Abstract: P684

Title: INTERIM RESULTS FROM ASSURE: A PHASE 3B SAFETY STUDY OF ACALABRUTINIB IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA

Abstract Type: Poster Presentation

Topic: Chronic lymphocytic leukemia and related disorders - Clinical

Background:

Acalabrutinib (acala) is a second-generation Bruton tyrosine kinase inhibitor approved for patients (pts) with treatment-naive (TN) or relapsed/refractory (R/R) chronic lymphocytic leukemia (CLL).

Aims:

To report interim safety results from ASSURE (NCT04008706), an ongoing global, phase 3b safety study evaluating acala monotherapy in pts with CLL in a real-world clinical practice setting.

Methods:

In this multicenter, open-label, single-arm study, pts aged ≥18 y with CLL requiring therapy and ECOG performance status ≤2 were enrolled into 1 of 3 cohorts (TN, R/R, or ibrutinib intolerant [IbrI; ibrutinib discontinued for any reason except disease progression]). Pts receive acala 100 mg twice daily for 48 cycles of 28 days each (beyond if still benefitting from drug) or until disease progression, toxicity requiring discontinuation, withdrawal of consent, loss to follow-up, death, or study termination, whichever comes first. The primary study objective is to evaluate the frequency of all treatment-emergent adverse events (TEAEs).

Results:

The first enrolled pt was dosed with acala in October 2019 (fully enrolled in October 2021); 552 pts had received treatment (TN, n=310; R/R, n=202; IbrI, n=40) and were included in this analysis. Median age overall was 69.5 y; 20% had del(17p)/*TP53*m and 68% had uIGHV. Median number of prior lines of therapy was 1 in the R/R cohort and 2 in the IbrI cohort. At data cutoff (June 15 2023), 64% of pts remained on treatment; reasons for discontinuation are in the **Table**. Median (range) duration of exposure reflected time on study and was 32.1 (0.2–43.6), 32.3 (0.6–41.5), and 20.5 (0.7–33.0) mo in the TN, R/R, and IbrI cohorts, respectively. Using Kaplan-Meier analysis, the estimated proportion of pts remaining on treatment at 30 mo (95% CI) was 71% (66, 76), 62% (55, 69), and 45% (27, 62) in the TN, R/R, and IbrI cohorts, respectively. The most common TEAEs are shown in the **Table**. Grade ≥3 TEAEs were reported in 57% of pts overall (TN, 54%; R/R, 63%; IbrI, 45%), most commonly COVID-19 (13%), pneumonia (7%), anemia (6%), and COVID-19 pneumonia (5%). Serious TEAEs were reported in 42% of pts overall (TN, 38%; R/R, 50%; IbrI, 25%), most commonly COVID-19 (12%), pneumonia (6%), and COVID-19 pneumonia (5%). TEAEs led to treatment discontinuation in 19% of pts (TN, 15%; R/R, 26%; IbrI, 18%), most commonly COVID-19 (n=22), COVID-19 pneumonia (n=9), hepatitis B reactivation (n=5), myalgia (n=3), and pneumonia (n=3). Events of clinical interest are reported in the **Table**; incidences of atrial fibrillation/flutter, hypertension, and major hemorrhage were low. Deaths were reported in 65 pts (12%) overall (TN, 7%; R/R, 19%; IbrI, 8%) including 56 pts with TEAEs with outcome of death. Most TEAEs with outcome of death were in pts with confirmed/suspected COVID-19 (n=41). TEAE deaths in pts without confirmed/suspected COVID-19 (n=15) included infections/infestations (n=4) and neoplasms (malignant/unspecified; n=4). No new safety risks were identified based on review of TEAEs or laboratory data review.

Summary/Conclusion:

In this interim analysis of ASSURE, the safety profile of acala in pts with CLL (TN, R/R, IbrI) in a real-world clinical setting was consistent with previous clinical studies. Unlike the previous studies, COVID-19 TEAEs, including those with outcome of death, were commonly observed as study enrollment spanned the COVID-19

pandemic (Niemann CU, et al. *Hemasphere*. 2022;6(10):e780); otherwise, rates of cardiac events were low, rates of infection were high but manageable with low mortality when COVID-19 deaths were excluded, and no new safety signals were reported.

