A Living NMA framework incorporating RWE in chronic lymphocytic leukemia (CLL) using the Oncoscope REAL-Time AI-assisted SLR



Andrew Briggs[1], Anna Forsythe[2], Saro Sarkisian[3], Mihaela Musat[2]

1. London School of Hygiene & Tropical Medicine, London, United Kingdom,
2. Oncoscope, Miami, FL, USA,
3. Frederick Health, Frederick, MD, USA.

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Session: Generating Decision-Ready Evidence for HTA and ICA

First-line CLL

The optimal choice of therapy remains uncertain in first-line and relapsed/refractory CLL.

NCCN preferred options[1]

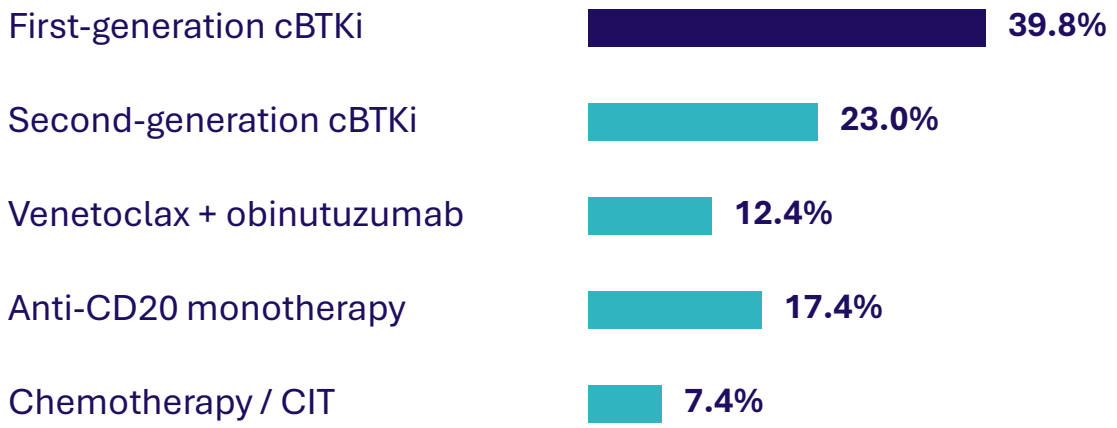
Fixed-duration venetoclax combinations and continuous second-generation BTK inhibitors are preferred options.

EHA first-line guidance[2]

Time-limited targeted therapy is preferred in the absence of TP53 aberrations. Treatment choice also reflects patient and disease factors.

Observed first-line use[3]

US ConcertAI cohort (n = 1,843)



Guidelines offer several targeted options, while treatment use varies across regimens

