Real World Outcomes of Pirtobrutinib Versus Venetoclax After Covalent BTK Inhibitor Exposure in CLL/SLL

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BACKGROUND

- The treatment landscape of relapsed or refractory CLL/SLL has rapidly evolved with the availability of noncovalent BTK inhibition
- Pirtobrutinib recently received traditional approval for patients previously treated with a covalent BTK inhibitor, creating a clinically relevant sequencing question against venetoclax based therapy
- Real world comparative data between these two strategies remain limited

METHODS

BEFORE MATCHING
570 vs 2,419

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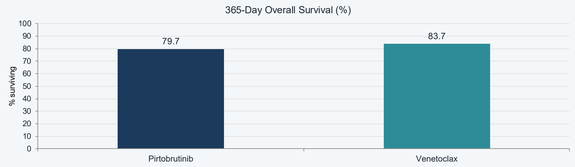
AFTER PSM MATCHING
548 vs 548

- Retrospective cohort study using the TriNetX Global Collaborative Network
- Adults with CLL/SLL previously exposed to a covalent BTK inhibitor (ibrutinib, acalabrutinib, or zanubrutinib)
- Patients initiating pirtobrutinib compared with patients initiating venetoclax
- Index date: first recorded pirtobrutinib or venetoclax use after covalent BTK exposure
- Propensity matching: demographics, prior BTK/rituximab/antineoplastic therapy, creatinine, hemoglobin, neutrophil and platelet count, albumin
- Primary outcome: all cause mortality within 365 days
- Secondary outcomes: infectious complications (365 days), cytopenias (180 days)

RESULTS



548 vs 548 — matched patients per cohort (pirtobrutinib vs venetoclax)

HR 1.299 — 95% CI 0.960–1.756, log-rank p=0.089

26.5% vs 25.0% — infectious complications, RR 1.058 (95% CI 0.865–1.294)

- Before matching: 570 received pirtobrutinib, 2,419 received venetoclax; 548 matched per cohort with well balanced baseline characteristics
- Death at 365 days: 92 patients (pirtobrutinib) vs 78 patients (venetoclax); difference not statistically significant
- At 180 days: neutropenia 17.7% vs 21.2% (RR 0.836); thrombocytopenia 28.8% vs 28.6% (RR 1.006)

CONCLUSION

- Pirtobrutinib demonstrated comparable 12 month survival, infection risk, and early hematologic safety relative to venetoclax
- Findings suggest pirtobrutinib is a practical sequencing option in the era of noncovalent BTK inhibition after covalent BTK exposure
- Results support individualized treatment selection based on prior therapy, comorbidity profile, cytopenia risk, treatment goals, and patient preference
- Prospective comparative sequencing studies are still needed

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