3903

Real-World Use of Fixed-Duration Ibrutinib+Venetoclax in Patients With Previously Untreated Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma: Pooled Analysis of REALITY-Worldwide and REALITY-2 Prospective Cohort Studies

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Key Takeaway

This largest prospective RW dataset to date confirms the efficacy and safety of FD Ibr+Ven for patients with CLL/SLL across all age groups (≥ 65 and < 65 years)

Conclusions

- High ORR confirmed in RW data after 9 treatment cycles; 90% ORR and 30% CR
- Low rate of treatment discontinuations due to TEAEs (3.9%) and dose adjustments (8.8%) confirm the well-tolerated profile of FD Ibr+Ven
- FD Ibr+Ven is well suited for outpatient administration, with no TEAEs or hospitalizations due to TLS and high physician agreement (88%) on the advantage of its route of administration, supporting the use of this all-oral regimen for patients with CLL/SLL

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Poster

https://www.congresshub.com/ASH2025/Oncology/Ibrutinib/Thieblemont

Acknowledgments

This study was funded by Johnson & Johnson and PCYC, an AbbVie company. Professional medical writing and editorial assistance were provided by Bradley Richardson, PhD, of Parexel, funded by Johnson & Johnson.

Disclosures

Catherine Thieblemont reports consultancy for Novartis, Johnson & Johnson, BeOne Medicines, AbbVie, Bristol Myers Squibb/Celgene, Takeda, Kite/Gilead, and Regeneron; research funding from Roche, AbbVie, and Kite/Gilead; and honoraria from ADC Therapeutics, AstraZeneca, Incyte, Sanofi, Amgen, Novartis, Cellectis, Johnson & Johnson, Bayer, Roche, BeOne Medicines, AbbVie, Bristol Myers Squibb/Celgene, Takeda, Kite/Gilead, and Regeneron.

Introduction

- Fixed-duration (FD) ibrutinib+venetoclax (Ibr+Ven) is approved as first-line (1L) treatment for chronic lymphocytic leukemia (CLL) in 78 countries across Asia, Europe, the Middle East, and South America, plus Australia, Canada, and New Zealand
- Clinical trials with up to 5.5 years of follow-up have demonstrated progression-free and overall survival benefits of 1L FD Ibr+Ven in patients (pts) with CLL/small lymphocytic lymphoma (SLL)[1-3]
- Despite the established benefit from clinical studies, there is a lack of supporting real-world (RW) evidence on the effectiveness and tolerability of FD Ibr+Ven outside of a clinical trial setting
- REALITY-WW (Worldwide) and REALITY-2 (Germany) are prospective observational cohort studies
  - REALITY-WW evaluated usage, factors for therapy decision, and clinical response of FD Ibr+Ven in routine clinical practice in pts with CLL across 58 sites in Europe, the Middle East, and Latin America[4]
  - REALITY-2 assessed treatment adherence, effectiveness, and safety outcomes in pts with CLL receiving Ibr+Ven in an RW setting in Germany[5]
- Here we present pooled data from REALITY-WW and REALITY-2 to understand the clinical response, safety, and factors for therapy decision of FD Ibr+Ven in routine clinical practice

Methods

- REALITY-WW and REALITY-2 included pts with untreated CLL/SLL from hospitals and medical institutions where Ibr+Ven was routinely used
- Pts included were aged ≥ 18 years with a confirmed CLL/SLL diagnosis requiring 1L treatment per International Workshop on CLL (iwCLL) 2018 criteria
  - Pts received 3 cycles of Ibr, followed by 12 cycles of FD Ibr+Ven (Ibr 420 mg/d; Ven, 5-week ramp-up to 400 mg/d)
  - The decision to start FD Ibr+Ven was made prior to and independent of pt enrollment
- The primary end point was overall response rate (ORR) per iwCLL 2018 criteria
- Secondary end points included treatment-emergent adverse events (TEAEs), tumor lysis syndrome (TLS) risk, and factors influencing physician decision-making

