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ORAL ABSTRACTS

614.ACUTE LYMPHOBLASTIC LEUKEMIAS: THERAPIES, EXCLUDING TRANSPLANTATION AND CELLULAR IMMUNOTHERAPIES

Feasibility and Outcome of Post-Induction Therapy Incorporating Dasatinib for Patients with Newly Diagnosed ABL-Class Fusion B-Lymphoblastic Leukemia (ABL-class Fusion B-ALL): Children's Oncology Group AALL1131

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Background: Approximately 2-3% of B-ALL patients have Philadelphia chromosome like (Ph-like) B-ALL with an ABL-class fusion (*ABL1, ABL2, PDGFRB*, or *CSF1R* fusions), but lacking *BCR::ABL1*. These patients are predicted to be sensitive to ABL-class tyrosine kinase inhibitors, such as imatinib or dasatinib. Ph-like B-ALL is associated with male sex, older age, higher initial white blood cell (WBC) count, elevated end of induction (EOI) minimal residual disease (MRD), and poor outcome. The AALL1131 Dasatinib arm was designed to evaluate response to therapy following induction of patients with ABL-class fusion B-ALL, when given dasatinib continuously on a modified Berlin-Frankfurt-Münster (MBFM) backbone.
Methods: Between February 2012 and March 2019, AALL1131 enrolled patients 1-30 years with newly diagnosed high risk (HR) B-ALL. AALL1131 was amended in August 2016, to include the Dasatinib arm for patients with ABL-class fusions involving ABL1, ABL2, PDGFRB, and CSF1R. Patients with Down Syndrome were not eligible for the Dasatinib arm. ABL-class fusion B-ALL patients with a predicted TKI-sensitive mutation were screened by low density array (LDA) PCR and confirmed by additional molecular testing. Following 4-drug induction, patients with HR B-ALL and ABL-class fusions received MBFM with dasatinib (60 mg/m ^{2}, maximum 140 mg) daily from start of consolidation through end of maintenance. Dasatinib was held only for toxicity.
Results: Twenty-two evaluable patients with HR B-ALL were non-randomly assigned to the Dasatinib arm. ABL-class 3' partners included *ABL1* (n=4), *ABL2* (n=4), *PDGFRB* (n=12), and *CSF1R* (n=2). Compared to all patients on AALL1131, patients treated

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on the Dasatinib arm were older (median age at diagnosis 14 versus 10 years, p=0.008), more often male (77% versus 56%, p=0.046), and had a trend towards an increased initial WBC (median WBC at diagnosis 44,000/μL versus 19,000/μL, p=0.086). Patients with ABL-class fusions had EOI MRD > 0.01% in 20 of 22 patients and available end of consolidation MRD >0.01% in 6 of 10 patients. Only 5 of 22 (22.7%) patients completed prescribed protocol therapy. Reasons for therapy discontinuation included induction failure (n=2), relapse (n=1), alternate therapy (n=1), determined to be in the patient's best interest (n=10), death (n=1), unknown (n=2). Compared to all patients on AALL1131, four-year disease-free survival was 52.5+18.1% versus 86.8+0.7% (p<0.0001) and overall survival 79.4+13.6% versus 89.2+0.4% (p<0.0001). Dasatinib was well tolerated with no unexpected treatment related toxicities.

Conclusion: Patients with ABL-class fusions were more likely male, EOI MRD+, and had poorer outcomes. Seventy-seven percent of patients enrolled on the Dasatinib arm did not complete prescribed therapy. While dasatinib was well tolerated, treatment failures occurred early, indicating alternate strategies are needed.

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