Abstract: P671

Title: REAL-WORLD TREATMENT EFFECTIVENESS IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) RECEIVING VENETOCLAX-BASED THERAPY AFTER BRUTON TYROSINE KINASE INHIBITORS: AN INTERNATIONAL STUDY

Abstract Type: Poster Presentation

Topic: Chronic lymphocytic leukemia and related disorders - Clinical

Background:

Data on real-world venetoclax (ven) effectiveness following covalent Bruton tyrosine kinase inhibitors (cBTKi), especially for patients (pts) who are intolerant or progress on cBTKis, as well as pts treated with ven+rituximab (VR), remains limited despite demonstrated clinical benefits in newly diagnosed or relapsed/refractory (R/R) chronic lymphocytic leukemia/small lymphocytic leukemia (CLL/SLL).

Aims:

The CLL Collaborative Study of Real-World Evidence (CORE), a retrospective, international, observational study, assessed clinical outcomes in pts who initiated ven after discontinuing cBTKis.

Methods:

CORE contributed data for adult pts with CLL/SLL initiating ven post-cBTKi. Clinical outcomes were overall response rate (ORR; i.e., proportion of pts with physician-defined complete/partial response as recorded in pts' medical charts among those with available response), progression-free survival (PFS; i.e., time from ven start to disease progression/death or last follow-up), and time to next treatment or death (TTNT-D; i.e., time from ven start to subsequent treatment start/death or last follow-up). Median (m) PFS and TTNT-D, and time-specific rates, were estimated using Kaplan-Meier methods. Outcomes were assessed overall and stratified by *reason for cBTKi discontinuation* (intolerance [DI]/progression [DP]), for *pts treated with VR*, and by *line of therapy* (1L cBTKi→2L ven/2L cBTKi→3L ven).

Results:

Of 2,253 included patients, 1,515 pts (67.2%) were treated with cBTKi; 705 pts (46.5% of 1,515) discontinued their cBTKi. The overall cohort included 200 pts (28.4% of 705) treated with ven post-cBTKi. Pts had a median age of 68.7 (IQR: 62.5, 76.4) with 69.0% male. Median follow-up was 16.4 months (mo; IQR: 6.0, 30.5). The outcomes were reported *by reason for cBTKi discontinuation* for DI: 85 pts and for DP: 75 pts; for 60 *pts treated with VR*;* and *by line of therapy* for1L cBTKià2L ven: 68 pts and for 2L cBTKià3L ven: 73 pts (4L ven+: 59 pts; not reported).

For the overall cohort of 200 pts, the ORR was 79.7% (DI: 84.7%; DP: 76.0%; VR: 71.8%). mPFS was 44.3 mo (DI: not reached [NR]; DP: 30.1 mo; VR: 39.5 mo; see Figure 1) with 12-mo PFS rate 85.5% (DI: 89.0%; DP: 81.8%; VR: 89.4%) and 18-mo rate 78.2% (DI: 87.2%; DP: 70.4%; VR: 79.4%). mTTNT-D was 39.5 mo (DI: NR; DP: 30.4 mo; VR: 37.4 mo) with 12-mo TTNT-D rate 83.6% (DI: 84.0%; DP: 85.9%; VR: 82.8%) and 18-mo rate 74.4% (DI: 78.8%; DP: 74.7%; VR: 75.8%).

For the 68 pts with 1L cBTKià2L ven, the ORR was 84.8%. mPFS was NR; with 12-mo PFS rate 90.8% and 18-mo rate 86.0%. mTTNT-D was 39.5 with 12-mo TTNT-D rate 85.8% and 18-mo rate 73.0%.

For the 73 pts with 2L cBTKià3L ven, ORR was 80.4%. mPFS was 44.3 mo with 12-mo PFS rate of 86.5% and 18-mo rate 82.1%. mTTNT-D was 44.2 mo with 12-mo TTNT-D rate 84.5% and 18-mo rate 78.4%.

Summary/Conclusion:

Our study shows that ven is effective post cBTKi; and is associated with durable remission and delayed time to

subsequent treatment in the R/R setting, with a mPFS of 44.3 months. Notably, clinical effectiveness was demonstrated both among patients who were intolerant to cBTKi as well as those who progressed after cBTKi and likely had more aggressive disease; it was also effective among patients treated with VR. Given the evolving CLL/SLL treatment landscape, these results provide further evidence to inform clinical practice and highlight the effectiveness of ven. Future studies including larger cohorts and longer follow-up will be undertaken to continue contributing to this body of evidence.

Figure 1. Clinical outcomes for the overall cohort and stratified by line of therapy (1L cBTKi → 2L ven/2L cBTKi → 3L ven), by reason for cBTKi discontinuation (intolerance/progression), and for pts treated with VR

		PFS			TTNT-D		
		Median (CI), months	Rate, % 12 months (CI)	Rate, % 18 months (CI)	Median (CI), months	Rate, % 12 months (CI)	Rate, % 18 months (CI)
Overall	Overall (N=200)	44.3 (38.9, NR)	85.5%	78.2%	39.5 (31.9, NR)	83.6%	74.4%
	1L→2L (N=68)	NR (39.5, NR)	90.8%	86.0%	39.5 (31.9, NR)	85.8%	73.0%
	2L→3L (N=73)	44.3 (36.3, NR)	86.5%	82.1%	44.2 (37.0, NR)	84.5%	78.4%
Intolerance	Overall (N=85)	NR	89.0%	87.2%	NR	84.0%	78.8%
	1L→2L (N=33)	39.5 (39.5, NR)	96.2%	91.6%	39.5 (39.5, NR)	89.2%	76.4%
	2L→3L (N=33)	NR	89.0%	89.0%	NR	87.2%	87.2%
Progression	Overall (N=75)	30.1 (20.4, NR)	81.8%	70.4%	30.4 (26.3, NR)	85.9%	74.7%
	1L→2L (N=15)	31.9 (13.2, NR)	77.8%	62.2%	31.9 (12.5, NR)	77.8%	53.3%
	2L→3L (N=30)	31.8 (22.1, NR)	82.6%	73.1%	37.4 (26.3, NR)	84.0%	75.2%
Venetoclax + rituximab	Overall (N=60)	39.5 (31.8, NR)	89.4%	79.4%	37.4 (31.6, NR)	82.8%	75.8%
	1L→2L (N=29)	NR (39.5, NR)	91.8%	91.8%	NR (39.5, NR)	84.3%	84.3%
	2L→3L (N=23)	36.3 (23.7, NR)	93.8%	85.9%	37.4 (31.6, NR)	85.9%	79.8%

Keywords: Chronic lymphocytic leukemia, Venetoclax