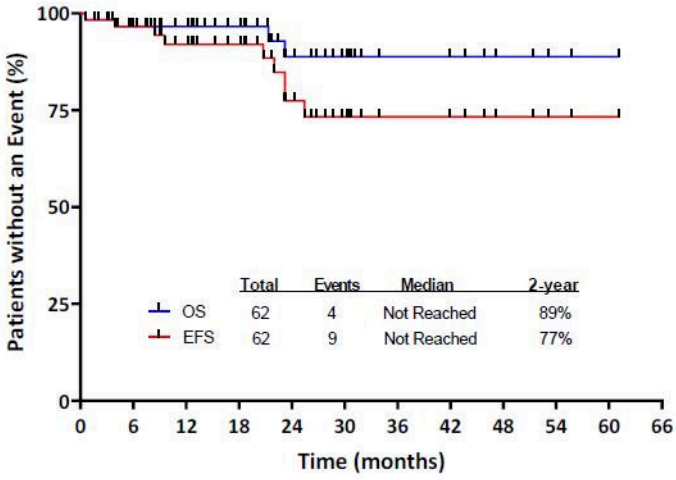

Figure 1

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