Abstract: P703

Title: IMPACT OF ACALABRUTINIB TREATMENT BY LINE OF THERAPY IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA: POOLED ANALYSIS FROM ELEVATE-TN, ELEVATE-RR, AND ASCEND

Abstract Type: Poster Presentation

Topic: Chronic lymphocytic leukemia and related disorders - Clinical

Background:

Acalabrutinib, a second-generation Bruton tyrosine kinase inhibitor (BTKi), has demonstrated comparable efficacy and an improved safety profile compared with ibrutinib (a first-generation BTKi) in a head-to-head trial in patients with relapsed/refractory (R/R) chronic lymphocytic leukemia (CLL) with a median of 2 prior lines of therapy (LOT) (Byrd et al. *J Clin Oncol*. 2021). A pooled analysis of 2 phase 3 studies demonstrated significantly improved progression-free survival (PFS) and overall survival (OS) among ibrutinib-treated patients who had 0 vs ≥3 prior LOT (O'Brien et al. *Am J Hematol*. 2019). The impact of acalabrutinib treatment in patients with CLL by number of prior LOT is unknown.

Aims:

To describe the impact of number of prior LOT on OS, PFS, and time to next treatment (TTNT) in patients with treatment-naive (TN) or R/R CLL receiving acalabrutinib monotherapy, overall and by del(17p) status.

Methods:

Data were pooled from 3 phase 3 studies (ELEVATE-TN [data cutoff: March 3, 2023], ELEVATE-RR [September 15, 2020], and ASCEND [September 3, 2021]) to include all patients treated with acalabrutinib monotherapy 100 mg twice daily. Median study follow-up was 74.5 mo in ELEVATE-TN, 40.9 mo in ELEVATE-RR, and 46.5 mo in ASCEND. Kaplan-Meier analyses were performed to evaluate OS, PFS, and TTNT for the overall population and patients with del(17p). Hazard ratios (HR) and log-rank *P*-values compared 1 vs 0 prior LOT and 2+ vs 1 prior LOT.

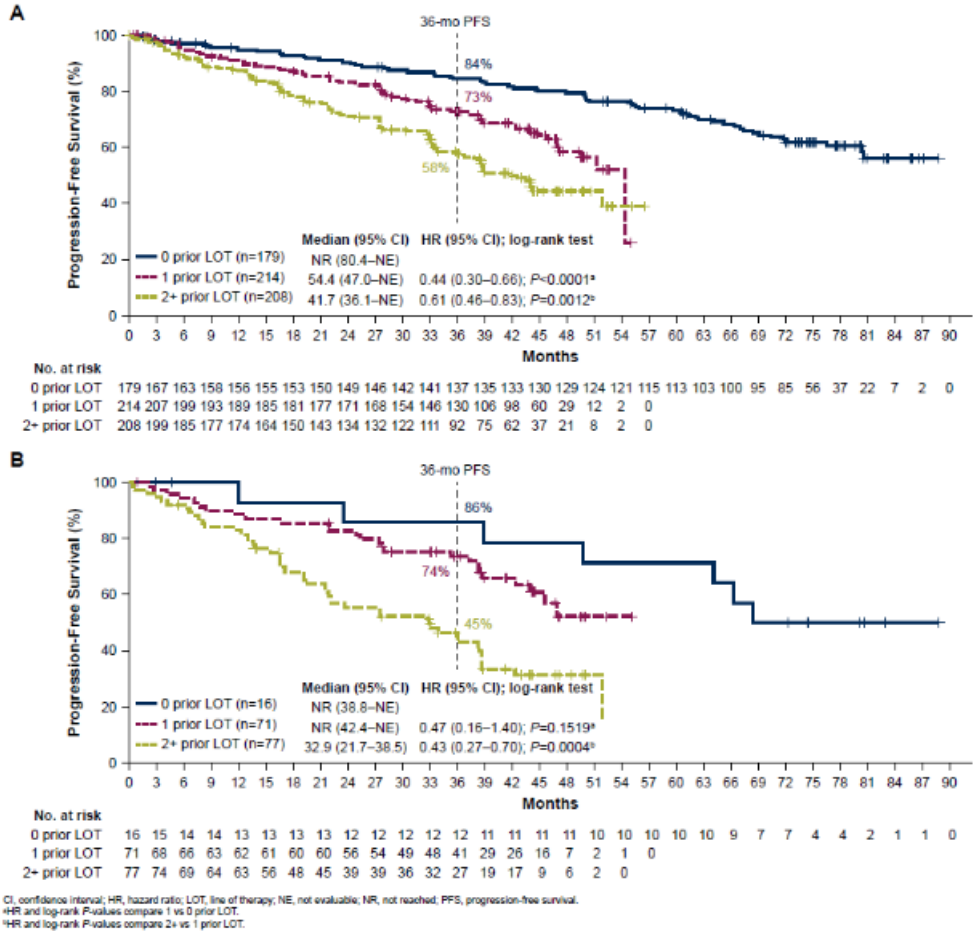
Results:

