Ibalizumab demonstrates real-world durability in people living with multi-drug resistant HIV

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BACKGROUND

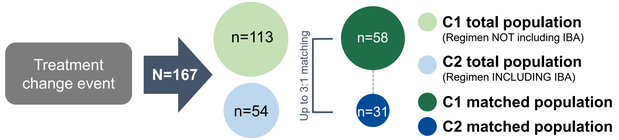
- In North America, approximately 1% of people with HIV-1 are heavily treatment-experienced (HTE) with multidrug resistant (MDR) strains.[1]
- This clinically complex population has extensive prior exposure to antiretrovirals (ARVs); however, establishing and maintaining virologic control can be challenging, as fewer fully-suppressive ARV regimens are available.[2,3]
- Ibalizumab (IBA) is a CD4-directed, post-attachment inhibitor of HIV indicated for treatment of HIV-1 in HTE adults with MDR who are failing their current ARV regimen.[4]
- IBA has a unique mechanism of action and demonstrates no evidence of cross-resistance with existing ARV classes.

METHODS

- PROMISE-US (NCT05388474) is a phase 4, multicenter, retrospective and prospective, observational, non-interventional registry study.
- The **primary objective** is to evaluate the long-term efficacy and durability of IBA in combination with other ARVs by comparing the clinical outcomes of participants receiving IBA treatment (Cohort 2; C2) against matched participants not receiving IBA (Cohort 1; C1).
- Here, we present results from the initial comparative analysis of matched participants from both cohorts (**Figure 1**). Participants were matched using baseline viral load (VL) and active agents in the optimized background regimen.

Figure 1. Study Design with Matching Cohorts

Inclusion criteria for this analysis in participants with MDR HIV:
- Switch to an alternative ARV regimen, defined here as a treatment change event
- Documented resistance to 1 ARV in at least 3 ARV classes



Baseline viral load (log_{10} copies/mL) Mean (SD)	**2.3** (1.35) n=98	*P*<0.001	**2.5** (1.50) n=56	*P*=0.0304
	3.4 (1.55) n=48		**3.2** (1.47) n=30	
Baseline CD4⁺ count (cells/mm³) Mean (SD)	**509** (302) n=102		**489** (307) n=57	
	334 (324) n=50	*P*=0.0013	**337** (278) n=31	*P*=0.0360

Primary endpoint
- Percentage of participants with <50 RNA copies/mL at Months 12 and 24

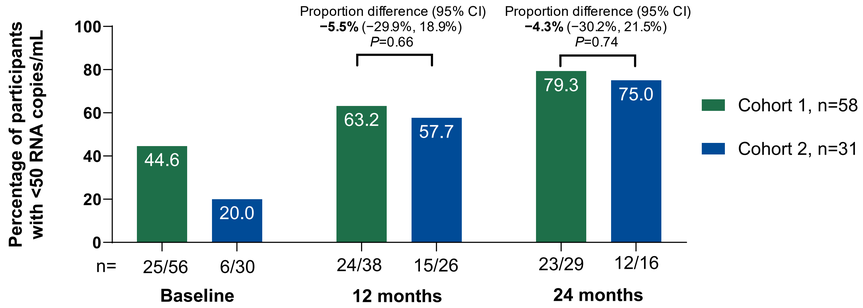
Secondary endpoints
- Percentage of participants with <50 RNA copies/mL at further timepoints
- Changes to CD4⁺ cell counts at Months 12, 24, and further timepoints

P-values for means were calculated using Student's t-test.
ARV, antiretroviral; C1, cohort 1; C2, cohort 2; IBA, ibalizumab; MDR, multidrug resistant; SD, standard deviation.