Table. Disposition, Most Common Treatment-Emergent Adverse Events (TEAEs; ≥15% [any grade] or ≥5% [grade ≥3] in any cohort), and Events of Clinical Interest

n (%)	TN cohort (n=310)		R/R cohort (n=202)		Prior ibrutinib cohort (n=40)		Total (N=552)	
Discontinued treatment	95 (30.6)		82 (40.6)		19 (47.5)		196 (35.5)	
Subject decision	12 (3.9)		5 (2.5)		2 (5.0)		19 (3.4)	
Adverse event[a]	51 (16.5)		53 (26.2)		7 (17.5)		111 (20.1)	
Condition under investigation worsened	9 (2.9)		18 (8.9)		6 (15.0)		33 (6.0)	
Development of study-specific discontinuation criteria	4 (1.3)		0		2 (5.0)		6 (1.1)	
Other	17 (5.5)		6 (3.0)		2 (5.0)		25 (4.5)	
Missing	2 (0.6)		0		0		2 (0.4)	
TEAEs (preferred terms)	**Any grade**	**Grade ≥3**	**Any grade**	**Grade ≥3**	**Any grade**	**Grade ≥3**	**Any grade**	**Grade ≥3**
Headache	129 (41.6)	4 (1.3)	77 (38.1)	3 (1.5)	28 (70.0)	0	234 (42.4)	7 (1.3)
COVID-19	120 (38.7)	34 (11.0)	92 (45.5)	35 (17.3)	14 (35.0)	2 (5.0)	226 (40.9)	71 (12.9)
Diarrhea	102 (32.9)	4 (1.3)	57 (28.2)	2 (1.0)	11 (27.5)	1 (2.5)	170 (30.8)	7 (1.3)
Contusion	82 (26.5)	0	43 (21.3)	0	9 (22.5)	0	134 (24.3)	0
Arthralgia	68 (21.9)	4 (1.3)	24 (11.9)	2 (1.0)	12 (30.0)	0	104 (18.8)	6 (1.1)
Nausea	55 (17.7)	1 (0.3)	35 (17.3)	0	8 (20.0)	0	98 (17.8)	1 (0.2)
Fatigue	59 (19.0)	2 (0.6)	26 (12.9)	5 (2.5)	8 (20.0)	1 (2.5)	93 (16.8)	8 (1.4)
Anemia	36 (11.6)	15 (4.8)	33 (16.3)	15 (7.4)	7 (17.5)	1 (2.5)	76 (13.8)	31 (5.6)
Constipation	52 (16.8)	2 (0.6)	13 (6.4)	0	2 (5.0)	0	67 (12.1)	2 (0.4)
Pneumonia	30 (9.7)	15 (4.8)	28 (13.9)	19 (9.4)	6 (15.0)	3 (7.5)	64 (11.6)	37 (6.7)
Vomiting	27 (8.7)	2 (0.6)	16 (7.9)	0	6 (15.0)	0	49 (8.9)	2 (0.4)
COVID-19 pneumonia	10 (3.2)	8 (2.6)	23 (11.4)	20 (9.9)	1 (2.5)	0	34 (6.2)	28 (5.1)
Neutropenia	14 (4.5)	11 (3.5)	19 (9.4)	12 (5.9)	1 (2.5)	1 (2.5)	34 (6.2)	24 (4.3)
Events of clinical interest[b]								
Cardiac events	60 (19.4)	21 (6.8)	31 (15.3)	10 (5.0)	9 (22.5)	1 (2.5)	100 (18.1)	32 (5.8)
Atrial fibrillation/flutter	20 (6.5)	7 (2.3)	4 (2.0)	1 (0.5)	2 (5.0)	1 (2.5)	26 (4.7)	9 (1.6)
Ventricular arrhythmias[c]	3 (1.0)	0	0	0	1 (2.5)	0	4 (0.7)	0
Hemorrhage	156 (50.3)	12 (3.9)	95 (47.0)	8 (4.0)	19 (47.5)	1 (2.5)	270 (48.9)	21 (3.8)
Major hemorrhage	12 (3.9)	12 (3.9)	9 (4.5)	8 (4.0)	1 (2.5)	1 (2.5)	22 (4.0)	21 (3.8)
Hypertension	29 (9.4)	10 (3.2)	12 (5.9)	7 (3.5)	2 (5.0)	1 (2.5)	43 (7.8)	18 (3.3)
Infections	229 (73.9)	76 (24.5)	152 (75.2)	81 (40.1)	30 (75.0)	8 (20.0)	411 (74.5)	165 (29.9)
Second primary malignancies excluding non-melanoma skin	29 (9.4)	16 (5.2)	17 (8.4)	7 (3.5)	3 (7.5)	2 (5.0)	49 (8.9)	25 (4.5)
Richter transformation and myeloid malignancies								
Richter transformation	4[d] (1.3)		2 (1.0)		0		6[d] (1.1)	
Chronic myeloid leukemia	0		1[d] (0.5)		0		1[d] (0.2)	
Acute myeloid leukemia	0		2[d] (1.0)		0		2[d] (0.4)	

[a]Data for treatment discontinuations due to adverse events (disposition data) were captured from the treatment termination case report form (vs the adverse event case report form for TEAEs leading to treatment discontinuation [safety data]).
[b]Includes new-onset and worsening of existing condition.
[c]All ventricular arrhythmia events were ventricular extrasystoles.
[d]Reported as an adverse event in 1 patient.

Keywords: Safety, Bruton's tyrosine kinase inhibitor (BTKi), Chronic lymphocytic leukemia, relapsed/refractory