HIV Cure

Target Product Profile

Steven Deeks, MD
Professor of Medicine
Division of HIV, Infectious Diseases, and Global Medicine
Zuckerberg San Francisco General
University of California, San Francisco
What will a cure need to do?

*Ideal product profile*

- A truly transformative intervention will need to address the needs of those unable to access, adhere, afford, tolerate and respond to ART
  - Effective for decades
  - Safe, affordable, scalable
  - Works in all populations, including those who are viremic
  - Prevents re-infection
- Aspirational but possible: Single-dose administration
Although the characteristics of an ideal cure are easily defined, those that might at a minimum be acceptable requires careful consideration and discussion from all stakeholders.
HIV Cure: Target Product Profile

- Leaders from industry, academia, advocacy groups, and funders were assembled in February 2019 to discuss cure and its global implementation
- Consensus reached that “target product profiles” for various cure strategies (e.g., immunotherapy, gene therapy)
- TPP should be applicable to all regions
- Process
  - Key stakeholders contacted
  - Delphi exercise completed
  - Consensus obtained, published
  - Living document maintained by HCAAP
Treatment evolution and a cure/remission

The first generation of cures are expected to complex and difficult-to-scale, as were the initial antiretroviral regimens.
What is a target product profile?

- An agreed set of minimally-acceptable and optimistic characteristics of a new product
- Helps to align all stakeholders by broadly defining the product the community wants to deliver to the field
- Will evolve based on scientific developments and changing patient needs

---

**Table: Target Product Profile**

<table>
<thead>
<tr>
<th>Minimums</th>
<th>Optimums</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Target population</strong></td>
<td>All people living with HIV</td>
</tr>
<tr>
<td><strong>Clinical efficacy</strong></td>
<td>Undetectable in plasma (below the 50 copies/ml limit of detection for 48 weeks)</td>
</tr>
<tr>
<td><strong>Safety and tolerability</strong></td>
<td>No grade 3-4 adverse events</td>
</tr>
<tr>
<td><strong>Frequency of adverse events</strong></td>
<td>&lt;5%</td>
</tr>
<tr>
<td><strong>Protection from infection</strong></td>
<td>None</td>
</tr>
<tr>
<td><strong>Special populations</strong></td>
<td>Safe and effective in all populations, including pregnant women, children, and neonates</td>
</tr>
<tr>
<td><strong>Dosing and administration</strong></td>
<td>Oral preferred, but parenteral (including intravenous) acceptable</td>
</tr>
<tr>
<td><strong>Maintenance regimen duration</strong></td>
<td>12 months</td>
</tr>
<tr>
<td><strong>Adverse events</strong></td>
<td>Limited to those no worse than grade 1 or 2</td>
</tr>
<tr>
<td><strong>Need for screening</strong></td>
<td>None</td>
</tr>
<tr>
<td><strong>Storage and handling</strong></td>
<td>Stable at ambient temperature (no cold chain required)</td>
</tr>
<tr>
<td><strong>Product registration path</strong></td>
<td>Approved by regulatory authorities</td>
</tr>
<tr>
<td><strong>Target delivery setting</strong></td>
<td>Any, including home or community centers</td>
</tr>
<tr>
<td><strong>Cost of goods sold</strong></td>
<td>Affordable</td>
</tr>
<tr>
<td><strong>Expected financing source</strong></td>
<td>National governments</td>
</tr>
</tbody>
</table>

---

**THE LANCET HIV**

Multi-stakeholder consensus on a target product profile for an HIV cure

Key areas of debate and consensus building

- Consensus that first generation cures might be cumbersome, non-scalable, expensive and less effective than ART
  - Need to start somewhere
  - Process will be iterative
  - First generation cures not meant to replace ART in those with access who are doing well

- Will PWH/clinicians/regulators accept any detectable viremia?
  - At what viral load threshold will transmission become a concern?

- Should a cure be comparable to ART in terms of safety?
  - No permanent, potentially disabling adverse events

- How important is a biomarker for a cure?
  - Higher tolerance of a less effective strategy if there is a way to prove the therapy was curative and unnecessary ART interruptions avoided

- Prevention of re-infection important public health implications
Acknowledgements

- **Bill & Melinda Gates Foundation**
  - Cathy Bansbach
  - Timothy Attoye
  - Adam Jiang
  - Mike McCune

- **International AIDS Society**
  - Rosanne Lamplough
  - Roger Tatoud

- **McKinsey & Company**
  - Matt Craven
  - Matt Wilson

- **Georgetown University**
  - Lauren Mathae

- **The Annenberg Foundation Trust at Sunnylands**
  - Rob Fallon
  - David Lane

- **Sunnylands working group**
  - Mark Dybul
  - Rosanne Lamplough
  - Ellen LaPointe
  - Sharon Lewin
  - Steve Deeks
  - Mike McCune
  - Joe Tucker
  - Wendy Wertheimer