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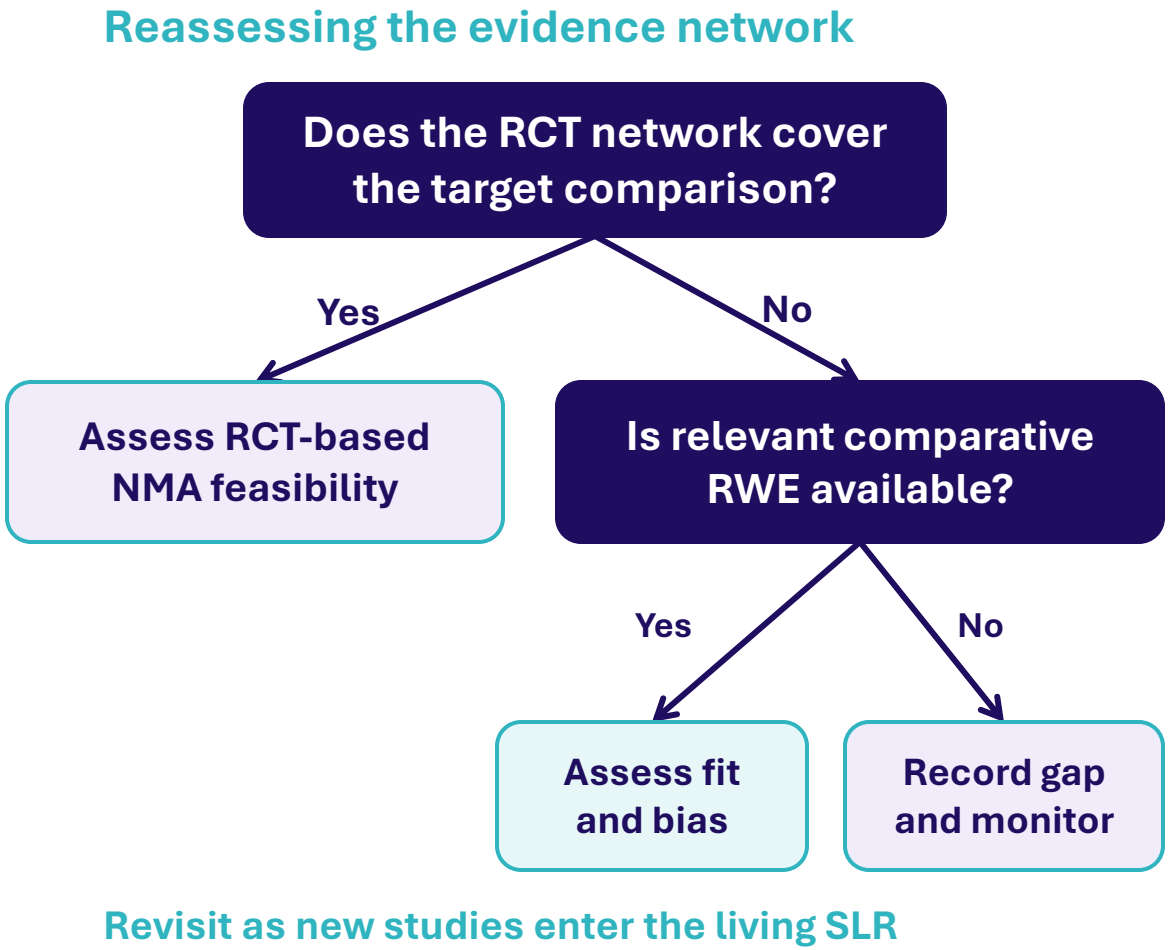
[1] NCCN Insights v2.2026 [2] Eichhorst et al. HemaSphere 2026 [3] Roeker et al. Cancers 2025

Implications for NMA

- Define the target comparison for the first-line population and outcome.
- RCTs and anchored indirect comparisons do not cover all relevant treatment options.
- EU-JCA increases the need for timely comparative effectiveness evidence.



A living SLR of interventional studies and RWE supports timely reassessment of the evidence available for NMA

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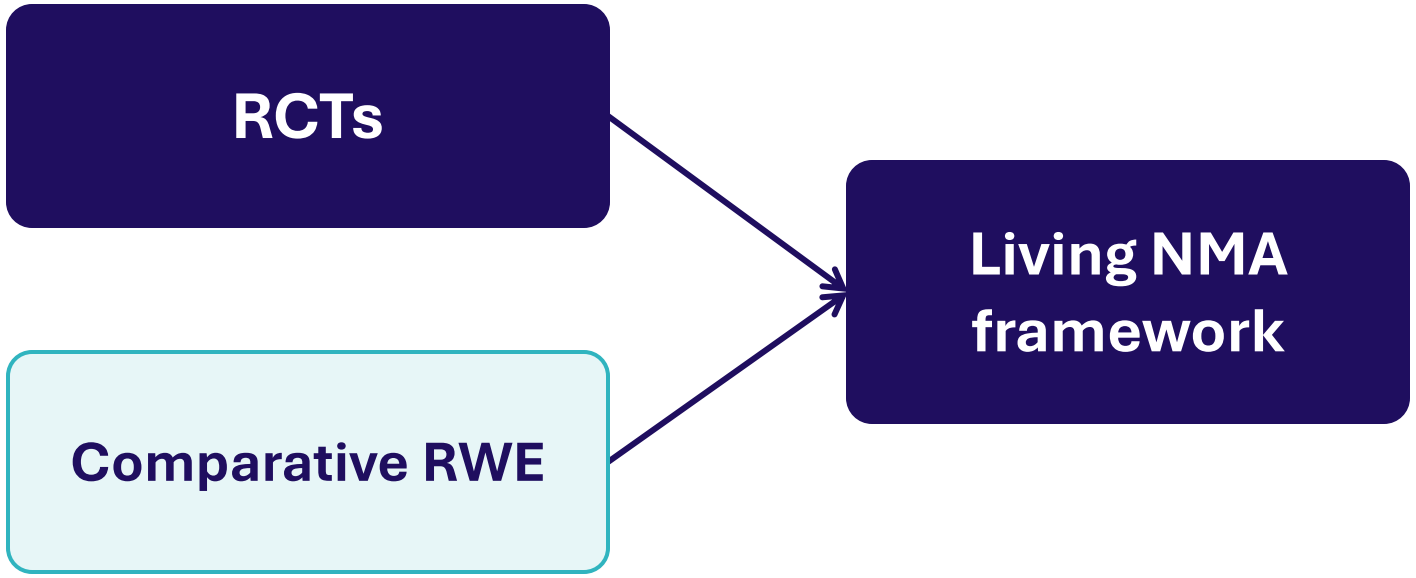
Objective

