Intramuscular Injection vs Intravenous Infusion of Ibalizumab for HTE PWH: The Results of TMB-302

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Background

- Ibalizumab (IBA) is a monoclonal antibody directed against domain 2 of the cluster of differentiation 4 (CD4) receptor whose binding blocks the post-attachment steps of HIV-1 replication.
- IBA is a long-acting injectable approved for the treatment of multidrug resistant HIV-1 infection in heavily treatment-experienced (HTE) people with HIV (PWH) in combination with other antiretrovirals agents[1].
- IBA maintenance dosing is currently administered every two weeks (Q2W) via intravenous infusion (IVI) over 15 minutes, or via undiluted intravenous push over 30 seconds. This requires specialized equipment and training which can limit access.
- Improving the administration of IBA will expand and simplify access for HTE PWH in need of new therapies to achieve their treatment goals.
- In TMB-302 (ClinicalTrials.gov Identifier: NCT03913195), the safety, efficacy, and treatment satisfaction of IBA administered as an intramuscular (IM) injection vs IVI was evaluated in both clinically stable HTE PWH on IBA therapy and HIV-uninfected volunteers (UI).

OBJECTIVES

Clinical study TMB-302 was conducted in two parts; the first assessed IBA maintenance doses delivered via IV push and these results have been presented previously[2]. This report focuses on the safety, efficacy, and patient reported outcomes of the second part of TMB-302, which evaluated IBA maintenance doses administered as IM injection.

- **Primary: A)** Evaluate the safety of administering IBA maintenance doses as an undiluted IM injection compared to 15 minute IVI. **B)** Compare the trough serum drug concentrations (C_{trough}) after IM vs. IVI. *These results will be presented elsewhere.*
- **Key Secondary: A)** Assess viral load (VL) for IVI compared with IM injection in PWH. **B)** Determine treatment satisfaction and preference for route of administration amongst all participants.

Methods

- TMB-302, an open-label non-randomized phase 3 study, enrolled clinically stable PWH with viral load (VL) < 1000 c/mL while on IBA-containing ARV regimens for at least 3 months, and HIV-uninfected individuals.
- Participants received the first 2 doses of IBA via IVI at Day 1/Baseline and again at Day 15. The next 4 doses of IBA through Day 71 were administered via IM injection. At Day 85, PWH reverted to diluted IVI dosing.
- The HIV treatment satisfaction questionnaire – status (HIVTSQs) and study medication satisfaction questionnaire - status (SMQs) were administered at the last IVI administration (Day 29) and after 8 weeks of IM administration (Day 85) and the HIV treatment satisfaction questionnaire – change (HIVTSQc) and study medication questionnaire - change (SMQc) were also administered on Day 85. All study participants were also asked to answer a one-question Preference Assessment at Day 85 comparing the experience on IM injections with IV infusion.

Methods (con't)

- HIVTSQ consists of 12 questions assessing various aspects of antiretroviral therapy and its impact on daily life for PWH. SMQ is a matched set of 11 questions for UI participants.
- Status questionnaire: each question is assessed on a scale of 0 (most negative response) to 6 (most positive response).
- Change questionnaire: each question is assessed on a scale of -3 (favors previous treatment) to 3 (favors current treatment), where 0 represents no change.

Results

- A total of 21 participants were enrolled, including 7 PWH.
- Two participants (1 in each treatment group) discontinued the study and treatment early. 1 PWH withdrew consent, and 1 UI participant withdrew because of an AE of rash during the IVI phase. Neither received IBA via IM injection.
- A total of 152 IM injections of IBA were administered during the study.