RESULTS

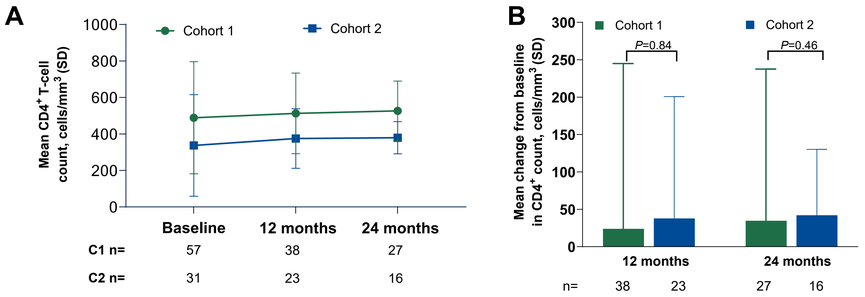
- As of the cut-off for interim analysis (1 August 2025), a total of 167 participants were enrolled in PROMISE-US.
  - Of these, 113 (68%) participants were in C1 (without IBA) and 54 (32%) participants were in C2 (with IBA).
- The significant baseline differences in VL and CD4+ counts of the full cohorts (**Figure 1**) led to 58 participants in C1 matched to 31 participants in C2 based on baseline VL and active agents in the optimized background regimen (OBR); the imbalance in CD4⁺ persisted even after matching.
- Median age (range) was 58.0 (28, 75) years with 71.9% participants assigned male at birth.
- The percentage of participants achieving RNA <50 copies/mL at 12 and 24 months were similar in both cohorts (**Figure 2**).
- Cohorts achieved similar CD4⁺-related outcomes at 12 and 24 months (**Figure 3**).

Figure 2. Viral Load Suppression Grows Similar Between Matched Cohorts Over Time



P-values were calculated using chi-square test. Not all patients have data at specific time points because of the nature of observational registries.
CI, confidence interval.

Figure 3. Mean CD4⁺ Count (A) and Mean Change in CD4⁺ (B) Over Time



P-values for mean change were calculated using mixed model repeated measures with baseline CD4⁺ count as covariate and treatment, visit, and treatment-by-visit interaction as fixed effects.
C1, cohort 1; C2, cohort 2; SD, standard deviation.

- The median (range) duration of ibalizumab exposure was 29 (10.8, 86.5) months (n=31).
- Most (61.3%) participants in C2 remained on ibalizumab for >24 months (**Figure 4**).
- The median (range) time in the study was 26 (3, 36) months.
- 3/31 patients discontinued IBA; of these, 1 withdrew consent and 2 died (there were no discontinuations due to adverse event or virologic failure).
- The median number of total ARV agents in the regimen (active and inactive) was 5.0 for both cohorts (range was 2–8 for C1 and 1–7 for C2).
- At 12 months, VL and CD4⁺ outcomes were similar for both cohorts, regardless of the number of active agents in the regimen (**Table 1**).

Figure 4. Exposure to Ibalizumab

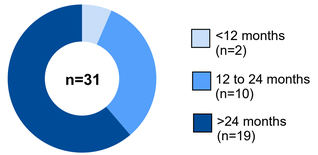


Table 1. 12-Month Endpoints Based on Number of Active Agents in Regimen

Number of active agents		Overall	1	2	3	4
Change from baseline in VL (log_{10} copies/mL)	Cohort 1	**−0.66** (1.28) *38*	**−1.28** (NA) *1*	**−0.75** (1.20) *20*	**−0.5** (1.37) *13*	**−1.82** (1.68) *2*
Mean (SD) *n*	Cohort 2	**−1.18** (1.65) *25*	**0** (NA) *0*	**−0.73** (1.78) *10*	**−0.92** (1.21) *7*	**−1.47** (1.38) *4*
Change from baseline in CD4⁺ count (cells/mm³)	Cohort 1	**23.8** (221.1) *38*	**99.0** (137.2) *2*	**48.2** (156.6) *18*	**−69.3** (242.7) *15*	**420.5** (285.0) *2*
Mean (SD) *n*	Cohort 2	**37.6** (163.2) *23*	**0** (NA) *0*	**52.6** (176.0) *9*	**−25.7** (90.0) *7*	**4.3** (120.5) *4*

NA, not applicable; SD, standard deviation; VL, viral load.

CONCLUSIONS

- Despite presenting with clinical indicators of more advanced HIV disease (such as significantly lower CD4⁺ count at baseline, even after matching), individuals receiving IBA-containing regimens demonstrated comparable rates of virologic suppression and immunologic recovery to those not receiving IBA.
- HTE patients may benefit from IBA, even those with low CD4⁺ count or limited active OBR.
- Interpretation of these findings is limited by the small sample size and differences in baseline disease severity between cohorts; future analyses will include larger numbers of participants.

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