Title: Safety and Efficacy of Zanubrutinib (Zanu) in a Subgroup of Older Patients (≥75 Years) With Treatment-Naive Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) From the Phase 3 SEQUOIA Study

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Background: In SEQUOIA (NCT03336333), zanu, a next-generation BTK inhibitor, demonstrated superior efficacy vs bendamustine + rituximab (BR) in treatment-naive pts with CLL/SLL. This subgroup analysis assessed zanu vs BR in older (≥75 yrs) pts.

Methods: Pts without del(17p) were randomized to receive zanu (arm A) or BR (arm B); arm C included pts with del(17p) receiving zanu. Pts in this analysis were restricted by age ≥75 yrs (elderly).

Result: As of April 30, 2024, median follow-up with zanu (for pts ≥75 yrs) was 62.1 mo (range, 1.4-74.1) in arm A and 66.5 mo (range, 5.0-73.3) in arm C. In arm A and B, 120 pts were aged ≥75 yrs, 64 pts received zanu and 56 pts received BR; median age was 78 yrs (range, 75-87). Arm C had 30 pts aged ≥75 yrs.

In arm A pts treated with zanu, ORR was 97%, with a complete response/complete response with incomplete hematopoietic recovery (CR/CRi) rate of 19% (vs 86% and 30% with BR in arm B). Estimated 60-mo PFS rate (95% CI) was 69% (55-80) with zanu and 44% (28-59) with BR. When COVID-19-adjusted, zanu PFS rate was 71% (56-81) and BR PFS rate was 44% (28-59). Estimated 60-mo OS rate (95% CI) was 82% (70-90) with zanu and 76% (62-86) with BR. When COVID-19-adjusted, zanu OS rate was 84% (72-91) and BR rate was 78% (64-87).

In arm C, ORR was 93% with a CR/CRi rate of 20% with zanu. The 60-mo PFS rate (95% CI) was 69% (49-83); 60-mo OS rate was 76% (56-88). In arm A and B, grade ≥3 adverse events (AEs) were observed in 77% with zanu and 89% with BR and serious AEs (SAEs) in 64% and 65% of pts, respectively. In arm C, rates of grade ≥3 AEs and SAEs were 67%, and 63%, respectively. AEs led to death in 9% and 13% of zanu-treated pts in arm A and arm C, respectively, and 17% of BR-treated pts in arm B.

Discussion: Zanu efficacy was comparable for elderly pts with/without del(17p). In elderly pts without del(17p), zanu demonstrated PFS benefit over BR; the safety profile with zanu was consistent with published data.

Conclusion: These data continue to support zanu as a valuable treatment option in the first-line CLL/SLL setting, including in elderly pts.

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