Abstract: P691

Title: IMPACT OF FIRST-YEAR DOSE MODIFICATIONS OF ACALABRUTINIB IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA

Abstract Type: Poster Presentation

Topic: Chronic lymphocytic leukemia and related disorders - Clinical

Background:

Acalabrutinib (acala), a second-generation, covalent Bruton tyrosine kinase inhibitor, demonstrated progression-free survival benefit and/or favorable tolerability vs comparators in patients (pts) with treatment-naive (TN) and relapsed/refractory (R/R) chronic lymphocytic leukemia (CLL) (Sharman et al. Blood. 2023; Ghia et al. HemaSphere. 2022; Seymour et al. Blood. 2023). Despite these benefits, 22% of pts with CLL treated with acala discontinued treatment (tx) within the first year in the real-world setting (Roeker et al. Blood. 2022). A previous analysis of ELEVATE-TN at median follow-up of 60 months (mo) demonstrated that pts with TN CLL who discontinued acala in the first year have poorer survival prognosis than pts who continued tx (Follows et al. Blood. 2023).

Aims:

To assess the impact of dose modifications or discontinuations that occur in the first year of acala tx on overall survival (OS) in an updated analysis in pts with TN CLL and in pts with R/R CLL.

Methods:

In the TN cohort, pts who received continuous acala 100 mg twice daily (BID) ± obinutuzumab (fixed duration, ≤6 cycles) in the phase 3 ELEVATE-TN trial (NCT02475681) were included. In the pooled R/R cohort, pts who received continuous acala 100 mg BID in the phase 3 ELEVATE-RR (NCT02477696) and ASCEND (NCT02970318) trials were included. Pts were divided into 3 subgroups: 1) pts with no dose reductions/interruptions >14 days in the first year; 2) pts with dose reductions/interruptions >14 days in the first year but who continued tx for ≥1 year; and 3) pts who discontinued tx in the first year. A conditional OS analysis was conducted; pts with <1 year of follow-up were excluded.

Results:

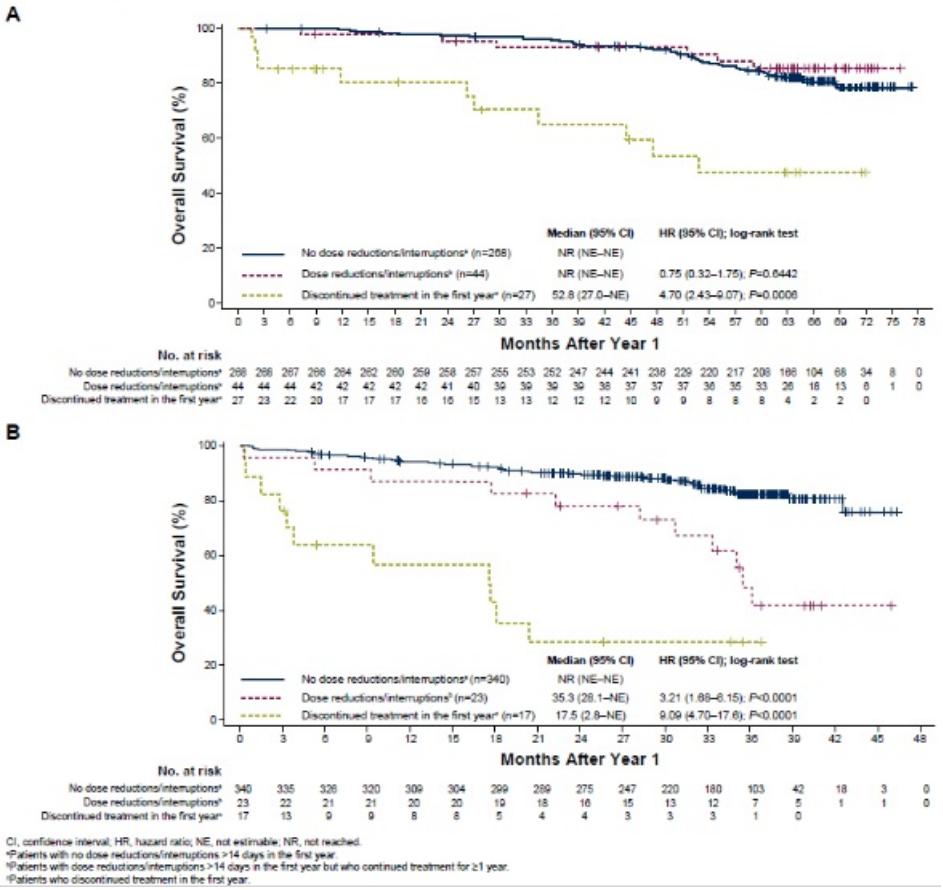
With median follow-up of 74.5 mo, the TN cohort included 339 pts with ≥1 year of follow-up. With median follow-up of 40.9 mo and 46.5 mo in the ELEVATE-RR and ASCEND trials, respectively, the R/R cohort included 236 and 144 pts, respectively, with ≥1 year of follow-up. In the TN and R/R cohorts, respectively, 268 (79%) and 340 (89%) pts had no dose reductions/interruptions >14 days, 44 (13%) and 23 (6%) pts had dose reductions/interruptions >14 days, and 27 (8%) and 17 (4%) pts discontinued tx in the first year. The most common reasons for tx discontinuation in the first year were adverse events (TN, n=15; R/R, n=8) and disease progression (PD) (TN, n=5; R/R, n=8). Pts who discontinued tx in the first year had >4-fold increased risk of death in the TN cohort (OS hazard ratio [HR]: 4.70, 95% confidence interval [CI]: 2.43–9.07, P=0.0006; **Figure 1A**) and >9-fold increased risk of death in the R/R cohort (HR: 9.09, 95% CI: 4.70–17.6, P<0.0001; **Figure 1B**) vs pts who did not require dose reductions/interruptions >14 days. When comparing pts who had dose reductions/interruptions >14 days vs pts who remained on tx without dose modifications, no statistically significant OS difference was observed in the TN cohort (HR: 0.75, 95% CI: 0.32–1.75, P=0.6442; **Figure 1A**), whereas in the R/R cohort, pts who had dose reductions/interruptions >14 days had >3-fold increased risk of death (HR: 3.21, 95% CI: 1.68–6.15, P<0.0001; **Figure 1B**). A sensitivity analysis excluding pts who discontinued tx due to PD before 1 year found similar results.

Summary/Conclusion:

In both the TN and R/R CLL cohorts, most pts did not require acala dose modifications. However, pts who

discontinued acala tx in the first year had significantly increased risk of death vs pts who remained on tx. Additionally, pts with R/R CLL who experienced acala dose modifications for >14 days in the first year had an increased risk of death vs pts who did not have dose modifications.

Figure 1. Overall survival by dose modification group in patients treated with acalabrutinib in **(A)** TN or **(B)** R/R CLL.



CI, confidence interval; HR, hazard ratio; NE, not estimable; NR, not reached.
[a]Patients with no dose reductions/interruptions >14 days in the first year.
[b]Patients with dose reductions/interruptions >14 days in the first year but who continued treatment for ≥1 year.
[c]Patients who discontinued treatment in the first year.

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