TREATMENT SATISFACTION

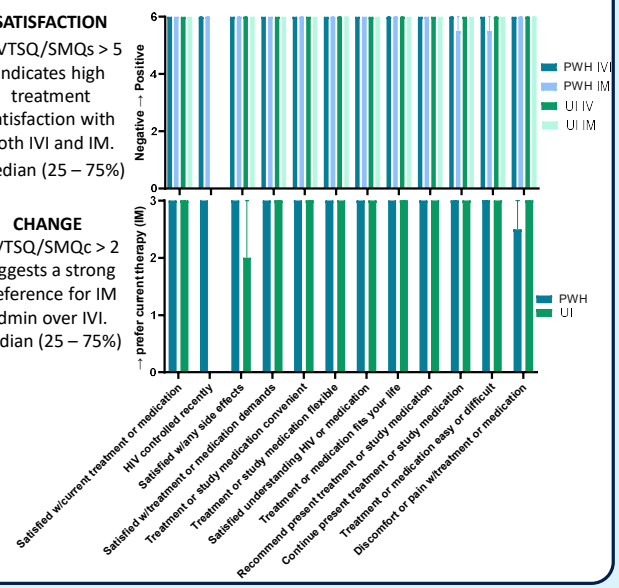
- Although there was no statistically significant difference in HIVTSQs/SMQs for Day 29 (IVI) vs 85 (IM), 83% of UI participants and 67% of PWH preferred administration of IBA via IM compared to IVI.

SATISFACTION

HIVTSQ/SMQs > 5 indicates high treatment satisfaction with both IVI and IM. Median (25 – 75%)

CHANGE

HIVTSQ/SMQc > 2 suggests a strong preference for IM admin over IVI. Median (25 – 75%)



Results (cont'd)

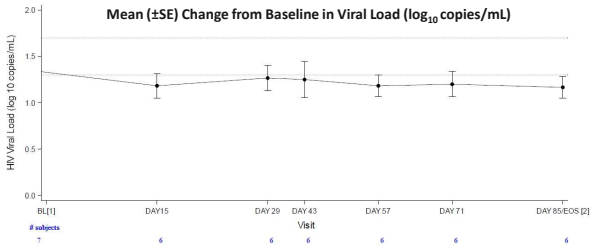
SUMMARY OF TEAEs

	HIV-infected (n = 6)	HIV-uninfected (n = 14)	Total (N=20)
Number (%) of subjects with			
TEAEs	4 (66.7)	10 (71.4)	14 (70.0)
Serious TEAEs	0	0	0
TEAEs with death outcome	0	0	0
TEAE leading to study drugs discontinuation	0	1 (7.1)	1(7.1)
Suspected adverse reaction[a]	1 (16.7)	4 (28.6)	5 (25.0)
Severe TEAE[b]	0	0	0
Class C TEAE[c]	0	0	0

CDC=U.S Centers for Disease Control and Prevention; TEAE=treatment emergent adverse event
a Possibly related to study drug
b Severity of Grade 3 or Grade 4 (severe or potentially life threatening)
c Per the CDC Classification System for HIV infection

- There were no clinically significant differences in the occurrences of TEAEs during IVI or IM. One TEAE of injection site pruritus was reported by 1 participant at 1 timepoint only. There were no clinically significant changes in hematology or chemistry assessments, CD4+ T-cell counts, or physical examination findings during the study.

EFFICACY



- Among PWH, VLs remained suppressed at all study timepoints following IVI and IM administration of IBA while on combined ARV therapy with no virologic failures observed.

Conclusions

- Administration of IBA as an **undiluted IM injection appears safe and well tolerated** in all study participants. PWH receiving IBA via IM injection **maintained viral suppression**.
- Both IM and currently approved IVI administration led to **high rates of treatment satisfaction**; however, IM injection was the **preferred method of administration for IBA amongst study participants.**
- Expanding the administration options for IBA to include IM is an important step to **increasing treatment flexibility for PWH**.

References:

1. Trogarzo®. Prescribing information. Theratechnologies Inc; 2023.
2. E. Dejesus, et al. (CROI 2022). IV PUSH ADMINISTRATION OF IBALIZUMAB: PHARMACOKINETICS, SAFETY AND EFFICACY. Poster #429.