Achievement of Virologic Suppression in the PROMISE-US Study in Subjects Viremic at Baseline

Smitha Gudipati[1], Princy N. Kumar[2], Charlotte-Paige Rolle[3], Christina Harbison[4], Namrata Shah[5], and Kaitlin R.A. Anstett[6] on behalf of the PROMISE-US Investigators

[1]Henry Ford Hospital, Detroit, MI, USA, [2]Georgetown University School of Medicine, Washington, DC, USA, [3]Orlando Immunology Center, Orlando, FL, USA, [4]Prism Health North Texas, Dallas, TX, USA, [5]Whitman Walker Institute, Washington DC, USA, [6]Theratechnologies, Inc., Montreal, QC, Canada

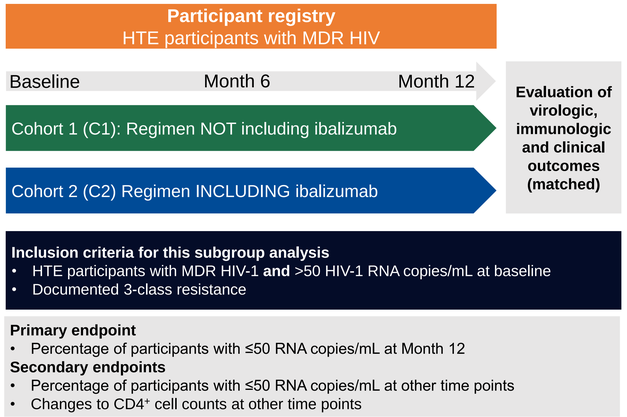
BACKGROUND

- It is estimated that there are over 1.2 million people with HIV in the US, and approximately 1% are heavily treatment-experienced (HTE) with multidrug resistant (MDR) HIV infection[1–3]
- In these participants, establishing and maintaining virologic control can be challenging as fewer antiretrovirals (ARVs) are available for a fully suppressive regimen[4,5]
- Ibalizumab (IBA), with its unique mechanism of action, is a promising candidate for managing patients with MDR HIV infection

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 ibalizumab in combination with other ARVs by comparing the clinical outcomes of participants receiving ibalizumab treatment (Cohort 2; C2) versus matched participants not receiving ibalizumab (Cohort 1; C1)
- We present results from an interim subgroup analysis of unmatched participants who were viremic at baseline (Figure 1)

Figure 1. Study Design



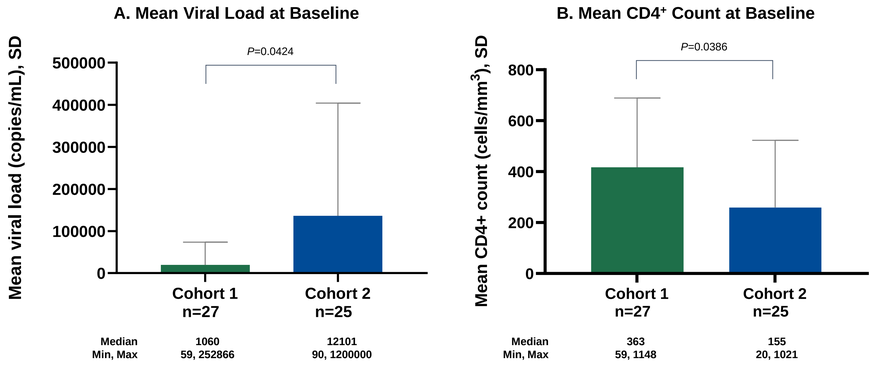
RESULTS

- As of 8 November 2023, a total of 112 participants were enrolled in the registry
- Of these, 27/70 (39%) participants in C1 and 25/42 (57%) participants in C2 had >50 RNA copies/mL at baseline (p=0.0279)
- Additionally, 59/70 (84%) participants in C1 and 21/42 (50%) participants in C2 had CD4⁺ counts >200 cells/mm³ at baseline (p=0.0002)
- Baseline characteristics for the viremic participants are shown in **Table 1** and **Figure 2**

