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# Risk of hypertension in patients (pts) with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) receiving treatment with zanubrutinib or pirtobrutinib: a comparative real-world study

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**Introduction:** Bruton tyrosine kinase (BTK) inhibitors are a standard of care treatment for pts with CLL/SLL, although concerns regarding cardiovascular toxicities, including hypertension, remain. Both zanubrutinib and pirtobrutinib have demonstrated a more favorable cardiovascular safety profile than the first-generation BTK inhibitor, ibrutinib. However, information regarding the occurrence of hypertension in pts treated with zanubrutinib or pirtobrutinib outside clinical studies is limited. This study compares the risk of new-onset and worsening hypertension in pts with CLL/SLL treated with zanubrutinib or pirtobrutinib using real-world data.

**Methods:** We conducted a retrospective cohort study in pts with CLL/SLL who initiated therapy with either zanubrutinib or pirtobrutinib between January 2023-October 2025 using the Symphony Health Solutions database. Index date was the first prescription date for zanubrutinib or pirtobrutinib. Primary outcomes were 12-month incidences of new-onset hypertension and worsening hypertension; a composite outcome of either new-onset or worsening hypertension was also assessed. New-onset hypertension was defined as initiation of antihypertensive medication in pts without baseline hypertension. Worsening hypertension was defined as either a ≥2-fold increase in antihypertensive dosage relative to baseline or the addition of a new antihypertensive medication in pts

with preexisting hypertension. Incidence proportions and event rates were compared between treatment cohorts. Inverse probability of treatment weighting (IPTW)–adjusted Cox proportional hazards models were used to estimate HRs and 95% CIs comparing the risk of hypertension between pts treated with zanubrutinib and pirtobrutinib. Prespecified subgroup analyses were conducted in pts aged ≥65 and ≥75 yrs.

**Results:** A total of 5374 pts initiating zanubrutinib and 841 pts initiating pirtobrutinib were included. Median follow-up was 16.0 months in the zanubrutinib cohort and 11.7 months in the pirtobrutinib cohort. In the zanubrutinib and pirtobrutinib cohorts, respectively, median age was 74 and 73 yrs, and 59.3% and 65.8% of pts were male. In the zanubrutinib cohort, 44.3% of pts received treatment in the first-line setting compared with 4.3% in the pirtobrutinib cohort. Among pts without baseline hypertension, 17.0% of pts treated with zanubrutinib developed new-onset hypertension within 12 months compared with 18.1% of pts treated with pirtobrutinib, corresponding to event rates of 1.72 and 1.97 per 100 person-months, respectively. Compared with pirtobrutinib-treated pts, the IPTW-adjusted HR for new-onset hypertension in zanubrutinib-treated pts was 0.99 (95% CI, 0.74-1.32; *P*=.942). Among pts with baseline hypertension, worsening hypertension occurred in 13.3% of pts treated with zanubrutinib and 10.5% of pts treated with pirtobrutinib. Compared with pirtobrutinib-treated pts, the IPTW-adjusted HR for worsening hypertension in zanubrutinib-treated pts was 1.18 (95% CI, 0.87-1.60; *P*=.299). Overall, 14.8% of pts treated with zanubrutinib and 13.7% of pts treated with pirtobrutinib experienced either new-onset or worsening hypertension. Compared with pirtobrutinib-treated pts, the IPTW-adjusted HR for the composite outcome in zanubrutinib-treated pts was 1.05 (95% CI, 0.85-1.28; *P*=.668). In 5055 pts aged ≥65 yrs (4391 treated with zanubrutinib, 664 treated with pirtobrutinib), the adjusted HRs were 1.02 (95% CI, 0.74-1.41; *P*=.901) for new-onset hypertension, 1.10 (95% CI, 0.80-1.52; *P*=.546) for worsening hypertension, and 1.07 (95% CI, 0.85-1.34; *P*=.560) for the composite outcome. Similar findings were observed in 3001 pts aged ≥75 yrs (2612 treated with zanubrutinib, 389 treated with pirtobrutinib). In analyses restricted to pts receiving 2L+ therapy (2993 pts treated with zanubrutinib, 805 pts treated with pirtobrutinib), the risk for new-onset hypertension was comparable

between zanubrutinib and pirtobrutinib (HR, 0.99; 95% CI, 0.72-1.36; *P*=.966); similar findings were observed for worsening hypertension (HR, 1.21; 95% CI, 0.87-1.69; *P*=.254) and the composite outcome (HR, 1.06; 95% CI, 0.85-1.32; *P*=.615).

**Conclusions:** In this real-world study, no statistically significant differences in hypertension risk were observed between zanubrutinib and pirtobrutinib. Similar findings were observed in pts aged ≥65 and ≥75 yrs and those in the 2L+ treatment setting, supporting similar hypertension risk profiles between these agents.