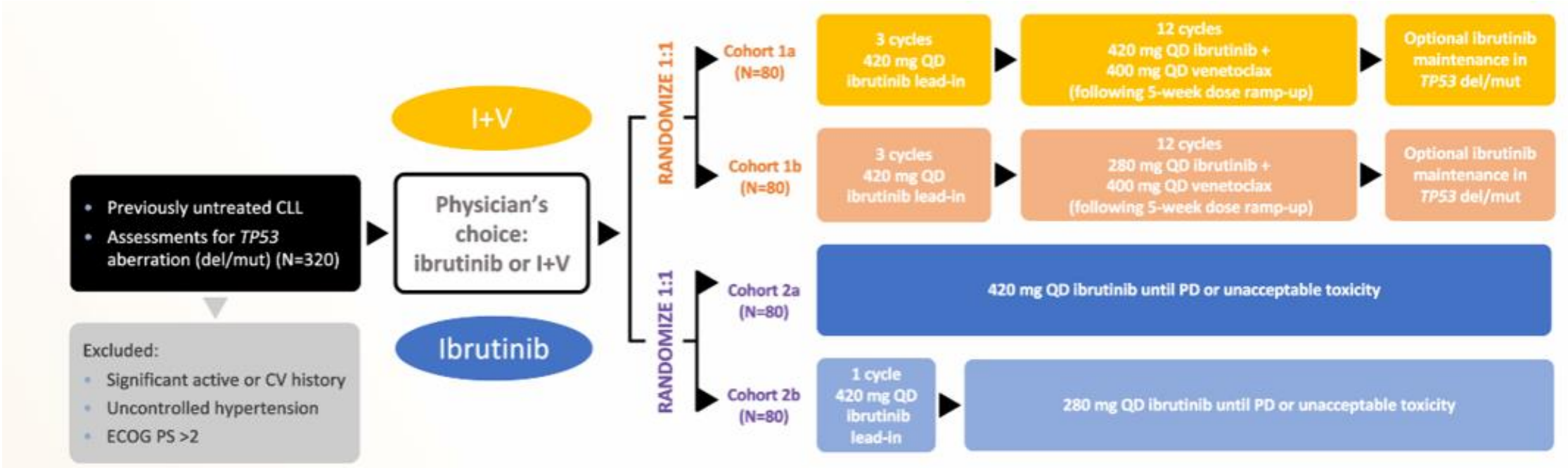
Tavola rotonda 27-11-2025

TAILOR Study Design



Stratification factors:
Number of medications currently prescribed for hypertension: 0 vs 1–2
Prior documented cardiac history: yes vs no
del(17p) or known *TP53* status: yes vs no

All cohorts will follow dose modification guidelines for AEs outlined in the protocol, based on recent label updates

- **Primary endpoint:** Best ORR (proportion of participants who achieve CR, CRi, nPR, PRL, or PR) over the course of the study
- **Secondary endpoints:** CR rate, DOR, PFS, OS, MRD negativity rate (Cohorts 1a and 1b only), AEs, discontinuation due to AEs, adherence rates, PROs

Abstract Number : abs25-7757

Abstract Title : Dose and BTK occupancy relationship in the prospective Phase 2 TAILOR study: Exploratory end point analysis of the ibrutinib monotherapy cohorts in patients with previously untreated chronic lymphocytic leukemia

Jacqueline Barrientos, Michael Doubek, Zsolt Lazar, Andrea Visentin, Javier de la Serna, Luca Laurenti, Alessandro Sanna, Laszlo Rejto, Lucrecia Yanez San Segundo, Paolo Sportoletti, Carl Gray, CelesteAnn Bremer, Aziz Ouerdani, Nicoline Treijtel, Brendan Hodkinson, John Loffredo, Claire Kavanagh, Sowmya Srikanthan, Ping Xu, Erin Franceschini, Christopher Abbazio, Brooke Patterson, Boo Messahel, Wasiulla Khan, Jan Burger, Lori Parisi, Mark Wildgust, Paolo Ghia, Jeff Sharman

TAILOR – ASH 2025

Exploratory analyses of the pharmacokinetics and pharmacodynamics data from the randomized Ibr monotherapy cohorts of the prospective phase 2 trial TAILOR study in pts with previously untreated CLL.

Results

Blood samples were evaluated from 21 pts: 10 from Cohort 2a and 11 from Cohort 2b. Pts had a median age of 76 years (range, 59-84) and 85.7% were aged ≥ 65 years. Of 21 pts, 7 had a TP53/del(17p) aberration and 14 of 18 assessed pts had unmutated IGHV. Data from additional patient samples will be included in the presentation.

Median predose BTK occupancy was similar between Cohorts 2a and 2b at C1D14 (99.4% [range, 98.7-99.9%] and 98.9% [range, 92.9-100.0%]), and C4D1 (99.5% [range, 98.3-100%] and 99.5% [range, 98.7-100.0%]). Median BTK occupancy for C1D14 and C4D1 combined was 99.4% for Cohort 2a and 99.2% for Cohort 2b. BTK occupancy was observed to be nearly complete for all Ibr plasma concentration levels measured at C1D14 and C4D1.