- **Develop a living RWE-informed NMA framework using the Oncoscope REAL-SLR database.**



Populations

First-line (1L) CLL
Relapsed/refractory (R/R) CLL

Outcomes

Overall survival (OS)
Progression-free survival (PFS)

Integrate trial and comparative real-world evidence to address CLL evidence gaps

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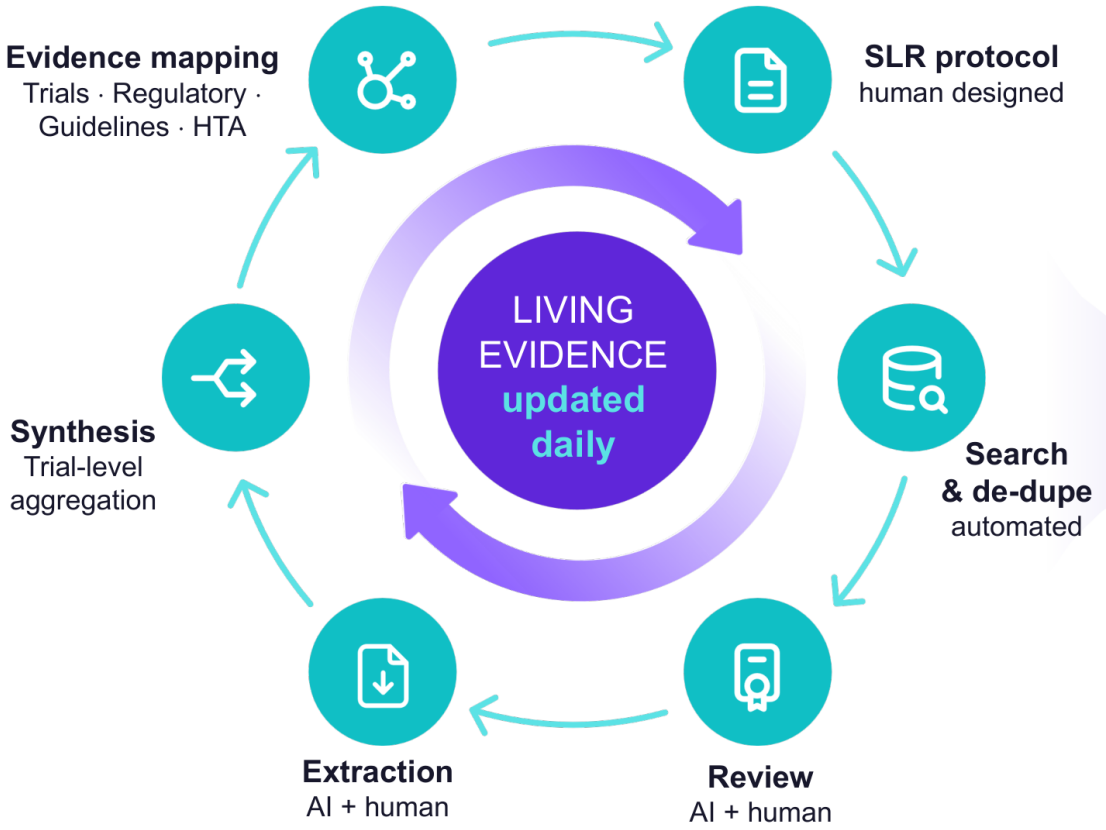
Methods: living SLR database

- PRISMA-compliant living evidence database with daily updates.
- Identify RCTs and comparative RWE reporting adjusted relative effects on OS and PFS.
- Document relevant effect modifiers in a living catalogue.



