Primary Efficacy Endpoint and Safety Results of Ibalizumab in a Phase 3 Study of Heavily Treatment-Experienced Patients with Multi-Drug Resistant HIV-1 Infection

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Presentation LB-6
Saturday, October 29
IDWeek 2016

Disclosures

- Dr. Lalezari receives research support from the following:

AbbVie
Arrowhead
Bavarian Nordic
Bristol-Myers Squibb
Calimmune
CytoDyn
Genocea Biosciences
Gilead Sciences
GlaxoSmithKline
Janssen
Merck
Novira Therapeutics
Sangamo BioSciences
TaiMed Biologics
ViiV Healthcare

Ibalizumab

- Humanized monoclonal antibody that primarily binds to second extracellular domain of CD4 receptor on T cells, away from binding site for MHC class II molecules
- Does not inhibit gp120 binding of HIV to CD4+ T cells
- Exerts its antiviral activity by blocking post-attachment conformational changes that are required for entry of virus into CD4+ cells
- Not immunogenic; not T cell depleting

Bruno and Jacobson, 2010, J Antimicrob Chemother

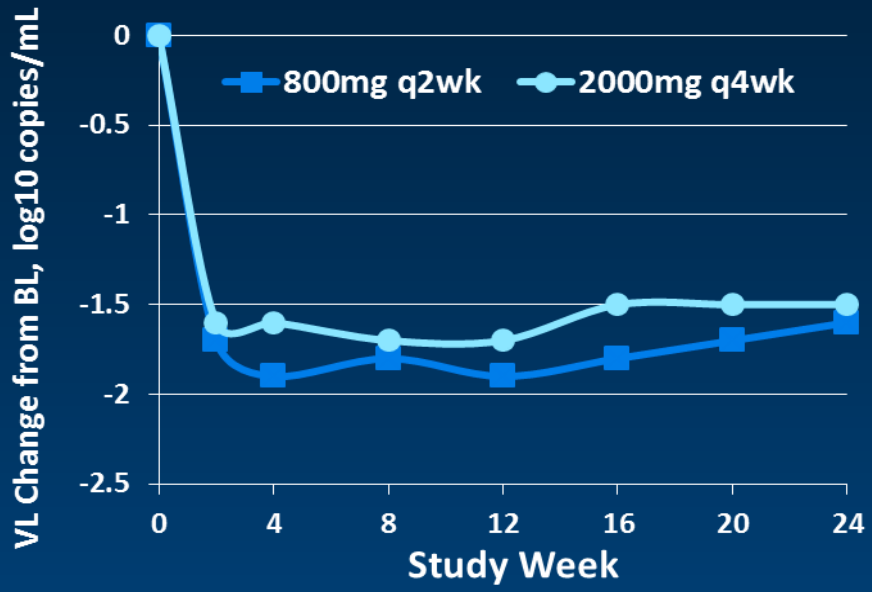
Ibalizumab – *In Vitro* Testing

- Broad spectrum anti-HIV activity
  - Active across clades
  - Active against CCR5, CXCR4 and dual/mixed tropic viruses

- No evidence of cross-resistance with existing ARTs
  - Synergistic with enfuvirtide
  - Additive or synergistic with all other classes of ARTs

- No drug-drug interactions with ARTs and/or other drugs
  - No significant liver or kidney metabolism
  - Metabolized by CD4 receptor internalization

Phase 2b: Antiretroviral Activity in Triple-Class Resistant Patients in Combination with OBR

