Outcomes ≥1 year after transitioning from treatment with ibrutinib (ibru) in the ASPEN study to zanubrutinib (zanu)

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ABSTRACT

Background: ASPEN (NCT03053440) compared BTK inhibitors (BTKi) zanu and ibru in patients (pts) with *MYD88*-mutated Waldenström macroglobulinemia (WM). LTE1 (NCT04170283) is a zanu long-term extension study. We report clinical outcomes ≥1 yr after transition from ibru in ASPEN to zanu in LTE1.

Methods: In LTE1, ibru-treated pts from ASPEN began zanu 320 mg/day. Disease response was assessed every 6 months by modified Owen criteria or as "no evidence of progressive disease" at investigator discretion. Safety and efficacy outcomes were analyzed ad hoc.

Results: Between Jun 26, 2020 and Jun 23, 2022, 47 ibru-treated pts from ASPEN enrolled in LTE1; most (79%) had relapsed/refractory WM prior to ASPEN. At LTE1 enrollment, median age was 73 yrs; median time from ASPEN discontinuation to zanu initiation was 0.07 months. As of Jun 23, 2023, 40 pts (85%) remained on study treatment. Median treatment duration was 50.4 months for ibru prior to transition and 15.3 months for zanu. During LTE1, grade ≥3/serious treatment-emergent AEs (TEAEs) occurred in 23%/13% of pts. Infections (6.4%; all COVID-19) were the only grade ≥3 TEAEs in >2 pts; no serious TEAEs affected >2 pts. Most ibru TEAEs of interest for BTKis did not recur/worsen after zanu transition (except infections [n=3, all COVID-19], anemia [n=1], neutropenia [n=1]). Six of 7 pts with cardiovascular AEs (8 events) in LTE1 had ≥1 ibru-emergent cardiovascular AE during ASPEN. No worsening or new hypertension occurred after zanu transition. There was no recurrence or worsening of atrial fibrillation (AF)/flutter; 1 new case of AF occurred (LTE1 day 12) in a pt with extensive cardiovascular history and concurrent pericarditis (LTE1 day 10). No cardiovascular TEAE led to death in LTE1. Two deaths occurred (both due to COVID-19). Overall response at end of ASPEN was maintained or improved at BOR in LTE1 in 96% (n=44/46) of efficacy-evaluable pts. Median [IgM] change was –36 mg/dL; [IgM] was stable/decreased in 29 pts (73%) from the last ASPEN response assessment to BOR in LTE1.

Conclusions: Following transition to zanu, at a median ibru treatment duration of 50.4 months, most ibru-emergent TEAEs of interest for BTKis did not recur/worsen at a 15-months median zanu treatment duration. Response was maintained or improved in 96% (n=44/46) of efficacy-evaluable pts. Although limited, these data suggest that transitioning ibru-tolerant pts with WM to zanu does not compromise safety or efficacy; long-term follow-up is ongoing.