P-565

A Prospective and Retrospective Observational Study of Multidrug-Resistant Patient Outcomes with and without Ibalizumab in a Real-World Setting: United States (PROMISE-US) Study Design and Baseline Characteristics

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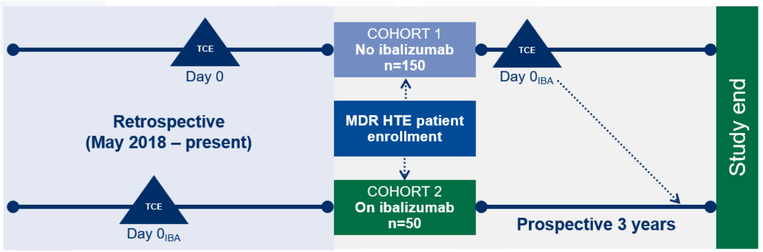
Background

- It is estimated that 12,000 people with HIV (PWH) live with unsuppressed multidrug resistant (MDR) HIV-1[a].
- MDR HIV is found most often in those with extensive prior exposure to ARVs. For these heavily treatment experienced (HTE) patients with MDR HIV-1, it can be challenging to establish and maintain virologic control, due to fewer active antiretrovirals (ARVs) available to construct a fully suppressive regimen.
- The efficacy of ibalizumab, a CD4-directed post-attachment inhibitor, in combination with an optimized background regimen has been demonstrated in the phase 3 studies TMB-301 and TMB-311[b,c]. However, there is still a need for long-term efficacy and safety data for ibalizumab in a real-world setting. Additionally, further understanding of the factors that contribute to maintaining virologic response in HTE individuals in a real-world setting is needed.

Key Question: How do HTE PWH on IBA-based regimens compare over the long-term to those without IBA in their regimens?

Methods



- PROMISE-US (ClinicalTrials.gov Identifier: 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 patients receiving ibalizumab treatment (Cohort 2; C2 or IBA) vs. matched patients not receiving ibalizumab (Cohort 1; C1).
- Baseline is defined as the date of the latest treatment change event (TCE) (the start date of ibalizumab in C2; the start date of current regimen in C1).
- If a participant in C1 is prescribed IBA they will not discontinue from the study; instead, they rollover into C2 and continue to be followed until end of study.
- This analysis represents a descriptive summary of subjects only and has not been matched for baseline characteristics.

Results

- By 8-Nov-2023, a total of 112 subjects were enrolled; 70 on C1, 42 on IBA, and 2 screen failures.
- Baseline characteristics, including race, ethnicity, sex, gender, and time since diagnosis, were similar between both cohorts (Table 1).

Table 1: Demographics of subjects enrolled in PROMISE-US

Characteristic	C1 (N = 70) n (%)	C2/IBA (N = 42) n (%)
Age (years) at enrollment		
Mean (SD)	58.5 (9.71)	53.8 (10.89)
Median	60.0	56.0
Min, Max	29, 77	28, 69
Sex at birth, n (%)		
Male	50 (71.4)	34 (81.0)
Female	20 (28.6)	7 (16.7)
Missing*	0	1 (2.4)
Race, n (%)		
American Indian or Alaska native	1 (1.4)	0
Black or African American	34 (48.6)	20 (47.6)
Native Hawaiian or other Pacific Islander	1 (1.4)	1 (2.4)
White	34 (48.6)	19 (45.2)
Missing	1 (1.4)	2 (4.8)
Ethnicity, n (%)		
Hispanic	11 (15.7)	8 (19.0)
Non Hispanic	59 (84.3)	33 (78.6)
Missing	0	1 (2.4)
Duration of HIV infection (years)		
Mean (SD)	26.443 (8.87)	27.717 (8.73)
Median	28.34	30.88
Min, Max	4.68, 42.42	5.29, 38.84

* Results are representative of data entered as 8-Nov-2023. Some data may be missing as due to incomplete data entry.

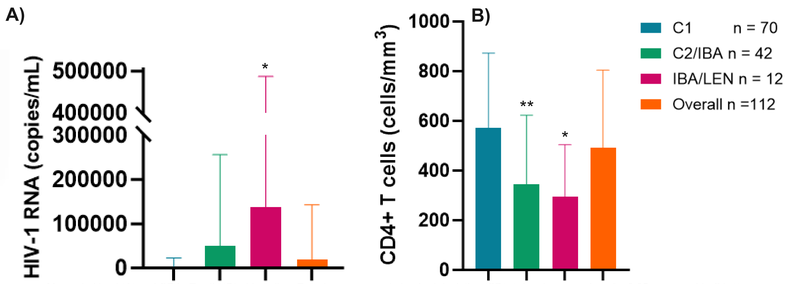
- The use of IBA was associated with HTE patients with higher baseline HIV viral loads and lower CD4 T cells (p-value of 0.0629 for VL and 0.001 for CD4 vs. C1 – Figure 1 and Table 2).
- Given the availability of the capsid inhibitor lenacapavir (LEN, approved 2023) as the second parenteral agent specifically for HTE PWH, we also investigated its use in combination with IBA. This subset of C2 demonstrated the highest baseline viral loads and lowest CD4 T cells counts.

