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Efficacy and Safety of Pirtobrutinib in Chronic Lymphocytic Leukemia / Small Lymphocytic Lymphoma

A Systematic Review and Meta-Analysis (PRISMA) · 8 studies

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Studies pooled · adults with CLL/SLL on pirtobrutinib 200 mg daily

0.43
PFS hazard ratio (IRC) · 95% CI 0.25–0.76 — significant

0.82
Overall-survival HR · 0.48–1.38 — not significant

0.65
Thrombocytopenia RR · 0.45–0.94 — significantly reduced

Background

CLL/SLL is the most common adult leukemia. BTK inhibitors improved outcomes, but resistance and adverse events remain challenges. Pirtobrutinib — a selective, *noncovalent* BTKi — has shown promising efficacy and tolerability in previously treated patients.

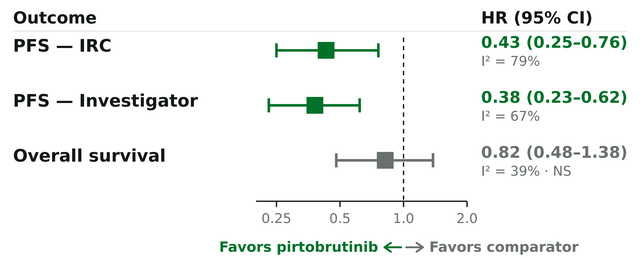
We pooled available evidence to quantify its efficacy and safety in CLL/SLL.

Methods

- **Design.** PRISMA-guided systematic review & meta-analysis.
- **Search.** Databases from inception to **January 2026**.
- **Population.** Adults ≥18 y with CLL/SLL on pirtobrutinib 200 mg daily, any prior therapy or BTKi exposure.
- **Outcomes.** Primary — ORR, PFS, OS, AEs/SAEs; secondary — TTNT, EFS.
- **Analysis.** Random-effects pooling of HRs and risk ratios with 95% CIs.

Efficacy: progression-free & overall survival

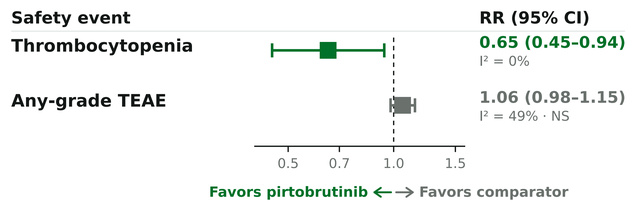
Pooled hazard ratios (random effects)



PFS significantly improved by IRC and investigator assessment; leave-one-out cut IRC-PFS heterogeneity to I²=36% with significance retained. OS trended favorable but was not significant.

Safety

Adverse events — pooled relative risk



Overall treatment-emergent AEs were comparable; thrombocytopenia was significantly reduced. See sensitivity findings (left) for grade ≥3, discontinuation, infection, and bleeding.

Sensitivity analyses

Significantly lower with pirtobrutinib

- ↓ **Grade ≥3 TEAEs**
- ↓ **Discontinuation due to AEs**
- ↓ **Neutropenia**

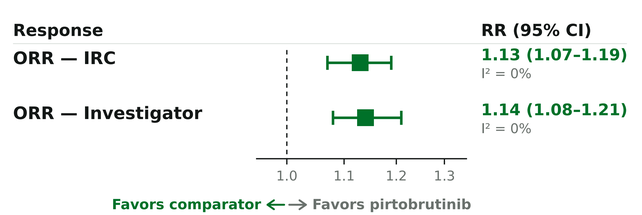
Significantly higher with pirtobrutinib

- ↑ **Infection**
- ↑ **Bleeding**

Directional findings from leave-one-out sensitivity analyses. Cardiovascular AEs were comparable between groups.

Response rate

Overall response rate — pooled relative risk



ORR significantly favored pirtobrutinib with no heterogeneity (I²=0%). Complete/partial response rates did not differ significantly and were heterogeneous.

Conclusions

- Pirtobrutinib **significantly improved PFS** in CLL/SLL with a generally manageable safety profile.
- No significant **OS** benefit was observed, but consistent PFS gains support its therapeutic role.
- Safety was favorable overall — reduced thrombocytopenia, grade ≥3 TEAEs, and discontinuations — with higher infection and bleeding risk to monitor.
- Larger, long-term studies are needed to confirm durability of efficacy and safety.