TITLE: Real World Analysis of Toxicities & Clinical Outcomes with BCR-ABL1 Tyrosine Kinase Inhibitors in B-Cell Acute Lymphoblastic Leukemia

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BACKGROUND: The rapid adoption of BCR-ABL1 TKIs in Ph+ B-ALL occurred despite a lack of comparative trials, leading to an absence of data regarding the additive toxicities of BCR-ABL1 TKIs with many standard chemotherapy regimens. BCR-ABL1 TKIs have been associated with severe adverse events and may significantly impact treatment-related morbidity and mortality.

OBJECTIVE: The objective of this study is to describe the cumulative toxicity imposed by BCR-ABL1 TKIs and chemotherapy regimens.

METHODS: A total of 48 patients with Ph+ B-ALL treated with a BCR-ABL1 TKI plus chemotherapy between January 2015 and October 2021 were eligible to assess treatment-related toxicity. High-intensity chemotherapy regimens included HyperCVAD, CALGB 10403, ECOG1910, and ECOG2993; low to moderate intensity regimens included EWALL-Ph-01, TKI + POMP, TKI + corticosteroids, and TKI monotherapy. Regimens containing blinatumomab and inotuzumab ozogamicin in combination with a TKI were assessed separately. The primary outcome was the occurrence of grade 3/4 toxicities, as defined by the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. The first occurrence of CTCAE toxicities was collected for each line of therapy patients received.

RESULTS: Among the 48 patients analyzed, 71 total lines of therapy were identified. Of these, 54.9% (n = 39) were classified as high-intensity, 29.6% (n = 21) were low-moderate intensity, 9.9% (n = 7) were blinatumomab, and 5.6% (n = 4) were inotuzumab ozogamicin. In high- and low-moderate intensity regimens, a median of 10 and 7 grade 3/4 toxicities occurred with dasatinib, respectively. In high- and low-moderate intensity regimens, a median of 8 and 2 grade 3/4 toxicities occurred with imatinib, respectively. Among all treatment regimens with dasatinib, toxicity-related discontinuation or dose reductions occurred in 51.2%. This contrasted with treatment regimens with imatinib, where no toxicity-related discontinuation or dose reductions occurred ($p = 0.002$). TKI combinations with blinatumomab and inotuzumab ozogamicin revealed no significant concerns.

CONCLUSIONS: The selection of BCR-ABL1 TKI did not influence the occurrence of grade 3/4 toxicity, regardless of chemotherapy regimen. However, a greater proportion of treatment regimens including dasatinib required dose reductions or discontinuation due to BCR-ABL1 toxicity compared to imatinib.