OUTCOMES OF PATIENTS NOT ACHIEVING PRIMARY ENDPOINT FROM AN IBALIZUMAB PHASE 3 TRIAL

E. DEJESUS[1], B. EMU[2], S. WEINHEIMER[3], Z. COHEN[4], B. CASH[5], S. LEWIS[3]

[1]Orlando Immunology Center, Orlando, FL, [2]Yale School of Medicine, New Haven, CT, [3]TaiMed Biologics, Irvine, CA, [4]Theratechnologies Inc, Montreal, Canada, [5]Syneos Health, Somerset, NJ.

Background

Ibalizumab (IBA) is a long-acting humanized immunoglobulin G4 monoclonal antibody that blocks entry of HIV into CD4⁺ T cells. Unlike other antiretroviral agents, IBA binds to a conformational epitope on the 2nd extracellular domain of the CD4 receptor, away from MHC II binding sites. It prevents HIV virus from infecting CD4⁺ immune cells while preserving normal immunological function.

IBA has been shown to have potent activity against a broad spectrum of primary clinical isolates (active across all major clades and against CCR5- and CXCR4-tropic virus) with no evidence of cross-resistance with existing ARV agents or drug-drug interactions.

IBA was approved by the FDA in March 2018 for the treatment of HIV-1 infection in heavily treatment-experienced adults with multidrug resistant (MDR) HIV-1 infection failing their current antiretroviral (ARV) regimen.

The application for marketing authorization of IBA was filed with the EMA through its centralized procedure in August 2018. The EMA review of the IBA file is under the accelerated assessment procedure.

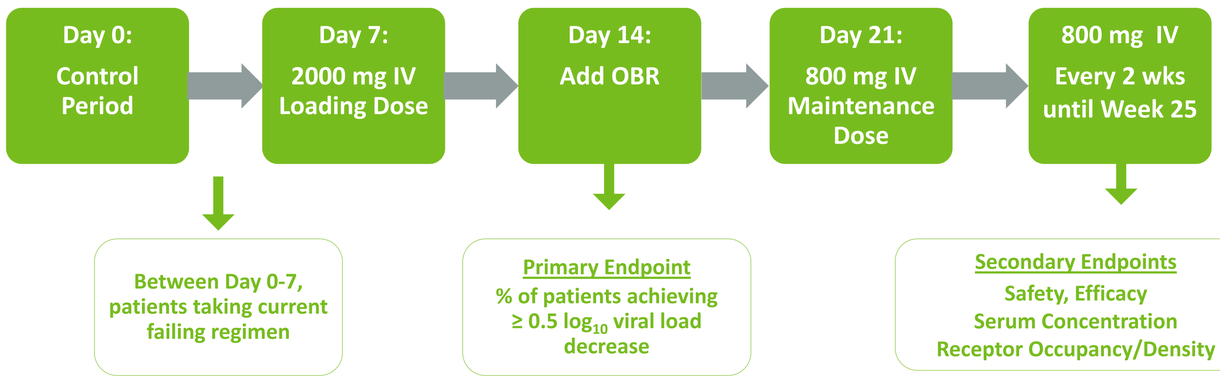
Here, we present the outcomes of patients not achieving the primary efficacy endpoint (≥ 0.5 $\log_{10}$ viral load decrease at Day 14). The outcomes in these patients are important given their significant resistance and potentially limited options.

TMB-301 Study Design

TMB-301 is a single arm, 24-week study of IBA plus optimized background regimen (OBR) in heavily treatment-experienced patients infected with MDR HIV-1.

Patients receiving their current failing ARV therapy, or no therapy, were monitored during a 7-day control period. Thereafter, a loading dose of 2,000 mg of intravenous (IV) IBA was the only ARV agent added to their regimen for 7 days. The primary endpoint of ≥ 0.5 $\log_{10}$ viral load decrease was assessed at Day 14 (seven days after the 2000 mg loading dose).

IBA was continued at doses of 800 mg IV every 2 weeks through 25 weeks on study treatment.



Baseline Characteristics

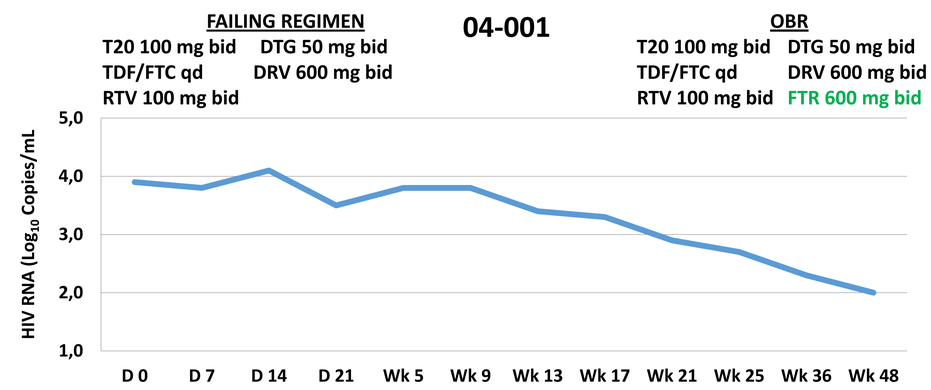
- N = 40
- Median age of 53 years 85% male 45% non-white
- Median duration of HIV infection of 23 years (range of 2-30)
- Median viral load of 35,350 copies/mL 18% with viral load ≥ 100,000 copies/mL
- Median CD4⁺ T cell count was 73 cells/µL
  - 17 patients with < 50 cells/µL (12 patients with < 10 cells/µL)
  - 10 patients with 50-200 cells/µL
- 28% were previously treated with ≥ 10 ARV agents
- 43% required investigational agent (fostemsavir) in OBR