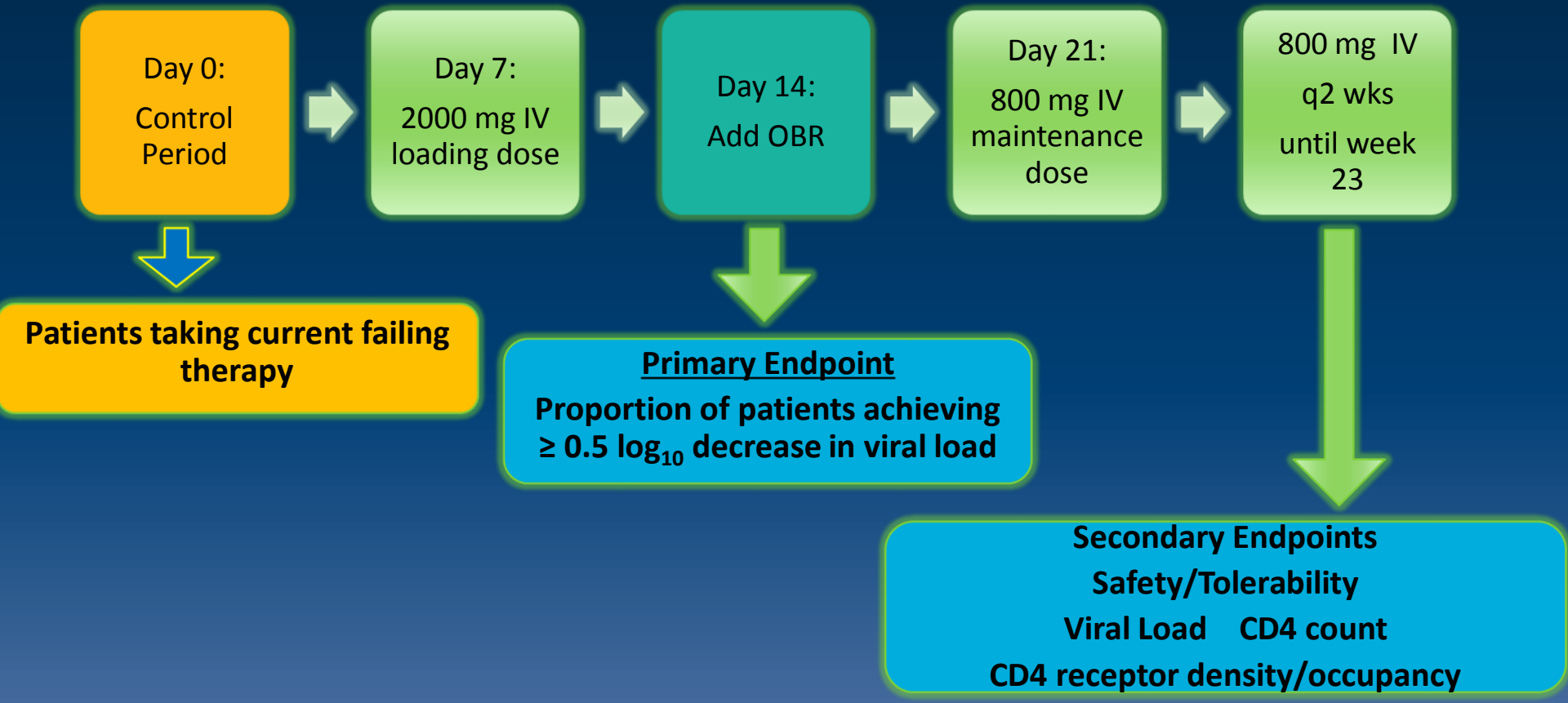


Mean change from Baseline VL at Week 24

800 mg q2wk: -1.6 log10 HIV RNA copies/mL
2000 mg q4wk: -1.5 log10 HIV RNA copies/mL

NOTE: Designated Orphan Drug and awarded Breakthrough Designation by FDA

TMB-301: Study Design



TMB-301: Study design

Day 0-6 (Control period):

- Patients monitored on current failing therapy
  - Viral load determined at Day 0 and Day 7

Day 7-13 (Monotherapy period):

- Patients continued on current failing therapy
- Received 2000 mg IV dose of Ibalizumab on Day 7
  - Viral load determined at Day 14

Day 14- Week 25 (Maintenance period):

- OBR initiated on Day 14
- Ibalizumab dosed 800 mg IV on Day 21 and every 2 weeks thereafter

TMB-301: Key Inclusion criteria

- HIV-1 viral load > 1000 copies/mL
- History of at least 6 months on ART
- Documented resistance to at least 1 ARV from 3 classes
- Have sensitivity to at least 1 ARV with which to construct an OBR
- Receiving stable ART for at least 8 weeks before Screening

TMB-301: Key Exclusion criteria

- Active AIDS-defining illness
- Immunomodulatory therapy, systemic steroids, or systemic chemotherapy within 12 weeks before Enrollment
- Prior exposure to ibalizumab
- Any Grade 3 or 4 lab abnormality