Table 1. Baseline Characteristics for Viremic (>50 RNA copies/mL) Participants

Characteristic	Cohort 1 n=27	Cohort 2 n=25
Mean age, years (SD)	56.7 (11.96)	52.7 (11.51)
Sex, % female	14.8	12.0
Mean duration of treatment, months (SD)	8.16 (2.66)	35.26 (23.67)
Mean duration of HIV infection, years (SD)	24.6 (9.74)	27.3 (8.33)

Figure 2. Baseline Viral Load (copies/mL) and CD4⁺ Count (cells/mm³)

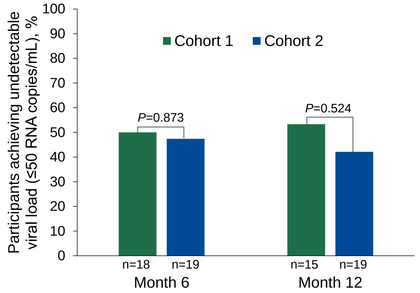


P-values for means were calculated using unpaired Welch's t-test.

- As of the cut-off date, not all participants had completed 6 and/or 12 months of follow-up
- Of participants with follow-up data available, 9/18 (50%) participants in C1 and 9/19 (47.3%) participants in C2 had an undetectable viral load (≤50 RNA copies/mL) at Month 6 (**Figure 3**)
- At Month 12, a total of 8/15 (53.4%) participants in C1 and 8/19 (42.1%) participants in C2 remained HIV undetectable (≤50 RNA copies/mL) (**Figure 3**)
- Median CD4⁺ at baseline was higher in C1 in comparison to C2, with follow-up results at Month 6 and Month 12 showing no consistent trends or differences between cohorts (**Table 2**)
- CD4⁺ counts increased on average in participants in C2 compared with participants in C1 (**Table 2**)

The two cohorts had significantly different viral loads and CD4⁺ counts at baseline (Figure 2). This indicates more severe disease in ibalizumab-treated participants compared to participants not receiving ibalizumab.

Figure 3. Percentage of Participants Achieving an Undetectable Viral Load



P-values comparing percentages calculated using relative risk according to Sheskin DJ, ISBN1584884401, 2004.

The two cohorts demonstrated similar proportions of participants with virologic suppression at 12 months.

Table 2. Mean and Median CD4⁺ Counts and Mean Change from Baseline

CD4⁺ cells/mm³	Cohort 1	Cohort 2	*P*-value
Median CD4⁺ count (min, max)			
Baseline (C1, n=27; C2, n=25)	363 (59, 1148)	155 (20, 1021)	**0.0091**
Month 6 (C1, n=16; C2, n=19)	274 (144, 1148)	225 (20, 917)	0.2268
Month 12 (C1, n=16; C2, n=19)	361 (54, 887)	206 (28, 984)	0.2819
Mean CD4⁺ count (SD)			
Baseline (C1, n=27; C2, n=25)	417 (272)	259 (264)	**0.0386**
Month 6 (C1, n=16; C2, n=19)	401 (274)	325 (278)	0.4228
Month 12 (C1, n=16; C2, n=19)	352 (230)	300 (276)	0.5474
Mean change from baseline (SD)			
Month 6 (C1, n=16; C2, n=19)	-53 (313)	+14 (112)	0.4264
Month 12 (C1, n=16; C2, n=19)	-80 (307)	+34 (116)	0.1770

Participants in C2 experienced a mean increase in their CD4⁺ counts, whereas participants in C1 saw a decline.

CONCLUSIONS

- Proportion of participants with virologic suppression and CD4⁺ cell counts were similar between the two cohorts at 6 and 12 months, despite having significantly different viral loads and CD4⁺ counts at baseline. The average change in CD4⁺ counts was positive in C2 and negative in C1, though these results did not reach statistical significance
- The results indicate that ibalizumab has the potential to offer adequate HIV viral suppression and support CD4⁺ T cell response, especially in participants with high viral loads and low CD4+ counts
- However, further studies and analyses are required due to the small sample size and unmatched disease severity at baseline between the two cohorts. The registry continues to actively enroll participants
- Ibalizumab may be a suitable treatment option for HTE patients with MDR who are struggling to achieve viral suppression on their current regimen

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AUTHOR CONTACT INFORMATION

SGudipa2@hfhs.org

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