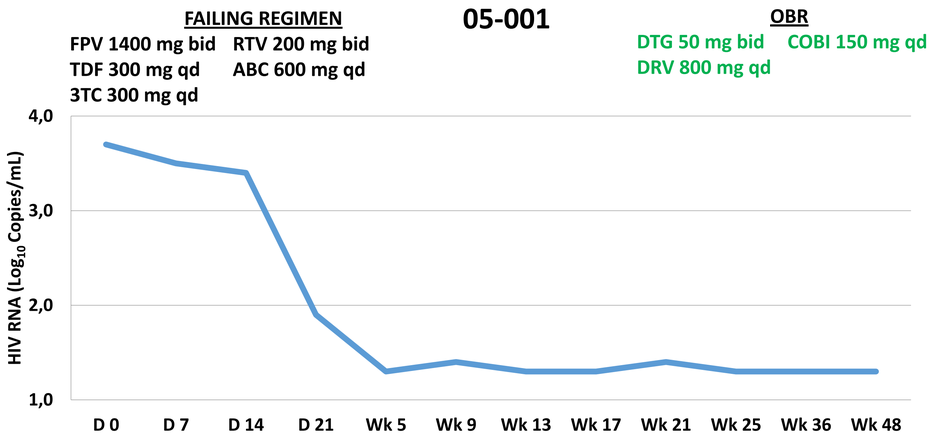
Results

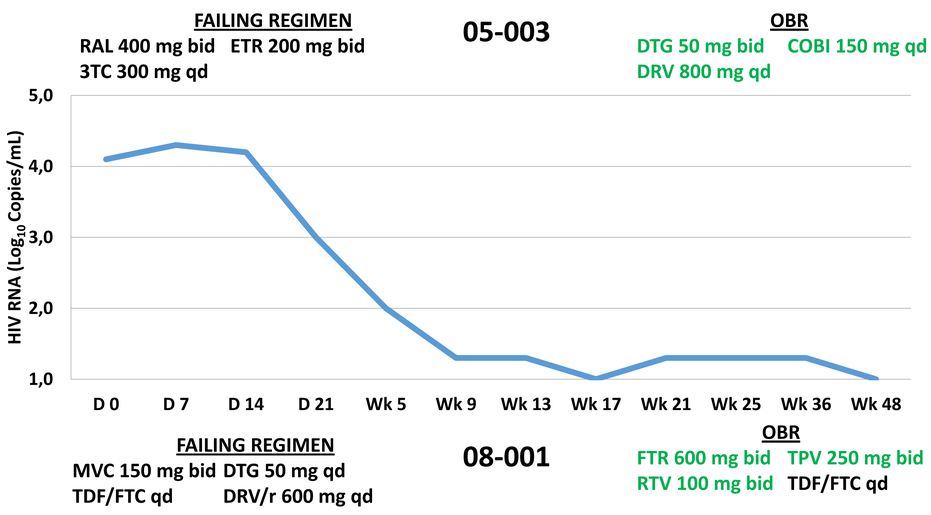
Day 14 — 7 days following loading dose of IBA			
	Day 7 Control	Day 14	
Percent with ≥0.5 $\log_{10}$ reduction	3%	83%	P<0.0001
Percent with ≥1.0 $\log_{10}$ reduction	0%	60%	
Mean VL decrease	0 $\log_{10}$	1.1 $\log_{10}$	P<0.0001

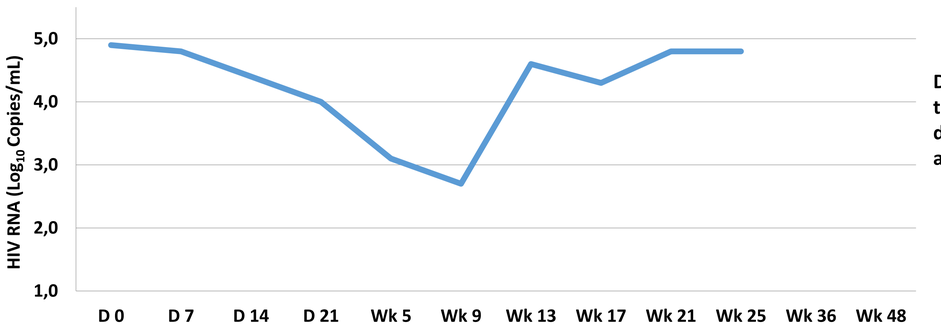
- **33 patients achieved ≥0.5 $\log_{10}$ reduction at Day 14**
- **7 patients did not achieve ≥0.5 $\log_{10}$ reduction at Day 14**