CLL STUDIES IN REAL-SLR

15 June 2026	4 November 2026
81 RCTs	**82 RCTs**
72 comparative RWE studies	**86 comparative RWE studies**

Daily evidence identification enables the living NMA to incorporate new studies

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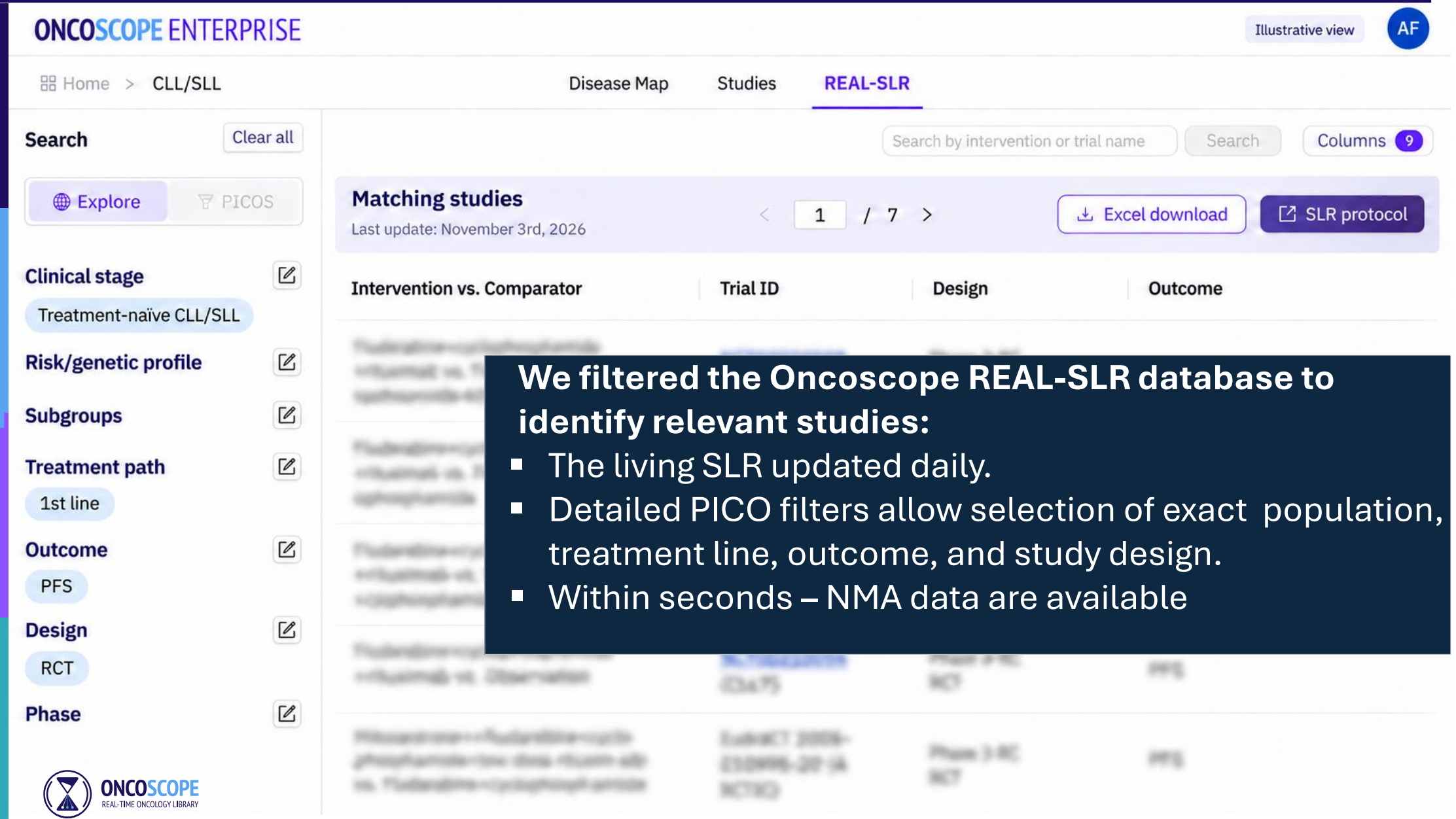
Methods: living SLR database