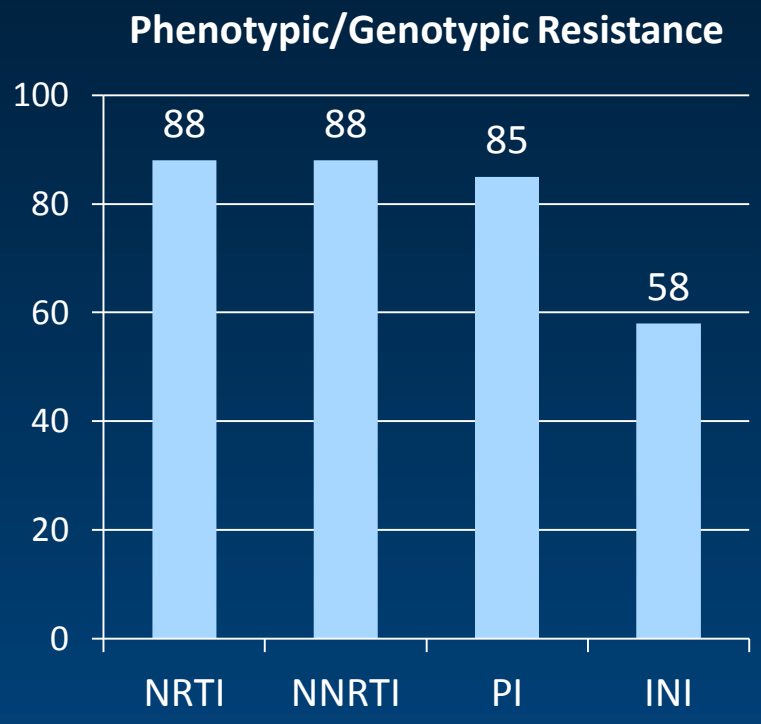
TMB-301: Patient Baseline Characteristics

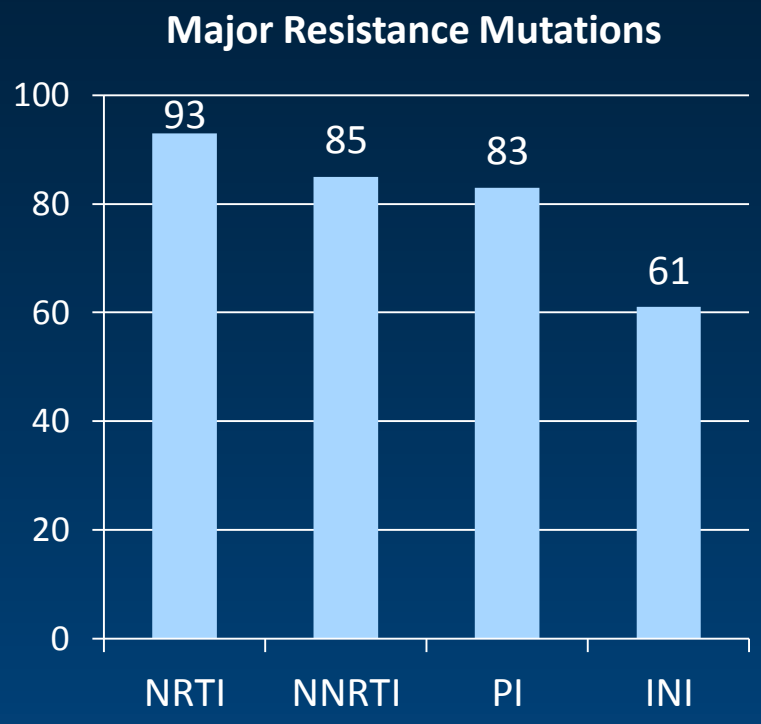
- N = 40
- 85% male; 45% non-white
- Mean duration of HIV infection 21 years

- Mean VL of 10^5 copies/mL
  - 18% with VL ≥ 10^5 copies/mL
- Mean CD4+ T cell count of 160 cells
  - 50% with <100 cells; 33% with <10 cells

- 28% treated with ≥ 10 previous ARVs
- 43% used second investigational agent in OBR

