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Blood 142 (2023) 3720–3721

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

903.HEALTH SERVICES AND QUALITY IMPROVEMENT -MYELOID MALIGNANCIES

Tumor Lysis Syndrome in Patients with AML Initiated on Venetoclax-Based Treatment without a Dose Ramp-up

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Introduction

Treatment with the combination of a hypomethylating agent (HMA) and venetoclax (VEN) is the standard of care for older patients (pts) with acute myeloid leukemia (AML). Venetoclax, an oral BCL-2 inhibitor, was initially approved for the treatment of chronic lymphocytic leukemia (CLL). In the early, pivotal studies assessing VEN safety, tumor lysis syndrome (TLS) was found to be a dose-limiting, potentially fatal toxicity. Dosing modifications were made to allow for safer initiation of the drug and, ultimately, a dose ramp-up was included in the dosing recommendation for CLL.

Given the risk for TLS with VEN initiation for CLL, it was hypothesized that the risk would be the same, or potentially greater, when treating pts with AML. Therefore, studies of VEN in AML have included a dose ramp-up. Although reported rates of tumor lysis syndrome in these studies have been much lower than expected, a dose ramp-up for pts with AML is included in the package insert for VEN and continues to be utilized in clinical trials.

Methods

We conducted a retrospective analysis of pts ≥18 years of age with newly diagnosed or relapsed/refractory AML treated with a standard dose hypomethylating agent (HMA), either azacitidine or decitabine, and VEN without a dose ramp-up (initiated at 400mg daily or 100mg daily if on concomitant voriconazole or posaconazole) at Thomas Jefferson University Hospital from January 1, 2018- August 1, 2021. The primary objective of this study was to determine the rate of laboratory and clinical TLS within 72 hours after chemotherapy initiation, as defined by the Cairo-Bishop criteria (Table 1). The secondary objectives were (1) to identify clinical and laboratory risk factors for the development of TLS in pts with AML who were treated with HMA-VEN without a VEN dose ramp-up and (2) to compare rates of TLS in pts with AML who were treated with HMA-VEN without a VEN dose ramp-up to historical rates of TLS in pts who underwent a VEN dose ramp-up. In the Phase 3 study of azacitidine and venetoclax the rate of TLS during the VEN dose ramp-up period (days 1-3 of treatment) was 1% (DiNardo CD, Jonas BA, Pullarkat V, et al. Azacitidine and venetoclax in previously untreated acute myeloid leukemia. N Engl J Med. 2020;383(7):617-629.).

Results

Ninety pts were included in the analysis. Seventy-one pts had newly diagnosed AML and 19 had relapsed/refractory disease. The majority of pts (58/90, 64%) had adverse risk disease by 2017 European LeukemiaNet Criteria. Median baseline white blood cell count at the time of therapy initiation was 3.25 (range 0.5-161.4). Sixty-one pts (68%) were receiving allopurinol prophylaxis at the time of HMA-VEN administration. Eighteen pts (20%) had a history of underlying renal disease. Fifteen pts (17%) were on medications, such as thiazide diuretics, aspirin, or levodopa, that can increase the risk of TLS at the time of treatment.

Zero pts met the defined criteria for laboratory or clinical TLS. One pt developed acute kidney injury and one pt developed a cardiac arrhythmia (atrial fibrillation) but neither had concomitant evidence of laboratory TLS.

Discussion

In this retrospective study of 90 pts with newly diagnosed or relapsed/refractory AML who were treated with HMA-VEN without a VEN dose ramp-up no pts developed clinical or laboratory tumor lysis syndrome. This is comparable to the rate of TLS (1%) seen in the registration trial of HMA-VEN where pts were treated with VEN 100 mg on day 1, 200 mg on day 2, and 400 mg on day 3 and thereafter. Starting pts with AML on full dose VEN on day 1, regardless of white blood cell count, renal function, or

concomitant medications, appears safe and could be implemented in clinical practice and clinical trials moving forward. This would simplify dosing for pts, pharmacists, and providers and allow for easier initiation of therapy.

Disclosures Keiffer: *Prelude Therapeutics:* Research Funding; *Cyteir Therapeutics:* Research Funding; *Abbvie:* Research Funding; *Astellas:* Membership on an entity's Board of Directors or advisory committees. **Kasner:** *Gilead:* Research Funding; *Kartos/Telios:* Research Funding; *Kronos:* Membership on an entity's Board of Directors or advisory committees; *Astellas:* Membership on an entity's Board of Directors or advisory committees; *BMS:* Research Funding; *Pfizer:* Research Funding. **Wilde:** *Gilead:* Research Funding.

Table 1. Cairo-Bishop Criteria for Clinical and Laboratory Tumor Lysis Syndrome

Laboratory TLS*	**Clinical TLS****
Uric acid ≥ 8mg/dL	Acute kidney injury (Creatinine >1.5X the upper limit of normal)
Potassium ≥ 6mEq/dL	Cardiac arrhythmia
Phosphorous ≥ 4.6 mg/dL	Seizure, tetany, or other symptoms of hypocalcemia
Calcium ≤ 7mg/dL	

* Defined as either a ≥25% change from baseline OR level above or below normal, as defined above, for any two or more serum values

** Defined as the presence of laboratory TLS plus one clinical feature not directly attributable to another source (i.e./ medication, infection, etc.)

Figure 1

https://doi.org/10.1182/blood-2023-184610