Results

Patients

- At data cutoff (REALITY-WW, August 2025; REALITY-2, March 2025), 181 pts from both studies received FD Ibr+Ven (REALITY-WW, 133; REALITY-2, 48)
- The median time on study was 6.7 months
- Median age was 66.0 years, with 42.5% of pts aged < 65 years and 57.5% of pts aged ≥ 65 years; 64.1% were male
- Median duration of treatment exposure was 6.6 and 3.3 months for Ibr and Ven, respectively

ORR in FD Ibr+Ven patients

- ORR was assessed in a subset of pts from REALITY-WW (88 pts) with ≥ 1 post-baseline assessment
- ORR was 89.8% (95% confidence interval [CI]: 83.44-96.10) at the end of 9 treatment cycles (3 months of Ibr and 6 months of Ibr+Ven) per iwCLL 2018 criteria, including complete response (CR; 29.5%), CR with incomplete hematological recovery (CRi; 1.1%), partial response (PR; 35.2%), and PR with lymphocytosis (PR-L; 23.9%). Stable disease (SD) occurred in 8.0% of pts (Figure 1)

TLS risk in FD Ibr+Ven patients

- Zero pts had TEAEs or hospitalizations due to TLS events
- The number of pts at high and intermediate risk of TLS declined between baseline and Cycle 3 from 20.4% and 39.2% to 12.7% and 23.2%, respectively (Figure 2)
- 138 of 181 pts at baseline and 108 of 181 pts at treatment Cycle 3 were assessed for TLS risk
- 8 pts (7 aged ≥ 65 years and 1 aged < 65 years) were hospitalized prophylactically after the Ven ramp-up period for TLS

Safety of FD Ibr+Ven in patients with CLL/SLL

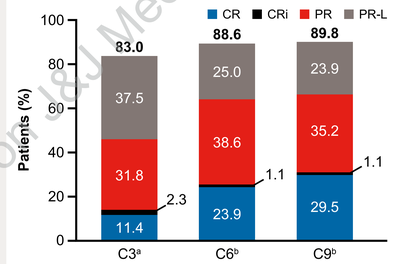
- Gastrointestinal disorders were the most common form of TEAE (31.5%) with diarrhea, dyspepsia, and nausea affecting 15.5%, 7.2%, and 6.6% of pts, respectively
- Muscle spasms (9.9%), fatigue (9.4%), and arthralgia (7.2%) were among other reported TEAEs
- The most common grade 3/4 TEAEs were neutropenia (1.7%), anemia (1.1%), back pain (1.1%), and myocardial infarction (1.1%)
- Treatment-emergent atrial fibrillation occurred in 5.0% of pts (grade 3/4, 0.6%) and hypertension in 2.8% of pts (no grade 3/4 events)
- Dose modification was observed in 10.5% (Ibr) and 3.3% (Ven) of pts, mainly due to treatment-associated TEAE/toxicity/TLS (Table 2)

Table 1: Baseline patient characteristics

Characteristic	All treated pts (N = 181)
Median time on study (range), months	6.7 (0.1-19.0)
Median age (range), years	66.0 (37.0-87.0)
Pts aged < 65 years, %	42.5
Pts aged ≥ 65 years, %	57.5
Sex, n (%)	
Female	65 (35.9)
Male	116 (64.1)
Median duration of treatment exposure (range), months	
Ibr	6.6 (0.1-15.9)
Ven	3.3 (0.1-11.4)
Median relative dose intensity (range), (%)[a]	
Ibr	97.1 (29.2-222.1)
Ven	77.7 (2.7-105.0)
ECOG PS, n (%)	
0-1	156 (98.1)[b]
2	3 (1.9)[b]
CIRS score > 6, n (%)	21 (12.5)[c]
< 65 years	4 (5.3)[d]
≥ 65 years	17 (18.3)[e]
***TP53* mutation, n (%)**	11 (6.4)[f]
Unmutated IGHV, n (%)	88 (50.6)[g]