TMB-301: Baseline Resistance Data



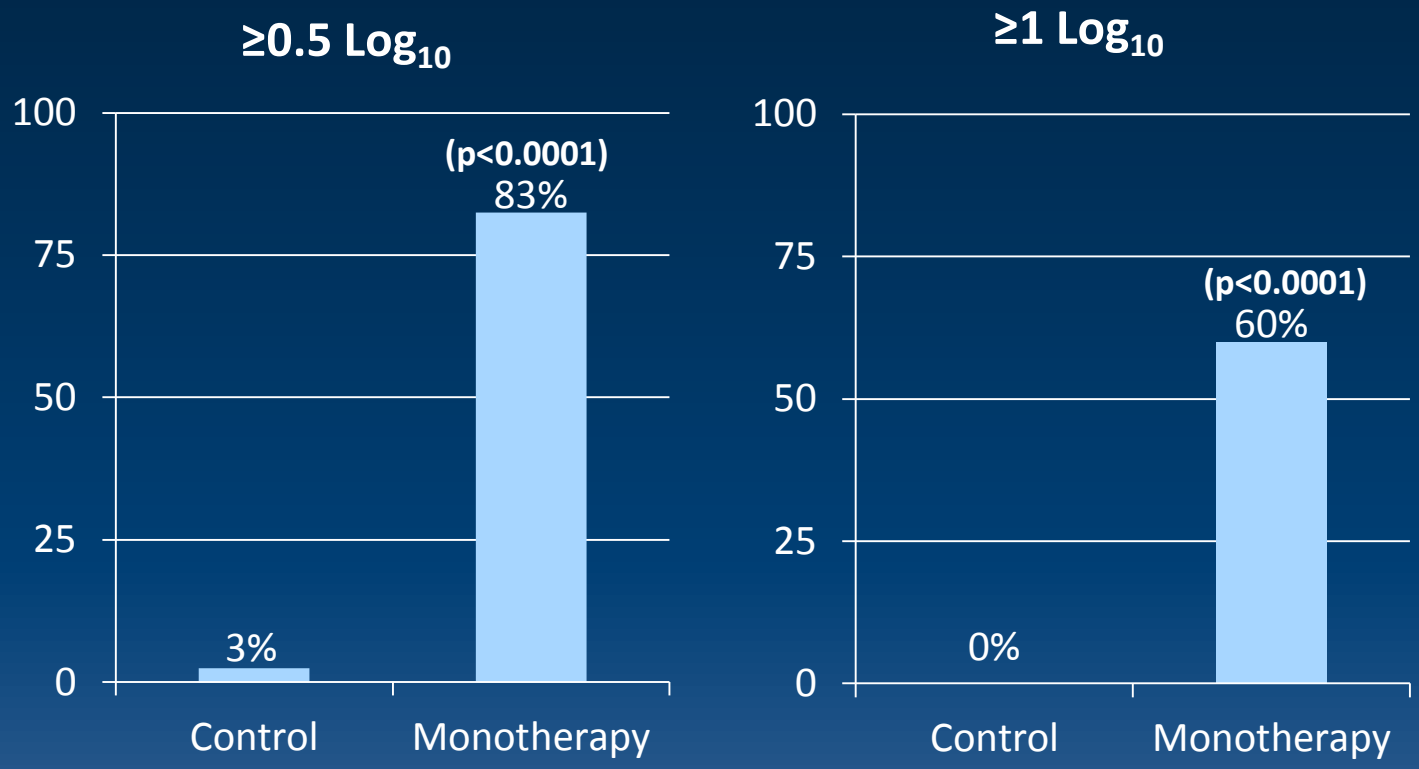


- 50% of patients had resistance to all drugs from at least 3 classes

Preliminary data pending verification of historical resistance testing

Primary Endpoint: VL Reduction at Day 14

Following 2000 mg loading dose of Ibalizumab (Day 7)



- Mean and median VL decrease of 1.1 $\log_{10}$ (p<0.0001)

TMB-301: Safety (Day 0 - 14)

- No discontinuations
- No treatment-related SAEs
- Treatment-Emergent AEs include:
  - Dizziness 10%
  - Asthenia/Fatigue 5%
  - Nausea/Vomiting 5%
  - Rash 2.5%

Conclusion / Practice Improvement

- Long-acting ART, administered IV every 2 weeks
- Significant antiretroviral activity
  - 83% with ≥ 0.5 $\log_{10}$ VL decrease after 7 days
  - Mean/median VL decrease of 1.1 $\log_{10}$ after 7 days
- Excellent short-term safety profile
- Novel mechanism of action providing new treatment to patients with limited options
  - No drug-drug interactions
  - No known risk of cross resistance
- Future results to address longer term outcomes (up to Week 25)
- Expanded Access Program is open for enrollment

ACKNOWLEDGEMENTS

Co-authors:

Dr. Jeffrey Fessel – San Francisco, CA
Dr. Shannon Schrader – Houston, TX
Dr. Princy Kumar – Washington, DC
Dr. Gary Richmond – Fort Lauderdale, FL
Dr. Christian Marsolais – Montreal, QC
Dr. Steve Weinheimer – Irvine, CA
Dr. Stanley Lewis – Irvine, CA

Thank You

Entire TMB-301 Study Team and Patients