Table 2: Baseline clinical HIV characteristics in PROMISE-US subjects

Characteristic	C1	C2/IBA	IBA/LEN*
HIV-1 RNA at enrollment (copies/mL)	(n = 70)	(n = 42)	(n = 12)
Mean	3,651	50,184	138,385
(SD)	(19,055)	(206,392)	(349,194)
Median	19	44	108
Min - Max	0 - 148,000	0 - 1,200,000	19 - 1,200,000
CD4+ T-cells at enrollment (cells/mm^3)	(n = 70)	(n = 42)	(n = 12)
Mean (SD)	571 (302)	345 (279)	294 (211)
Median	579	283	311
Min - Max	34 – 1436	13 – 1231	32 – 609
Composition of OBR, n (%)	(n = 68**)	(n = 32**)	(n = 6**)
PI	45 (66.18)	14 (43.75)	1 (16.67)
NNRTI	21 (30.88)	7 (21.88)	0 (0)
NRTI	52 (76.47)	21 (65.63)	2 (33.33)
INSTI	54 (79.41)	20 (62.50)	1 (16.67)
IBA	0 (0)	32 (100)	6 (100)
FTR	17 (25)	10 (31.25)	3 (50)
LEN	2 (2.94)	6 (18.75)	6 (100)
MVC	5 (7.35)	1 (3.13)	0 (0)
cGSS***	(n = 63**)	(n = 31**)	(n = 6**)
Mean (SD)	2.2 (0.75)	2.7 (0.96)	2.9 (1.4)
Median	2.0	2.5	2.5
Min, Max	1.0 – 3.5	1.5 – 5.5	2.0 – 5.5

* Any regimen including the two drugs and may have additional ARVs in the OBR; ** cGSS was calculated as per Gonzalez-Serna et al. J. Antimicrob. Chemother, 2017, P. 496 –503. ** Due to missing data, OBR and cGSS only reported for the subset of participants with complete data entry. *** Because commercial resistance testing is not available for ibalizumab, fostemsavir, or lenacapavir, all 3 agents are always considered fully active. cGSS, combined genotypic sensitivity score; FTR, fostemsavir; IBA, ibalizumab; INSTI, integrase strand transfer inhibitor; LEN, lenacapavir; MVC, maraviroc; NNRTI, non-nucleotide reverse transcriptase inhibitor; NRTI, nucleotide reverse transcriptase inhibitor; OBR, optimized background regimen; PI, protease inhibitor; SD, standard deviation.

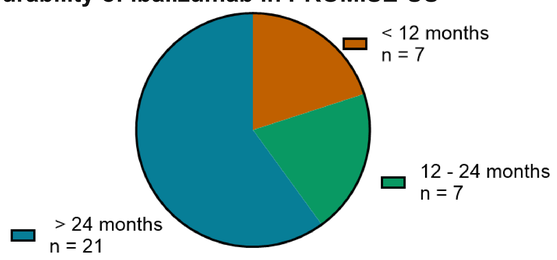
Figure 1: Baseline viral load and CD4+ T cells in PROMISE-US



Mean viral load (A) and CD4+ T cells (B) at baseline. Error bars represent standard deviation (SD). * denotes a p-value of > 0.05 compared to C1, ** a p-value of > 0.001 compared to C1.

- Combined genotypic susceptibility scores (cGSS) values were comparable between the two cohorts (Table 2). However, since commercial resistance testing is not available for IBA, fostemsavir (FTR), or LEN they are considered fully active and therefore this measure may overestimate regimen sensitivity in C2 subjects who were more likely to have these in their regimens.
- 80% of C2 subjects had been on ibalizumab for greater than 12 months during the follow-up period. (Figure 2).
- IBA was well-tolerated with no infusion reactions reported. No subject in C2 discontinued due to a treatment emergent adverse event (data not shown).

Figure 2: Durability of ibalizumab in PROMISE-US



Total=35

Length of time (in months) for subjects in C2/on ibalizumab in the PROMISE-US registry. Includes retrospectively and prospectively entered data (where available).

Conclusions

- Ibalizumab was more frequently selected for use in advanced HTE patients with lower baseline CD4 cell counts and higher viral loads than other regimens. Despite this, IBA demonstrated good durability with the majority of subjects staying on therapy for >24 months. This study will help further characterize the efficacy and safety profile of agents used in combination for this population with high unmet need to help guide treatment selection.

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a . Millham LRI et al. J Acquir Immune Defic Syndr. 2020 Feb 1;83(2):148
b. Emu B et al. N Engl J Med 2018;379:645-654
c. Theratechnologies, Data on File.

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