TAILOR – ASH 2025

Conclusions

In this exploratory end point analysis of the prospective phase 2 TAILOR study, both study cohorts had > 99% median post-baseline BTK occupancy regardless of Ibr dosage group.

These results indicate that high BTK occupancy levels can be maintained after proactively reducing Ibr dose to 280 mg QD after 1 cycle with 420 mg QD, with concomitant lower serum Ibr concentration in pts randomized to the proactively dose reduced Cohort 2b. Further analyses are needed to determine whether the observed BTK occupancy and lower Ibr serum concentrations are associated with similar efficacy and better safety outcomes.

- **La riduzione di dose di Ibrutinib da 420 mg a 280 mg con simile occupazione del BTK ci autorizza ad usarlo a dosaggio ridotto?**

- **Cambia qualcosa dal punto di vista prescrittivo?**

- **Vantaggio farmaco-economico incide sulla vs scelta?**

Abstract Number : abs25-7205 Constantine Tam

Sustained efficacy of zanubrutinib (zanu) vs bendamustine + rituximab (BR) in treatment (tx)-naive chronic lymphocytic leukemia/small lymphocytic lymphoma (TN SLL/CLL) and continued favorable survival in non-randomized patients (pts) with del(17p): 6-year follow-up in the phase 3 SEQUOIA study

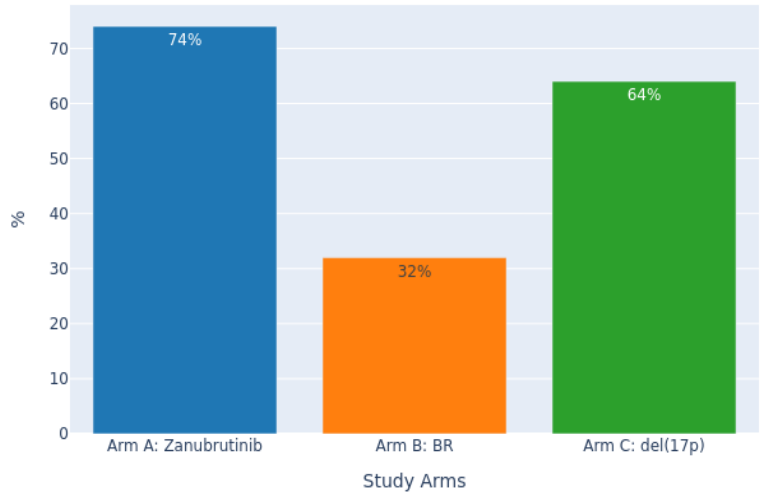
SEQUOIA Study: 6-Year Outcomes

Phase 3 SEQUOIA: Zanubrutinib vs BR in TN CLL/SLL

- Median follow-up: ~72 months
- Arms: A (Zanu), B (BR), C (del17p)
- Zanubrutinib shows sustained PFS superiority and longer TTNT

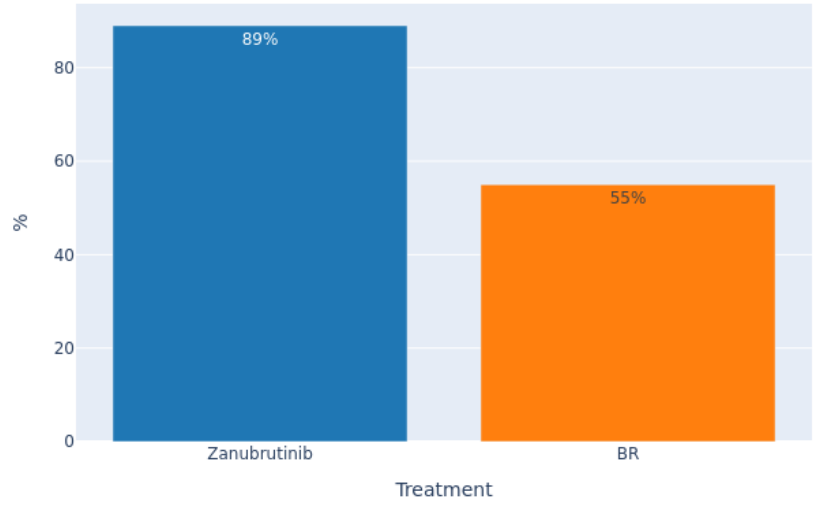
72-Month PFS

Hr=0,28; P<0,0001 ARM A vs B



72-Month TTNT

HR: 0,22



- **Zanubrutinib mantiene efficacia robusta e profilo di sicurezza favorevole a lungo termine, con beneficio anche nei pazienti ad alto rischio (del17p), supportando il suo uso come opzione di prima linea in CLL/SLL.**

- **64% di PFS a 72 mesi in pz con del 17p rende Zanubrutinib il farmaco di scelta per I pazienti non trattati con alto rischio biologico?**