We filtered the Oncoscope REAL-SLR database to identify relevant studies:

- The living SLR updated daily.
- Detailed PICO filters allow selection of exact population, treatment line, outcome, and study design.
- Within seconds – NMA data are available

Evidence base

- CLL evidence available as of June 15, 2026

Population / outcome	All studies	RCTs	Comparative RWE
First-line PFS	32	31	1
R/R PFS	15	13	2
First-line OS	21	10	11
R/R OS	12	8	4

CLL database

81

RCTs

72

Comparative RWE

Analysis-specific counts; studies may contribute to more than one outcome

PFS analyses are largely RCT-based; comparative RWE contributes more to OS

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What changed since the June abstract?

First-line CLL/SLL • 15 June to 4 November 2026

2 RCTs with OS or PFS*

- **Orelabrutinib vs. rituximab** + chlorambucil - new **PFS** comparison
- **Ibrutinib + venetoclax vs. chlorambucil + obinutuzumab (GLOW)** updated long-term follow-up **OS and PFS**

3 Comparative RWE studies

- **Zanubrutinib vs. acalabrutinib vs. ibrutinib** - updated comparative **OS**
- **Venetoclax-based vs. cBTKi-based** vs. Other regimens reports comparative **OS**
- **Ibrutinib** vs. chemotherapy reports **OS**

