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POSTER ABSTRACTS

613.ACUTE MYELOID LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Changes in White Blood Cell Counts Early during Treatment of Acute Leukemia Using Differentiating Chemotherapies

Amyah C. Harris[1], *Christopher S. Bell*[1], *Gabriela S. Hobbs, MD*[2], *Hanno Hock, MD PhD*[2], *Philip C. Amrein, MD*[2], *Rupa Narayan, MD*[2], *Amir T. Fathi, MD*[1], *Andrew M. Brunner, MD*[3]

[1] Massachusetts General Hospital, Boston, MA
[2] Division of Hematology/Oncology, Massachusetts General Hospital, Boston, MA
[3] Division of Hematology/Oncology, Dana-Farber Cancer Institute, Boston, MA

Background: Differentiation syndrome (DS) is a life-threatening complication that can occur with a number of therapies used for the treatment of acute myeloid leukemia (AML). It is best characterized in patients treated with All-trans retinoic acid (ATRA) and Arsenic for acute promyelocytic leukemia (APL), or for patients receiving an IDH inhibitor for *IDH1/2* mutant AML, but can also be seen with other therapies such as with FLT3 inhibitors, and in novel therapies under development such as menin inhibitors. It is critical to identify DS early, as corticosteroids can mitigate complications. The diagnosis of DS is made by recognizing a constellation of symptoms, typically including a rising white blood cell count, peripheral edema, rash, shortness of breath, pulmonary edema, and fevers. We evaluated white blood cell (WBC) count changes during treatment according to whether patients DS or not on chemotherapy.

Methods: We identified adult patients who received ATRA+Arsenic for newly diagnosed APL, as well as patients with AML harboring a mutation in *IDH1* or *IDH2* who were treated with monotherapy IDH inhibitors (enasidenib or ivosidenib) at any point during their treatment for active AML and treated at MGH. Patients were treated at MGH between 2015 and 2023. Patients were 18 or older and had a confirmed pathological diagnosis. We interrogated the medical record to identify patients with clinical documentation of DS during treatment, as well as the treatments used for management and clinical complications. Descriptive statistics were used to identify differences in median WBC counts between patients with DS and those without DS, and comparisons were made using Wilcoxon or chi square testing as appropriate.

Results: We identified 33 patients with APL who received ATRA+Arsenic, and 35 patients with AML harboring an *IDH1/2* mutation treated with monotherapy IDH inhibition. Our analysis revealed that 26% (18/68) of patients had clinical documentation of differentiation syndrome, including 21% (14/33) of patients treated with ATRA+Arsenic and 11% (4/35) of patients on IDH inhibitors.

In APL, the median day of a recorded diagnosis of DS was 4 days after treatment start (range 1-14 days). Patients with APL who developed DS had a higher initial WBC at treatment start compared to those who did not develop DS (6.7 vs 1.05 K/uL, p=0.03). There was no difference in hemoglobin, platelets, ANC, and percentage of peripheral blood blasts (Table 1). The WBC in DS patients started rising during the first week of treatment and peaked on Day 15 (Figure 1). Regarding treatment approaches for DS, the majority of patients were treated with steroids, (78%, 11/14) while 43% (6/14) received cytoreduction, most commonly with gemtuzumab.

In IDH-mutant AML, the median day of a recorded diagnosis of DS was 35 days after treatment start (range 16-69 days). Patients with IDH-mutated AML on IDH Inhibitor monotherapy who experienced DS had a similar finding of an early temporal rise in WBC to those with APL on ATRA+Arsenic, although this rise started on day 12 and peaked on day 16 of monotherapy. Of note, these peaks occurred prior to the documentation of a clinical DS diagnosis. In contrast to APL, patients with IDH-mutant AML who developed DS had a lower baseline ANC (p=0.03) and higher percentage of peripheral blasts circulating than those without DS (p=0.03). All patients with IDH inhibitor associated DS received dexamethasone.

Discussion: Patients with DS during treatment for APL on ATRA+Arsenic, as well as patients with DS with IDHmut AML on IDH inhibitors, had similar early peaks in the WBC count, occurring around 2 weeks from the start of treatment. In this small group, the IDHmut AML showed a rise in WBC that preceded the actual DS diagnosis. Understanding the timing of and risk factors for DS may help to identify at risk patients early for mitigation strategies.

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