PF613

Real-World First-Line Fixed-Duration Ibrutinib+Venetoclax Treatment in Patients With Chronic Lymphocytic Leukemia: Analysis From the Prospective REALITY-Worldwide Study

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Key Takeaway

REALITY-WW demonstrates the effectiveness and tolerability of FD Ibr+Ven in routine clinical practice, including in elderly patients and those with high-risk features

Conclusions

ORR was high throughout treatment, reaching 94.5% by the end of 15 treatment cycles

FD Ibr+Ven is well tolerated in a diverse RW population, with low rates of neutropenia (14.8%), and no increase in TLS risk after the Ibr lead-in period. The low rates of atrial fibrillation (3.8%) were comparable to those reported with other BTKis, supporting this as a BTKi class effect

Low rates of Ibr discontinuation due to TEAEs (2.9%) show the robustness of FD Ibr+Ven in an RW setting

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Poster

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Disclosures

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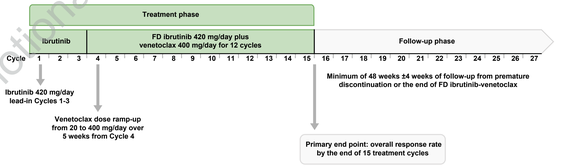
Introduction

- Fixed-duration (FD) ibrutinib + venetoclax (Ibr+Ven) has demonstrated noninferiority to continuous Ibr, with similar 3-year progression-free survival (PFS) and overall survival (OS) rates in patients with previously untreated chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL)[1]
- FD Ibr+Ven also achieves OS rates comparable with an age-matched general European population[2]
- FD Ibr+Ven is approved in 78 countries[3] and real-world (RW) data have been reported on its use
- Pooled analysis from the REALITY-worldwide (WW) and REALITY-2 studies indicated that FD Ibr+Ven has a manageable safety profile and is effective in clinical practice[4]
- The Spanish LI+VE RW study reported a tolerable safety profile, low rates of discontinuations, and 6-month OS/PFS rates of 100%/98.9%[5]
- In the Thrive study, rates of discontinuations were favorable when compared with historical trials, including in patients aged ≥ 65 years without del17p[6]
- Here we present analysis from the REALITY-WW RW prospective study, with a median time on study of 9.6 months

Methods

- Patients aged ≥ 18 years with first-line CLL/SLL requiring treatment were enrolled over 63 sites in Brazil, France, Israel, Italy, and the United Kingdom
- Decision to start treatment with FD Ibr+Ven was taken prior to, and independent of, the patient's enrollment in the study
- Patients received a 3-cycle lead-in of Ibr (420 mg once daily), followed by 12 cycles of FD Ibr+Ven (with Ven dose ramp-up from 20 to 400 mg over 5 weeks) (**Figure 1**)
- Data were collected every ~ 12 weeks during routine clinic follow-up visits until subsequent treatment or study completion
- The primary end point was best overall response rate (ORR) by the end of 15 treatment cycles; ORR included complete response (CR), CR with incomplete hematological recovery (CRi), partial response (PR), and PR with lymphocytosis (PR-L)
- Secondary end points included PFS, OS, and safety

Figure 1: Study design for REALITY-WW



Results

Patients

- As of March 2026, all patients are now fully enrolled. 175 patients are still on study treatment, and 16 patients have completed study treatment
- 18 patients discontinued study treatment prematurely
- The median age was 66 years, with 54.1% of patients aged ≥ 65 years and 19.1% ≥ 75 years
- Median time on study was 9.6 months

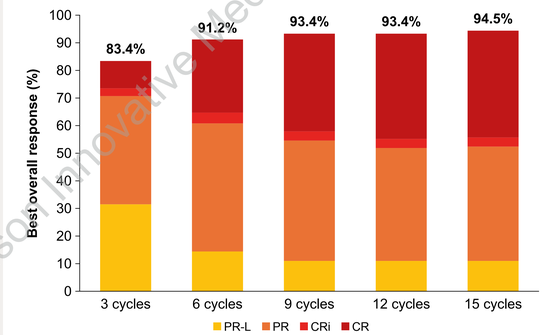
Table 1: Patient baseline characteristics

Characteristic	Treated patients (N = 209)
Median age (range), years	66.0 (39-87)
Patients aged ≥ 65 years, n (%)	113 (54.1)
Patients aged ≥ 75 years, n (%)	40 (19.1)
Sex, n (%)	
Male	137 (65.6)
Female	72 (34.4)
Initial diagnosis, n (%)	
CLL	200 (95.7)
SLL	9 (4.3)
CIRS score, n (%)[a]	
> 6	23 (12.0)
ECOG PS, n (%)[b]	
0-1	172 (97.2)
2	5 (2.8)
IGHV status, n (%)[c]	
Unmutated	87 (42.9)
Mutated	57 (28.1)
Not available	55 (27.1)
Not assigned to a group	4 (2.0)
***TP53*, n (%)[d]**	
Mutation present	6 (3.0)
No mutation present	167 (82.7)
Not available	29 (14.4)
Del17p, n (%)[c]	
Mutation present	25 (12.3)
No mutation present	130 (64.0)
Not available	48 (23.6)

[a]191 assessed. [b]177 assessed. [c]203 assessed. [d]202 assessed.
CIRS, Cumulative Illness Rating Scale; ECOG PS, Eastern Cooperative Oncology Group performance status.

