Real-world treatment patterns and outcomes of Zanubrutinib in chronic lymphocytic leukemia and small lymphocytic leukemia (CLL/SLL)

Margaret Li Krackeler, MD[1], Bryant H Chee, MD[2]; Arthur K Orchanian, MD[2]; Lisa Law, MD[3]; Alfredo Lopez, MD[1]; Susan Buchanan, MS PA-C[4]; Gregory A. Maglinte, PhD MPH[4]; Raymond Liu, MD[1]; Zheng Zhu, MS[3]; Lori Sakoda, PhD[2]; Jahan Tavakoli, MD[1]

[1]Department of Hematology Oncology, Kaiser Permanente San Francisco, San Francisco, CA, USA; [2]Department of Internal Medicine, Kaiser Permanente San Francisco, San Francisco, CA, USA; [3]Division of Research, Kaiser Permanente San Francisco, San Francisco, CA, USA [4]BeiGene USA, San Mateo, CA, USA

Kaiser Permanente Research

BeiGene

Background

- Zanubrutinib (zanu) is a next-generation selective Bruton's tyrosine kinase inhibitor (BTKi) with superior efficacy and lower rates of cardiac events seen in clinical trials over first-generation ibrutinib (ibru) in CLL/SLL patients (pts). [1-4]
- Herein we present real-world treatment patterns and outcomes based on a formulary change from ibru to zanu in pts with CLL/SLL in an integrated community oncology practice.

Methods

- Retrospective analysis of CLL/SLL pts 18 years and older who received at least 3 months of zanu from October 1, 2018 to September 15, 2023 at Kaiser Permanente Northern California.
- Outcomes:

  •Treatment duration (defined as first fill to last fill of prescription), dose reduction rates, discontinuation rates, mortality

  •Treatment-emergent adverse events (TEAEs: AEs reported during BTKi use), treatment-limiting adverse events (TLAEs: AEs leading to BTKi discontinuation), cardiotoxicity TEAEs and TLAEs.

Table 1. Demographics	Overall (n=281)	Ibru to Zanu (n=190)	Zanu only (n=91)
Age at 1st BTKi fill, *median (range)*	**71** (64,76)	**69** (62,75)	**74** (66,80)
Sex, n (%) Male Female	**181** (64) **100** (36)	**117** (62) **73** (38)	**64** (70) **27** (30)
Race/ethnicity, n (%) White Black Other	**210** (75) **28** (10) **43** (15)	**138** (73) **22** (12) **30** (16)	**72** (79) **6** (7) **12** (14)
Charlston Comorbidity Index, mean (SD)	**2 .1** (1.8)	**2.0** (1.8)	**2.4** (1.8)
Insurance type, n (%) Commercial Medicaid Medicare	**87** (31) **7** (2.5) **186** (66)	**60** (32) **7** (3.7) **122** (64)	**27** (30) **0** (0) **64** (70)

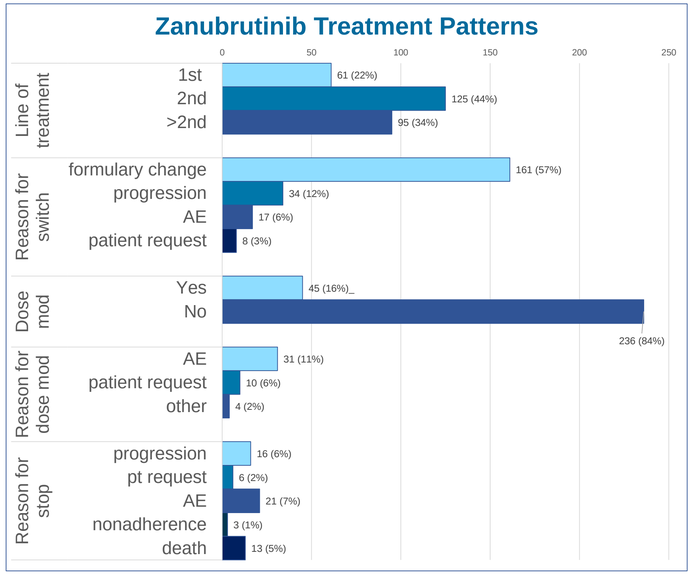
Table 2. Outcomes	While on Ibru (n=190)	While on Zanu (n=281)	After Ibru-Zanu Switch (n=190)	After Initiating Zanu Only (n=91)
Median Follow Up, mos. (range)	**46** (15,115)	**23.7** (3.3,26)	**24.4** (5.5,26)	**8.2** (3.3,25)
Median treatment duration, mos.	**20.8** (0.2,89)	**20.5** (3,25)	**22.8** (3,25)	**6.6** (3,25)
TEAE, n (%)	**69** (36.3)	**88** (31.3)	**56** (29.5)	**32** (35.2)
TLAE, n (%)	**21** (11.1)	**22** (7.8)	**14** (7.4)	**8** (8.8)
Cardiotoxicity, n (%)				
TEAE	**18** (9.5)	**6** (2.1)	**5** (2.6)	**1** (1.1)
TLAE	**8** (4.2)	**2** (0.7)	**2** (1.1)	**0** (0)
CTCAE grade of TLAE ≥3, n (%)	**7** (3.6)	**4** (1.4)	**3** (1.6)	**1** (1.1)

Results

- 281 pts received at least 3 mos of zanu: 190 pts switched from ibru, and 91 pts received zanu only
- 26 pts (9%) with del(17), 267 pts (95%) with unmutated IGHV, 13 pts (5%) with complex karyotype
- Lower TEAE, TLAE and cardiotoxicity rates seen with zanu use than with ibru use
- Special interest AE: atrial fibrillation

  •TEAE: 8 pts (4%) on ibru, 3 pts (1%) on zanu

  •TLAE : 3 pts (1.6%) on ibru, 1 pt (0.3%) on zanu
- Most common TLAEs:
  - On ibru: atrial fibrillation (1.6%), fatigue (1.6%)
  - On zanu: cytopenia (1.4%), rash/bruising (1%)
- Most TLAEs were reported as Grade1/2 by CTCAE (>67% of total TLAEs)
- Of the 281 zanu pts, 79% remain on treatment with median follow up of 24 months
- 13 pts died (8 from infection, including 5 from COVID), with no reports of treatment-related deaths.



Conclusion

- In the real-world setting post-formulary change, Zanubrutinib is effective and safe in patients with or without prior ibrutinib use
- Zanu use had lower rates of cardiotoxicity and TLAE than observed with ibru use with decreased rates after switch
- Limitations of study: Difference in follow-up time between ibru and zanu use; pts with <3mo of therapy were excluded
- In real world settings, discontinuation and dose reductions were most often due to low grade AEs by CTCAE

Contact & References

- **Margaret Krackeler, MD**
  Margaret.x.Krackeler@kp.org
- **Jahan Tavakoli, MD**
  Jahan.x.Tavakoli@kp.org

KAISER PERMANENTE®