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Blinatumomab With Tyrosine Kinase Inhibitor for Ph-Positive B-Acute Lymphoblastic Leukemia (B-ALL): Multicenter Retrospective Review.

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INTRODUCTION

Ph-positive B-ALL has long been considered an adverse cytogenetic abnormality in ALL, and it is generally recommended to proceed with a stem cell transplant (SCT) in first remission. Historically, the addition of Tyrosine Kinase Inhibitors **(TKI)** to the stander chemotherapy backbone improved long-term survival, with better results noted in the second-generation than in first-generation TKIs. Recent reports on a **non-chemotherapy-based** approach with the combination of immunotherapy **(Blinatumomab) and TKI** showed encouraging results and potentially eliminated the need for consolidative SCT .In this retrospective analysis, **we reviewed all Ph-positive B-ALL treated with blinatumomab and TKI at two major academic centers.**

AIM

The study aims to assess the effectiveness and safety of combining **Tyrosine Kinase Inhibitors (TKIs) with Blinatumomab** in treating Philadelphia chromosome-positive B-cell acute lymphoblastic leukemia.

METHOD

A retrospective review of adolescents and adults (14 years or older) with Ph-positive B-ALL patients who received blinatumomab with TKI at two major institutions (KFSHRC & KFMC) between 7/2018 and 7/2023.

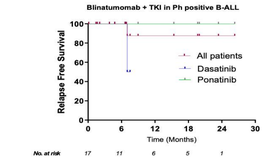
- Patients who **received up to 3 cycles of chemotherapy** before being transitioned to therapy with blinatumomab and TKI were considered as **frontline** if there was no history of relapsed disease.
- **Relapse/refractory patients** with Ph-positive B-ALL treated with blinatumomab and TKI were also included in the R/R cohort, excluding patients with prior single-agent exposure to blinatumomab or ponatinib.
- Patients with **a history of CNS disease** were included.
- **Chronic myeloid leukemia** in a lymphoid blast phase (LBP-CML) treated with blinatumomab and TKI were also included.
- Patients were assessed for toxicity as well as for efficacy.

RESULTS

We identified **17 patients**, with a median age of **40 years** (range, 15-78): 9 patients (53%) were frontline Ph-positive B-ALL, 5 (29%) were R/R Ph-positive B-ALL, and 3 (18%) were LBP-CML. **All patients in all cohorts achieved complete remission**.

- Of 7 evaluable patients in the **frontline cohort**, all achieved complete molecular response (CMR) using PCR for BCR:ABL (CMR=100%), with a median follow-up of 6.9 months.
- In the **R/R cohort**, all patients achieved CMR using PCR for BCR:ABL, with a median follow-up of 6.7 months.
- In the 3 patients with **LBP-CML**, 2 achieved CMR using PCR for BCR:ABL, and 1 achieved MMR (0.036%), with a median follow-up of 19.7 months.
- Only **4 patients proceeded to SCT**, two with BP-CML and two with newly diagnosed Ph-positive B-ALL.
- All patients proceeded with SCT in CMR except 1 with LBP-CML with positive PCR for BCR::ABL at 0.03%, although with undetectable MRD by flowcytometry (<0.01%).
- Patients were treated with **dasatinib (n=4) or ponatinib (n=13).**
- The median number of blinatumomab cycles was 4 (range, 1-5). One death occurred in a patient treated with dasatinib and blinatumomab likely secondary to infectious complication.

Variables	All patients (n=17)	ND Ph-positive B-ALL (n=9)	R/R Ph-positive B-ALL (n=5)	LBP-CML (n=3)
Age yrs, Median [range]	40 [15-78]	40 [16-52]	25 [15-78]	53 [49-53]
Male, n (%)	14 (82)	7 (78)	4 (80)	3 (100)
Fusion protein				
P190, n (%)	10 (59)	7 (78)	3 (60)	0
P210, n (%)	7 (41)	2 (22)	2 (40)	3 (100)
Prior chemotherapy, n (%)	14 (82)	6 (67)	5 (100)	3 (100)
CNS involvement n (%)	4 (24)	3 (33)	1 (20)	0
TKI used				
Dasatinib, n (%)	4 (23)	2 (22)	1 (20)	1 (33)
Ponatinib, n (%)	13 (77)	7 (78)	4 (80)	2 (67)
SCT, n (%)	4 (24)	0	2 (40)	2 (67)



CONCLUSION

Although with short follow-up, **combining TKI with blinatumomab seems to have a high complete molecular response** rate in patients with newly diagnosed and relapsed/refractory Ph-positive B-ALL. Similar to prior reports, patients with newly diagnosed Ph-positive B-ALL perhaps they could be spared the toxicities associated with chemotherapy and the need for allogeneic hematopoietic stem-cell transplantation in the first remission using this approach. Further evaluation of this novel strategy is warranted.

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