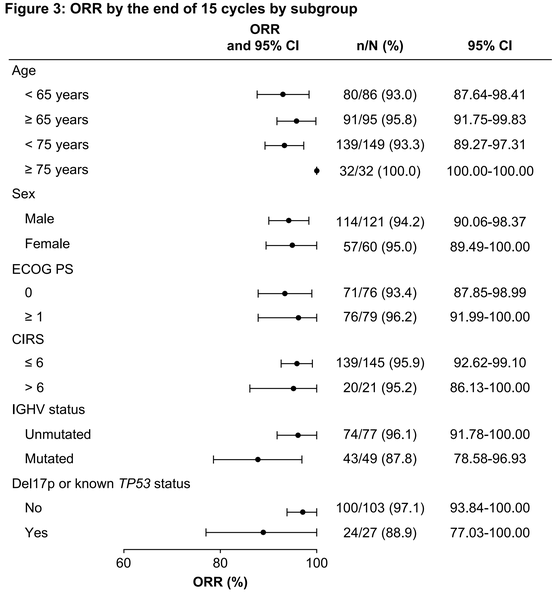
Overall response rate in FD Ibr+Ven–treated patients with at least 1 postbaseline assessment

Figure 2: ORR by the end of 3, 6, 9, 12, and 15 treatment cycles



At 3 cycles = 8.3% with stable disease (SD), 1.1% with progressive disease (PD), and 7.2% not evaluable (NE). At 6 cycles = 4.4% SD, 1.1% PD, and 3.3% NE. At 9 cycles = 3.3% SD, 1.1% PD, and 2.2% NE. At 12 cycles = 3.3% SD, 1.1% PD, and 2.2% NE. At 15 cycles = 2.8% SD, 1.1% PD, and 1.7% NE.

Figure 3: ORR by the end of 15 cycles by subgroup



CI, confidence interval.
Analysis set includes patients with at least 1 postbaseline assessment; CIs are based on normal approximation (Wald's CI).

- Among the 181 treated patients who had ≥ 1 postbaseline disease assessments, ORR was 94.5% (95% CI, 91.2-97.8) by the end of 15 treatment cycles, including a CR in 38.7%, CRi in 3.3%, PR in 41.4%, and PR-L in 11.0% (**Figure 2**). Additionally, 5 patients had stable disease, 2 had progressive disease, and 3 were not evaluable
- When evaluating all response assessments available by the end of each treatment cycle, ORR was 83.4% by the end of 3 treatment cycles, 93.4% by the end of 9 treatment cycles, and 94.5% by the end of 15 treatment cycles
- ORR was generally consistent across patient subgroups (**Figure 3**)

Safety in FD Ibr+Ven–treated patients

- Overall median duration of exposure was 9.1 months, with 8.6 months (range: 0.1-17.3) and 6.3 months (range: 0.0-14.1) for Ibr and Ven, respectively
- Any-grade treatment-emergent adverse events (TEAEs) were reported in 148 (70.8%) patients, the most common of which were infections (20.6%) and diarrhea (18.7%) (**Table 2**)
- Severe TEAEs were reported in 36 (17.2%) patients and serious TEAEs in 31 (14.8%)
- 8 (3.8%) patients had reported atrial fibrillation, 2 (1.0%) of which were severe; 4 of these patients had either an interruption or reduction of Ibr dose. Of these 8 patients, 2 had a history of cardiac disease and 4 had a history of hypertension
- 6 (2.9%) patients had TEAEs leading to discontinuation of Ibr, 23 (11.0%) leading to modification of Ibr dose, and 50 (23.9%) leading to interruption of Ibr dose
- No cases of clinical/laboratory tumor lysis syndrome (TLS) were reported
- Of the 57 patients who were classified as having high TLS risk at baseline, 26 had a reduction to intermediate or low risk, and no patients had an increase in TLS risk between baseline and Cycle 4
- 2 patients aged ≥ 75 years discontinued Ibr due to TEAEs

Table 2: TEAEs occurring in ≥ 5% of patients

Treatment-emergent adverse event	Any grade, n (%)	Severe, n (%)
Infections and infestations[a]	43 (20.6)	8 (3.8)
Diarrhea	39 (18.7)	0
Neutropenia	31 (14.8)	12 (5.7)
Muscle spasms	19 (9.1)	0
Arthralgia	19 (9.1)	0
Nausea	17 (8.1)	0
Fatigue	15 (7.2)	0
Contusion	13 (6.2)	0
Thrombocytopenia	12 (5.7)	3 (1.4)
Hypertension	11 (5.3)	1 (0.5)

[a]System organ class.

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B-cell Malignancies

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