IDWeek #1027

Long-term Efficacy, Safety, and Durability of Ibalizumab-based Regimens in Subgroup of TMB-202 Participants

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THERA technologies

Introduction

- Antiretroviral regimens for patients with MDR HIV have been associated with suboptimal virologic suppression, due to drug cross-resistance and regimen complexity.
- Yet, in treatment-experienced (TE) HIV patients with limited available options, ART durability is essential for preventing further resistance and decreasing HIV-associated morbidity and mortality.
- Ibalizumab (IBA), the first long-acting, post-attachment inhibitor approved to treat multi-drug resistant (MDR) HIV, may support regimen durability given its novel mechanism of action and directly observed administration.

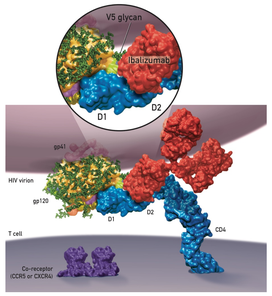

Fig 1. Ibalizumab mechanism of action

Objective

We analyzed the safety, efficacy, and durability of response in 12 patients who started IBA in TMB-202, a Phase 2b study which was conducted from October 14, 2008 to January 26, 2011.

Methods

- In TMB-202, 113 patients with MDR HIV received either 2000 mg IBA every 4 weeks (n=54) or 800 mg IBA every 2 weeks (n=59) for 24 weeks with an optimized background regimen (OBR).
- Of 96 patients who completed TMB-202, 56 transferred into an investigator-sponsored investigational new drug protocol (PI-IND).
- 12 patients later enrolled into an expanded access protocol, TMB-311, where efficacy and safety were monitored until IBA was commercially available (approval in March 2018).

Methods (cont'd)

TMB-202 Study Design

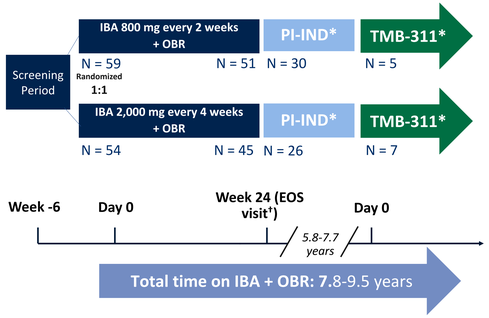

Fig 2. TMB-202 study design through PI-IND and completion of TMB-311

*Enrolment into the PI-IND and TMB-311 studies was decided by the principal investigator
†Protocol Amendment 2 (May 15, 2009): duration of study changed from 48 weeks to 24 weeks.

Results

Baseline characteristics

- 12 patients from TMB-202 entered TMB-311
  - 5 from the 800 mg Q2W group
  - 7 from the 2000 mg Q4W group
- There were no significant differences in baseline characteristics between the 2 dosing arms.

Table 1. Baseline characteristics (TMB-202 entry) for the 12 patients from TMB-202 that entered TMB-311

	Overall (N = 12)
Sex (% male)	100
Median age (years)	55
<50 years (%)	17
≥50 years (%)	83
White (%)	92
Median duration of HIV infection (years)	22*
Median viral load (copies/mL)	4.4 $\log_{10}$
Median CD4 count (cells/µL)	135
CD4 10-50 (%)	25
CD4 50-200 (%)	58
CD4 >200 (%)	17
Median OSS#	1
OSS = 0 (%)	8
OSS = 1 (%)	58
OSS = 2 (%)	25
OSS >2 (%)	8

*Date of HIV diagnosis was unknown for 1 patient; #Overall Susceptibility Score

Results (cont'd)

Long-term Virologic Suppression

- At the completion of TMB-202:
  - 11/12 achieved virologic suppression (VL <200 c/mL); 8/12 had VL <50 c/mL.
- All 12 patients were suppressed (VL < 200 c/mL) at their last TMB-311 visit.
  - 11/12 had VL <50 c/mL