Note: Counts precede NMA eligibility evaluation

Five additional study records to assess for indirect comparisons

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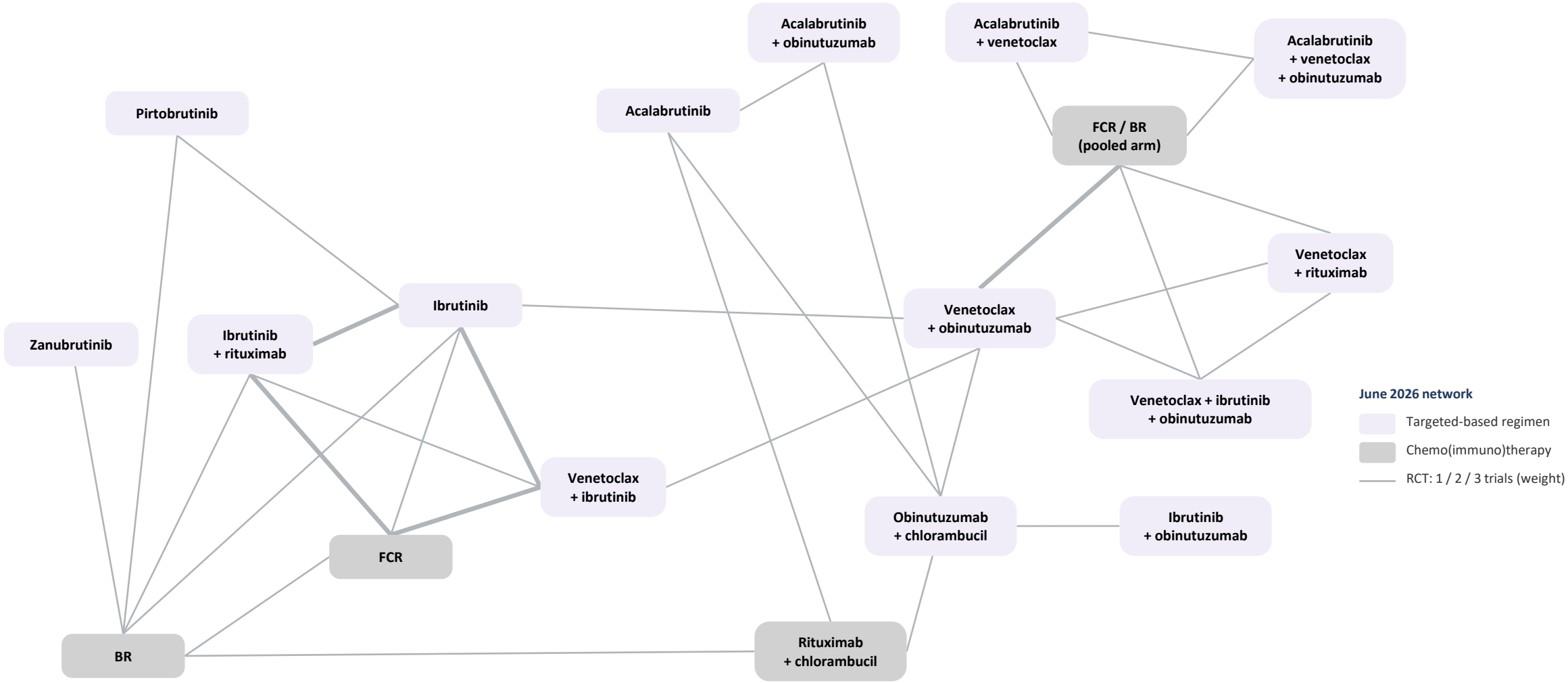
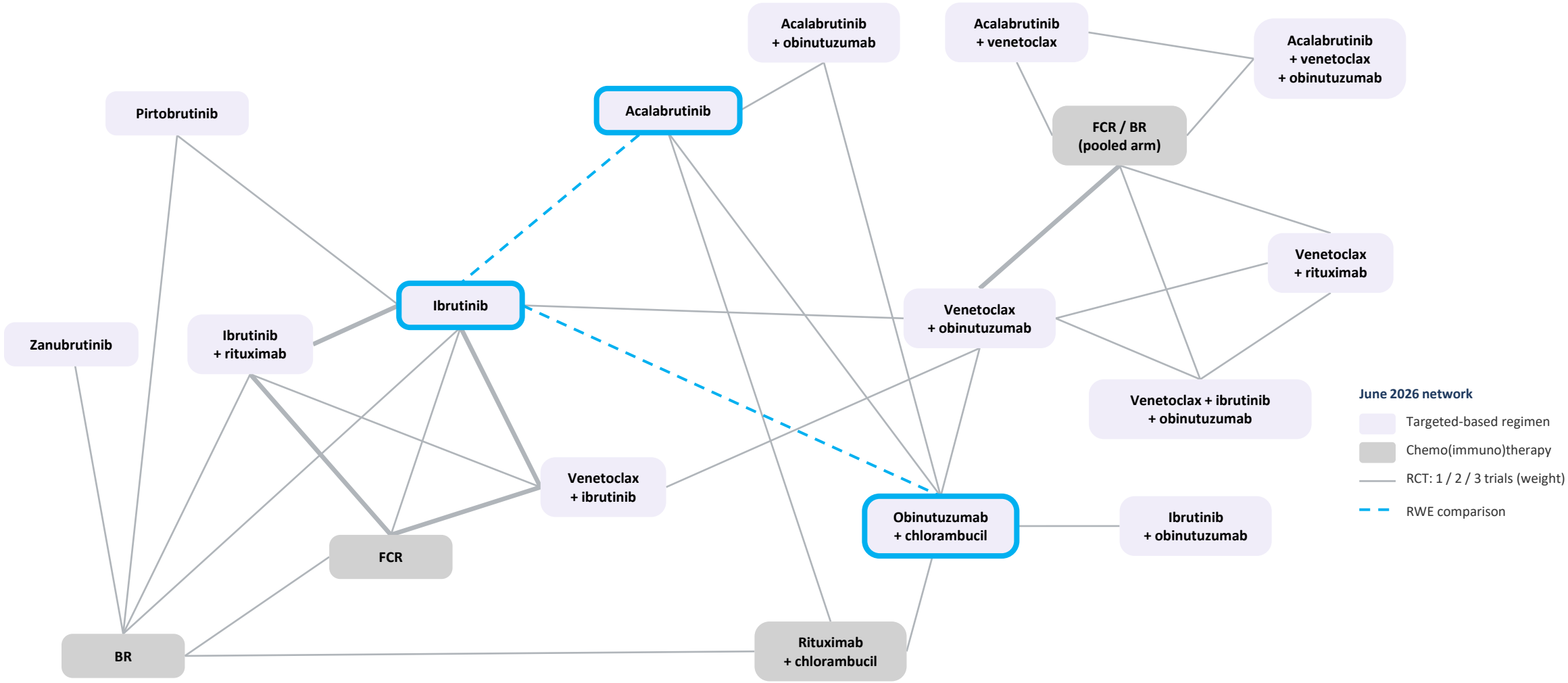
*1 new RCT and 1 update of previously identified RCT