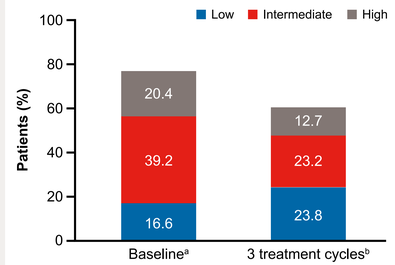
[a]Relative dose intensity (%) = (Average daily dose (mg) / Expected dose intensity per protocol (mg))*100. [b]159 assessed. [c]168 assessed. [d]75 assessed. [e]93 assessed. [f]173 assessed. [g]174 assessed.
CIRS, Cumulative Illness Rating Scale; ECOG PS, Eastern Cooperative Oncology Group performance status.

Figure 1: Overall response rates



n = 88; [a]5 (5.7%) and [b]2 (2.3%) pts not evaluable.
C, Cycle.

Figure 2: TLS risk



[a]n = 138; 39 (21.5%) not assessed and 4 (2.2%) missing. [b]n = 108; 33 (18.2%) not assessed and 40 (22.1%) missing.

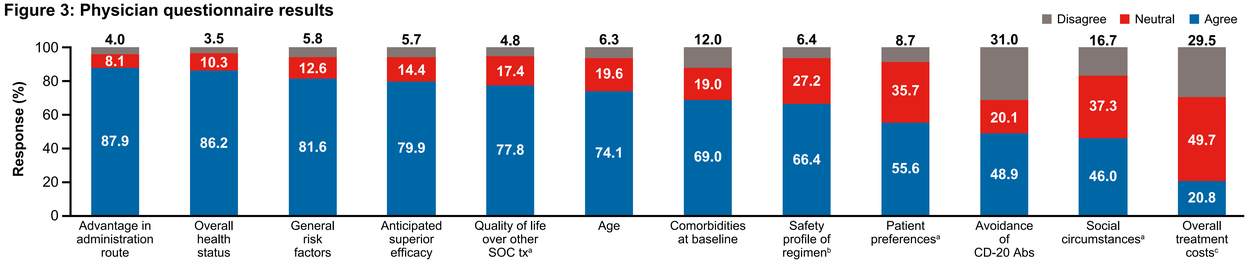
Table 2: Summary of safety in FD Ibr+Ven patients

Summary of adverse events	Treated pts (N = 181)
Any TEAE	112 (61.9%)
Serious TEAE	23 (12.7%)
Grade 3/4 TEAE	19 (10.5%)
TEAEs leading to discontinuation of ≥ 1 study treatment	7 (3.9%)
TEAEs leading to dose reduction of ≥ 1 study treatment	16 (8.8%)
TEAEs leading to interruption of ≥ 1 study treatment	41 (22.7%)

Factors influencing the decision to initiate FD Ibr+Ven

- Administration route advantage (87.9%), overall health status (86.2%), and general risk factors (81.6%) were the most common factors associated with decision to initiate FD Ibr+Ven (Figure 3)
- Avoidance of CD-20 antibodies (48.9%), social circumstances (46.0%), and overall treatment costs (20.8%) were among the least important factors (Figure 3)

Figure 3: Physician questionnaire results



n = 174, physician's treatment decision questionnaire performed.
Note: Agree/Strongly agree combined, Disagree/Strongly Disagree combined. Neutral indicated neither agreed or disagreed. [a]Answers only available for 126 pts or [b]125 pts (REALITY-WW). [c]Answers only available for 173 pts.
Ab, antibody; SOC, standard of care; tx, treatment.

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B-cell Malignancies

Presented by C Thieblemont at the 67th ASH Annual Meeting; December 6-9, 2025; Orlando, FL, USA