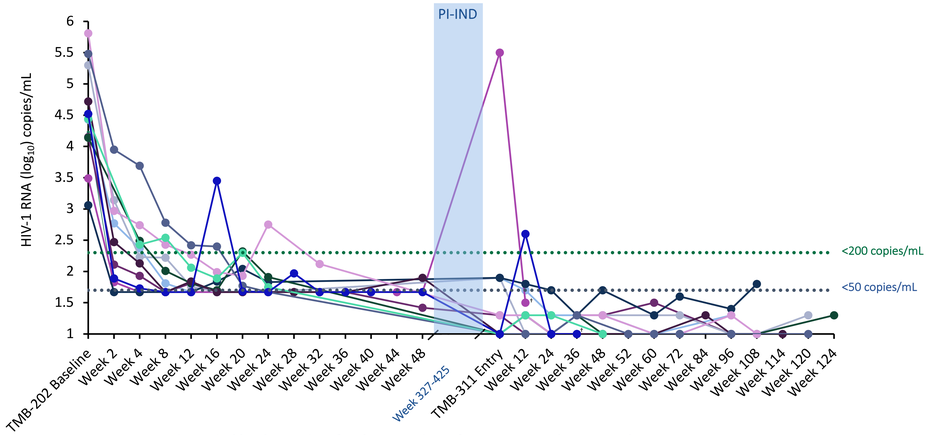

Fig 3. Viral load over time for the 12 patients from TMB-202 that entered TMB-311

†Patient death from unrelated cause

Long-term CD4+ T cell Counts

- Patients gained an average of 99 CD4 cells/µL relative to TMB-202 baseline at week 96 of TMB-311

Table 2. CD4+ T cell counts (cells/mm³)

	Baseline TMB-202	Δ Week 25 TMB-202 (n=12)	Δ Week 96 TMB-311 (n=9*)
Mean	135	+64	+99

*2 patients died and 1 patient transitioned to commercial IBA prior to Week 96

Safety

- Two patients died from unrelated causes (injury and metastatic tonsil cancer)
- No patients were withdrawn or lost to follow-up during TMB-311

Safety (cont'd)

- There were no treatment-emergent adverse events (TEAE) or therapy discontinuations *related to IBA* during follow-up

Table 3. Safety overview after start of TMB-311 for the 12 patients who entered from TMB-202

	Overall (N = 12)
At least one TEAE	92%
Serious TEAE*	42%
TEAE with death outcome	17%
TEAE leading to discontinuation	0%
TEAE related to study drug	0%
Severe TEAE†	50%

*Excludes death; can include a life-threatening AE, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect, or an important medical event.
†Severity = Grade 3 or higher.

Results (cont'd)

Durability of Response

- Overall, the 12 patients remained on IBA for an average of 8.9 years (range 7.8-9.5)
- During this period, 8/12 did not require addition of new ARVs to their OBR to maintain suppression.

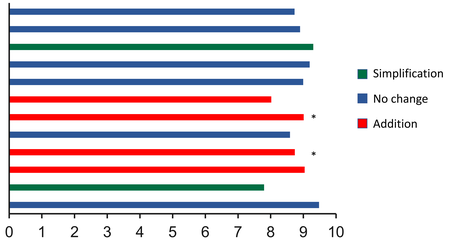

Fig 4. Duration of ibalizumab-based regimen for the 12 patients who entered TMB-311 from TMB-202.

Ritonavir (booster) was the only addition to the OBR

Conclusions

- Data from 12 patients who received IBA for an average of 9 years validate the long-term efficacy and safety of IBA in TE patients.
- Importantly, for most patients, the durability of virologic response was maintained with minimal adjustments to the OBR.
- Patients gained an average of 99 cells/µL at W96 of TMB-311 relative to TMB-202 baseline, supporting IBA's impact on immunologic recovery.
- Average of 9 years on IBA-based regimens reflects a favorable safety profile and high tolerability of IBA infusion Q2W.
- Altogether, in TE HIV patients with limited options, these data demonstrate the durability of viral suppression when combining the long-acting ARV IBA with short acting oral agents.

References

1. TMB-202 Clinical Study Report, September 2018.
2. Theratechnologies, Data on File
3. TMB-311 Clinical Study Report, March 2019.
4. Khanlou H et al. IDSA 2011. LB-9