PFS network in first-line CLL – RCTs only (June 2026)



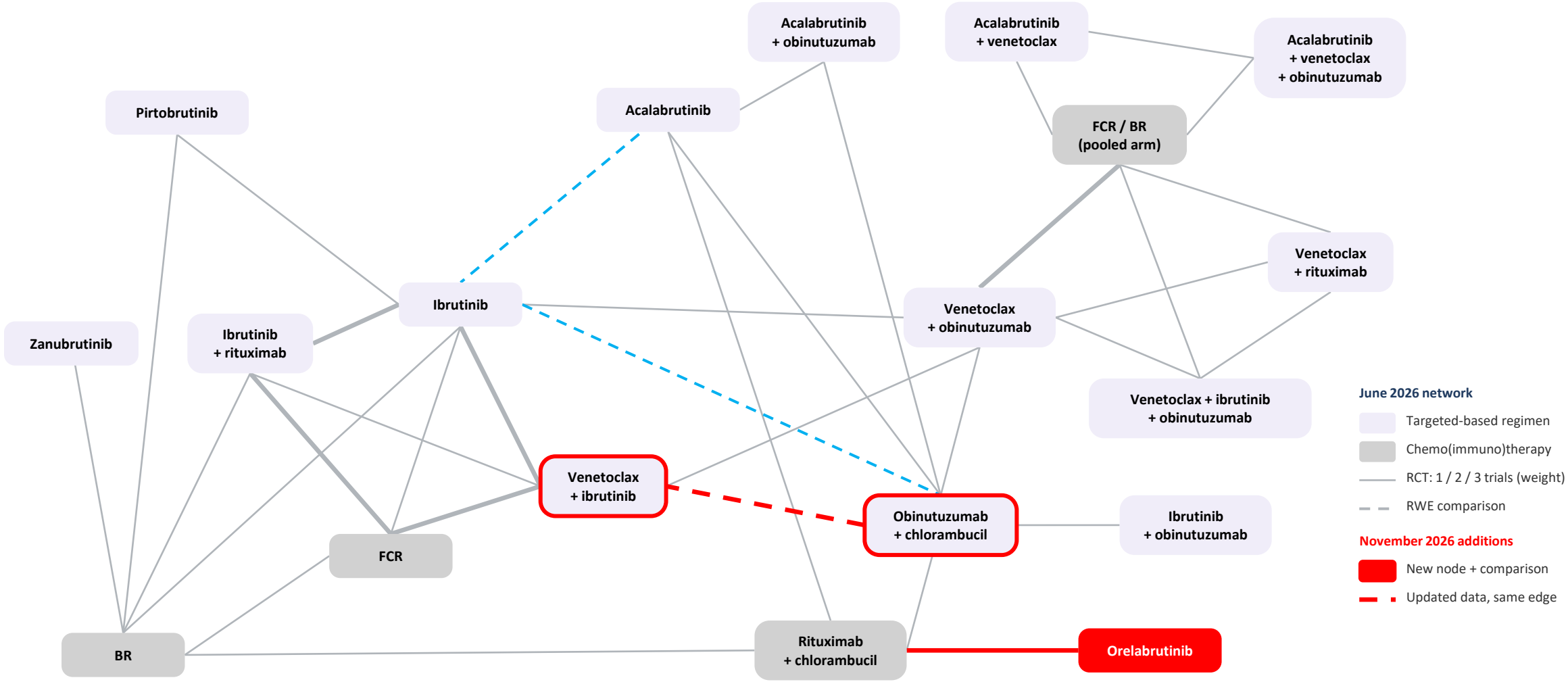
No indirect connection between important BTKi comparisons through RCTs only

PFS network in first-line CLL – RCTs + RWE (June 2026)



RWE adds important network connections

PFS network in first-line CLL – November 2026



November adds a new randomized comparison and updated follow-up data for an existing edge

