2. ABSTRACT

- **Title**

An observational study of patients with Philadelphia chromosome-negative relapsed or refractory acute lymphoblastic leukemia in the US.

- **Keywords**

Philadelphia chromosome-positive (Ph+) disease, relapsed/refractory acute lymphoblastic leukemia (ALL), treatment, healthcare utilization, real-world

- **Rationale and Background**

For patients with relapsed or refractory (R/R) acute lymphoblastic leukemia (ALL), treatment options have been limited and prognosis unfavorable. With the recent approval of BLINCYTO® (blinatumomab) in the US, it is important to understand its "real-world" utilization and to assess and understand its effectiveness and safety when administered in clinical practice. This observational study was conducted using medical record review at multiple clinical sites in the US and aimed to provide data on the real-world treatment and outcomes of patients with Philadelphia chromosome-negative (Ph-) R/R ALL, including the utilization of healthcare resources, and use, effectiveness, and safety of blinatumomab.

- **Research Question and Objectives**

Primary Objectives

o To describe treatment patterns, drug utilization, and healthcare resource utilization in patients with Ph- R/R ALL

Secondary Objectives

o To estimate the proportion of patients who receive allogeneic hematopoietic stem cell transplantation (alloHSCT) following salvage treatment for Ph- R/R ALL

o To estimate the incidence of selected adverse events (AEs) among patients receiving salvage treatment for Ph- R/R ALL

o To estimate complete remission (CR) among patients with Ph- R/R ALL receiving blinatumomab as first salvage

o To estimate CR + CR with incomplete peripheral blood count recovery (CRi) + CR with partial hematological response (CRh) in Ph- R/R ALL patients receiving blinatumomab and among all Ph- R/R ALL patients receiving salvage treatment

o To estimate minimal residual disease (MRD) response within 12 weeks of treatment initiation in Ph- R/R ALL patients receiving blinatumomab and among all Ph- R/R ALL patients receiving salvage treatment

o To estimate overall survival (OS) in Ph- R/R ALL patients receiving blinatumomab and among all Ph- R/R ALL patients receiving salvage treatment

o To estimate relapse-free survival (RFS) in Ph- R/R ALL patients receiving blinatumomab and among all Ph- R/R ALL patients receiving salvage treatment

- **Study Design**

A retrospective chart review study of Philadelphia chromosome-negative R/R ALL patients in the US.

- **Setting**

The study population was comprised of patients initiating treatment for Ph- R/R ALL at 20 selected cancer centers in the US.

- **Subjects and Study Size, Including Dropouts**

The study sample included 191 patients. This is a purely descriptive study and the final sample size is sufficient to address the primary objectives which include describing characteristics, treatment patterns and outcomes.

- **Variables and Data Sources**

 Endpoint/Outcome Variables

- Treatment patterns (e.g., types and order of treatments received)
- Drug utilization (e.g., dose and duration of treatment)
- Selected healthcare resource utilization (e.g., number and length of hospitalizations)
- Receipt of alloHSCT following salvage treatment for Ph- R/R ALL
- Incidence of selected adverse events (e.g., cytokine release syndrome)
- Best response within 8 weeks of initiation of salvage treatment; best responseb
- OS from time of initiation of salvage treatment
- RFS from time remission achieved with salvage treatment

- Exposure Variables
  - Exposure was considered initiation of treatment for Ph- R/R ALL and will be further described by treatment type (e.g., blinatumomab; salvage chemotherapy) and dosage.

- Salvage chemotherapy was defined as chemotherapy regimens included in the National Comprehensive Cancer Network (NCCN) guidelines for the management of adult ALL patients with refractory or relapsed disease.

- **Results**

Of 191 enrolled patients, 126 received blinatumomab (BLN) (86 as 1st, and 73 as most recent salvage) while 131 had standard of care chemotherapy (SOC) (102 as 1st, and 98 as most recent) in any line of salvage. The median age of patients was 46 years (range, 18–79). Patients (n, %) received 1 (80, 41.9%), 2 (55, 28.8%), 3 (30, 15.7%), or ≥4 (26, 13.6%) lines of salvage following R/R diagnosis. The median number of lines of treatment was 2, and 38.4% (28/73) had 3+ therapies before BLN as most recent salvage. Median blinatumomab treatment duration was 29.0 (IQR, 21.0–66.5) days; patients received 1 (57, 45.2%), 2 (24, 19.0%), 3 (25, 19.8%), or ≥4 (18, 14.3%) cycles. Median SOC salvage duration was 31.0 (11.0–75.0) days. The most common 1st salvage-only treatments were blinatumomab (n=45/191, 23.6%) and SOC (n=34/191, 17.8%}; patients with 2 lines of salvage received SOC-blinatumomab (n=16/191, 8.4%), SOC-SOC (13, 6.8%), and blinatumomab-SOC (13, 6.8%); patients with 3 lines of salvage received SOC-SOC-SOC (n=9/191, 4.7%), SOC-blinatumomab-SOC (5, 2.6%), SOC-SOC-blinatumomab (4, 2.1%), and blinatumomab-SOC-SOC (4, 2.1%). About a fifth of those treated with Blinatumomab as first salvage (20.9%) and 10.8% of those on chemotherapy received HSCT following salvage treatment. In the secondary analysis set, 32.9% of patients who received blinotumomab as most recent salvage and 13.3% of those on chemotherapy received HSCT following their salvage treatment. Patients who received blinatumomab tended to have lower leukemic BMB percentage (< 50%) at time of salvage (BLN,27.9%;SOC, 19.6%). Incidence of Gr ≥3 treatment-emergent AEs due to blinatumomab included cytokine release syndrome (3.2%) and neurologic events (13.5%).

- **Discussion**

Blinatumomab appeared to be well tolerated and the real-world efficacy and safety of blinatumomab were found to be comparable to clinical trials results. In addition, blinatumomab is being utilized as salvage treatment in patients with R/R B-ALL who are not responding to SOC, and has shown to reduce healthcare utilization versus SOC.

- **Marketing Authorization Holder(s)**

Amgen, Inc
Thousand Oaks, CA

- **Names and Affiliations of Principal Investigators**

See Section 3 for complete list of investigators.