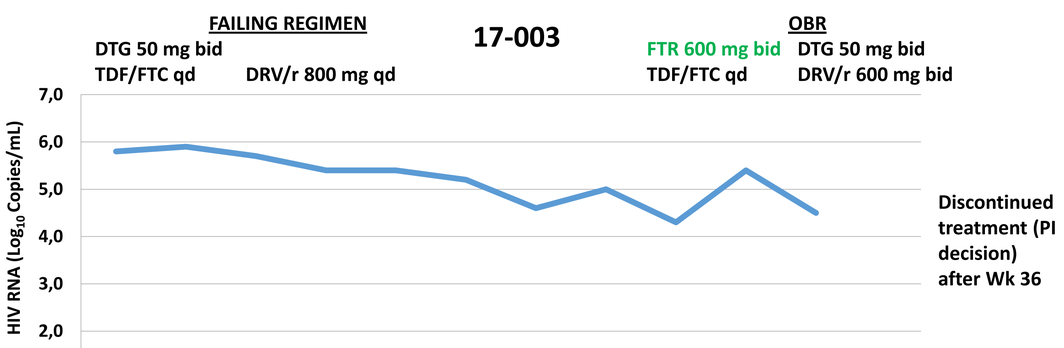
Week 25 — IBA + OBR	
Percent with VL<50 copies	43%
Percent with VL<200 copies	50%
Mean VL decrease	1.7 $\log_{10}$
Percent with ≥1.0 $\log_{10}$ reduction	55%
Percent with ≥2.0 $\log_{10}$ reduction	48%

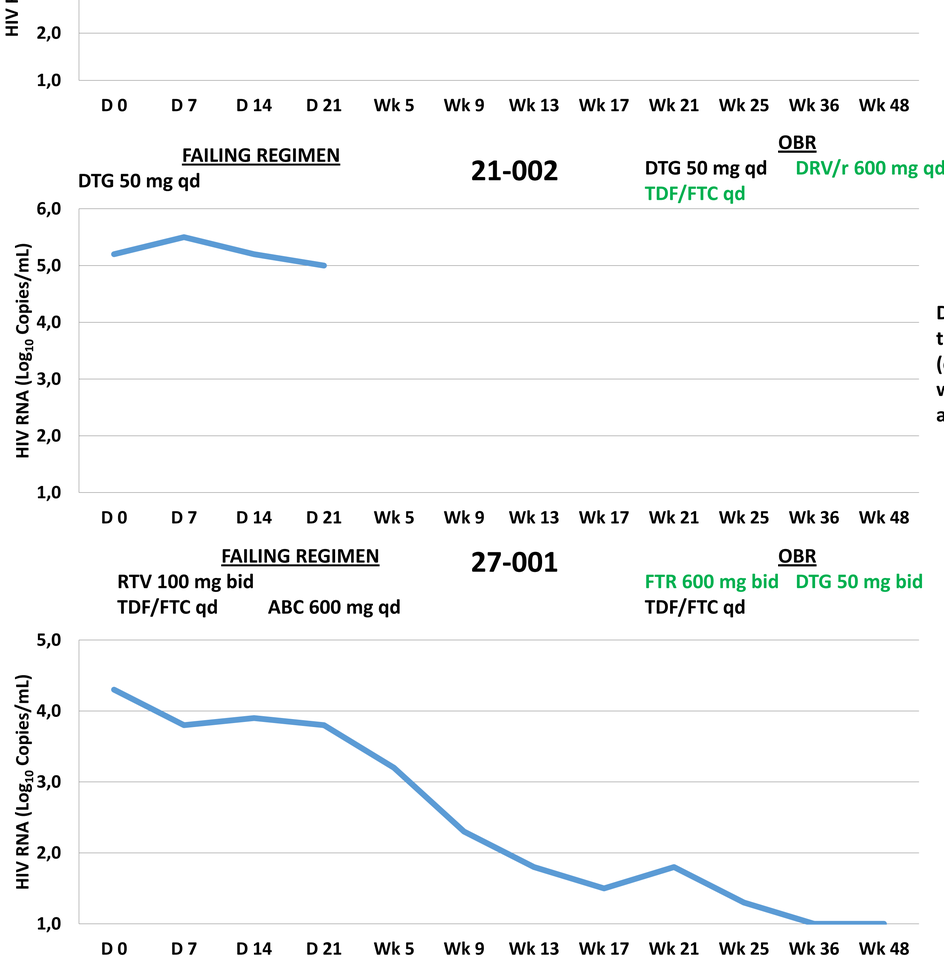












Conclusion

- Although some patients did not achieve a ≥0.5 $\log_{10}$ reduction in viral load seven days after the IV loading dose of IBA, some went on to experience viral suppression at Week 25 with IBA in combination with an OBR.
- Virologic responses with MDR HIV-1 may take longer to achieve.