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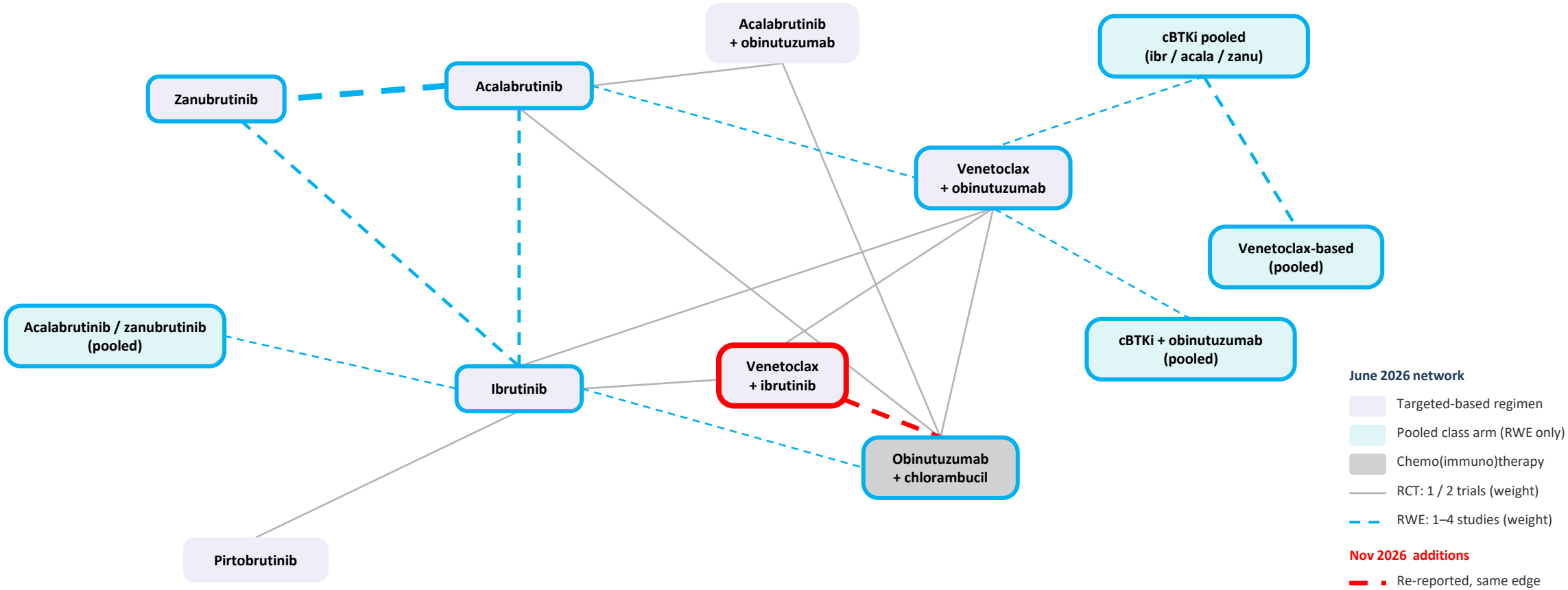
OS network in first-line CLL



RWE helped bridge BTK inhibitors. November adds updated follow-up data

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What RWE adds to the CLL evidence network

June abstract snapshot → November evidence update

June · Where RWE could bridge gaps

First-line PFS

Acalabrutinib vs. ibrutinib

First-line OS

Candidate links among BTK inhibitors and to venetoclax + obinutuzumab

Relapsed/refractory OS

Venetoclax alone vs. venetoclax-based combinations

November · What changed

2 RCTs + 3 comparative RWE studies

First-line PFS or OS records absent from the June workbook

PFS and OS

Updated PFS and OS data for previously published studies

New comparisons to assess

Orelabrutinib RCT for PFS and ibrutinib vs. chemotherapy RWE for OS

Note: Candidate RWE links require eligibility assessment.

RWE can bridge gaps. Living updates can add evidence to existing comparisons.

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Conclusions and next steps

- **REAL-SLR provides the evidence foundation for a living RWE-informed NMA in CLL.**

Study limitations

- Every time-specific snapshot will change as new evidence emerges.
- The abstract identifies potential bridges without reporting pooled NMA effects.

Next steps

- Continue daily study identification and refresh the effect-modifier catalogue.
- Assess RWE comparability and bias before integrating eligible evidence.



A living NMA can assess new evidence as the CLL treatment landscape evolves



Thank you

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Anna Forsythe

Founder & CEO

anna@oncoscope.com

+1-646-477-0936

WhatsApp and phone

oncoscope.com

