Ibalizumab (Trogarzo)

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Last Updated: July 9, 2020
Ibalizumab (Trogarzo)

Trogarzo
[tro-gar-zo]

Entry Inhibitor

Intravenous Infusion: Loading Dose followed by Dosing Every 2 Weeks

Source: Photograph courtesy of Theratechnologies, Inc.
Ibalizumab (Trogarzo)

• **Indication:**
  - Heavily treatment-experienced adults with multidrug resistant HIV-1 failing their current antiretroviral regimen

• **Dosing (Intravenous):**
  - Loading dose: 2,000 mg IV
  - Maintenance dose: 800 mg IV every 2 weeks

• **Contraindications**
  - None

• **Use During Pregnancy**
  - Insufficient data

• **Common Adverse Events (≥5%)**
  - Diarrhea (8%), dizziness (8%), nausea (5%), and rash (5%)
Host Receptors and HIV Entry

HIV

Host Receptors

CD4

CCR5

CXCR4

CD4 Cell
HIV Cell Entry: Binding to Host Cell CD4 Receptor

- CD4 binding site
- gp120
- gp41

Intracellular Space
Host Cell
HIV Cell Entry: Binding to Host Cell CD4 Receptor

HIV

CD4 binding site

CD4

Intracellular Space

Host Cell

CCR5

CCR5
HIV Cell Entry
Binding to Host Cell CD4 Receptor

HIV

CD4

CCR5

CCR5

Intracellular Space
Host Cell
CD4 Receptor

[Diagram showing the structure of CD4 receptor]

- Extracellular Region (370 aa)
- D1-D4 Domains
- Transmembrane region (25 aa)
- Cytoplasmic tail (38 aa)

CD4 Receptor and Ibalizumab Binding
Ibalizumab
CD4 Directed Post-Attachment HIV Inhibitor

HIV

Ibalizumab

CD4 Receptor

Intracellular Space
Host Cell

CCR5
CCR5
Ibalizumab
Summary of Key Studies

• **Salvage Antiretroviral Therapy**
  - TMB-301: Ibalizumab plus OBR for Adults Failing ART
Ibalizumab
Ibalizumab for Antiretroviral Salvage

TMB-301: Study
Ibalizumab Added to OBR for Adults Failing ART
TMB-301: Study Design

TMB-301: Study Design

• Study design:
  - Single-arm, open label study of ibalizumab (IBA) added to optimized background therapy (OBR) for individuals failing ART.
  - Primary endpoint: proportion achieving ≥0.5 log_{10} decrease in HIV RNA 7 days after initiating IBA therapy (day 14 of study).
  - Secondary endpoints: virologic outcomes, safety, and tolerability at 24 weeks.

• Inclusion Criteria:
  - Adults with HIV, on ART for ≥6 months, HIV RNA >1,000 copies/mL, and ≥3 class drug resistance (but ≥1 remaining active drug).

### Baseline Characteristics of the 40 Participants in TMB-301

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N = 40</th>
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<tbody>
<tr>
<td>Median age (range)—years</td>
<td>53 (23-65)</td>
</tr>
<tr>
<td>Male</td>
<td>34 (85%)</td>
</tr>
<tr>
<td>Non-white</td>
<td>18 (45%)</td>
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<tr>
<td>Mean duration since HIV diagnosis—years</td>
<td>20 ± 8</td>
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<tr>
<td>Mean CD4 count—cells/mm³</td>
<td>150 ± 182</td>
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<tr>
<td>Mean HIV RNA—copies/mL</td>
<td>100,287</td>
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<tr>
<td>Participants with HIV RNA &gt;100,000 copies/mL</td>
<td>7 (18%)</td>
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Ibalizumab Added to OBR for Adults Failing ART
TMB-301: Efficacy at Day 14

IBA Monotherapy = after 7 days of IBA added to failing ART (functional monotherapy)
Control = after 7 days of baseline failing ART

Ibalizumab Added to OBR for Adults Failing ART
TMB-301: Efficacy at Week 24

Optimized background regimen (OBR) added at day 14

Ibalizumab Added to OBR for Adults Failing ART

TMB-301: Efficacy at Week 25, by Baseline CD4 Cell Count

Week 25 Virologic Response (Intention-to-Treat Analysis)

**Conclusions**: “In patients with multidrug-resistant HIV-1 infection who had advanced disease and limited treatment options, ibalizumab had significant antiviral activity during a 25-week study. Evidence of the emergence of diminished ibalizumab susceptibility was observed in vitro in patients who had virologic failure.”

Acknowledgment

The National HIV Curriculum is an AIDS Education and Training Center (AETC) Program supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling $800,000 with 0% financed with non-governmental sources. This project is led by the University of Washington’s Infectious Diseases Education and Assessment (IDEA) Program.

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