A total of 601 patients were included (0 prior LOT, n=179; 1 prior LOT, n=214 [ELEVATE-RR, n=132; ASCEND, n=82]; 2+ prior LOT, n=208 [ELEVATE-RR, n=135; ASCEND, n=73]). Patients with 0 prior LOT were older (age ≥65 years: 84.4%) vs those with 1 or 2+ prior LOT (51.9% and 62.0%, respectively). Proportions of patients with del(17p) (8.9%, 33.2%, 37.0%), del(17p) and/or *TP53* mutation (12.8%, 40.2%, 45.2%), and complex karyotype (17.3%, 28.0%, 32.2%) were lower in those with 0 prior LOT vs those with 1 or 2+ prior LOT, respectively. Most common reasons for treatment discontinuation were adverse events (17.9%, 13.1%, 22.6%) and disease progression (14.0%, 23.4%, 31.7%) in those with 0, 1, and 2+ prior LOT, respectively. In the overall population, patients with 0 prior LOT had a significantly lower risk of death (OS HR: 0.55, 95% confidence interval [CI]: 0.33–0.93, *P*=0.0185), disease progression or death (PFS HR: 0.44, 95% CI: 0.30–0.66, *P*<0.0001) (**Figure 1A**), and initiating subsequent therapy (TTNT HR: 0.48, 95% CI: 0.32–0.70, *P*=0.0001) vs those with 1 prior LOT. Compared to patients with 2+ prior LOT, those with 1 prior LOT also had significantly lower risk of death (OS HR: 0.54, 95% CI: 0.36–0.79, *P*=0.0016), disease progression or death (PFS HR: 0.61, 95% CI: 0.46–0.83, *P*=0.0012), and initiating subsequent therapy (TTNT HR: 0.67, 95% CI: 0.49–0.90, *P*=0.0070). Findings were consistent in patients with del(17p), wherein patients with 1 prior LOT had a significantly lower risk of death (OS HR: 0.46, 95% CI: 0.25–0.82, *P*=0.0072), disease progression or death (PFS HR: 0.43, 95% CI: 0.27–0.70, *P*=0.0004) (**Figure 1B**), and initiating subsequent therapy (TTNT HR: 0.54, 95% CI: 0.34–0.87, *P*=0.0091) vs those with 2+ prior LOT. Analysis of the del(17p) subgroup in patients with 1 vs 0 prior LOT was insufficiently powered due to small sample size of patients with 0 prior LOT (n=16).

Summary/Conclusion:

In this pooled analysis of 3 phase 3 trials of patients with TN or R/R CLL, the overall population and those with del(17p) had significantly better OS, PFS, and TTNT outcomes when receiving acalabrutinib earlier rather than in later LOT.

Figure 1. Kaplan-Meier plot of progression-free survival in the **(A)** overall study population (ELEVATE-TN, ELEVATE-RR, and ASCEND) and **(B)** patients with del(17p) by number of prior LOT (1 vs 0 and 2+ vs 1).



CI, confidence interval; HR, hazard ratio; LOT, line of therapy; NE, not evaluable; NR, not reached; PFS, progression-free survival.
[a]HR and log-rank *P*-values compare 1 vs 0 prior LOT.
[b]HR and log-rank *P*-values compare 2+ vs 1 prior LOT.

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