Treatment and Care: Product portfolio

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EDCTP Stakeholder Meeting on HIV/AIDS
3-4 September 2013
Summary

- Brief overview HIV Treatment Pipeline
- Key Questions & Challenges
- EDCTP role
Targets for Antiretroviral Drugs in HIV Life Cycle

Reeves & Piefer, 2005
## Approved products & Sponsors

### 2003 - 2012

<table>
<thead>
<tr>
<th>Product</th>
<th>Year</th>
<th>Sponsor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emtricitabine</td>
<td>2003</td>
<td>Gilead</td>
</tr>
<tr>
<td>Etravirine</td>
<td>2008</td>
<td>Janssen</td>
</tr>
<tr>
<td>Rilpivirine</td>
<td>2011</td>
<td>Janssen</td>
</tr>
<tr>
<td>Atazanavir</td>
<td>2003</td>
<td>BMS</td>
</tr>
<tr>
<td>Fosamprenavir</td>
<td>2003</td>
<td>Vertex/GSK</td>
</tr>
<tr>
<td>Tipranavir</td>
<td>2005</td>
<td>BI</td>
</tr>
<tr>
<td>Darunavir</td>
<td>2006</td>
<td>Janssen</td>
</tr>
<tr>
<td>Enfuvitide</td>
<td>2003</td>
<td>Trimeris / Hoffman LaRoche</td>
</tr>
<tr>
<td>Maraviroc</td>
<td>2007</td>
<td>Pfizer</td>
</tr>
<tr>
<td>Raltegravir</td>
<td>2007</td>
<td>Merck</td>
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</table>

### ARV Class

<table>
<thead>
<tr>
<th>ARV Class</th>
<th>Total Products</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Approved</th>
<th>Submitted</th>
<th>Discontinued</th>
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<tbody>
<tr>
<td>NRTI (NtRTI)</td>
<td>12</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>7</td>
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<td>NNRTI</td>
<td>8</td>
<td>1</td>
<td>1</td>
<td>3</td>
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<td>3</td>
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<td>Protease Inhibitor</td>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td>4</td>
<td>2</td>
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<td>Fusion Inhibitor</td>
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<td></td>
<td>1</td>
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<tr>
<td>CCR5RI/2RI</td>
<td>4</td>
<td>1</td>
<td></td>
<td>1</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Intergrase Inhibitor</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Attachment Inhibitor</td>
<td>4</td>
<td>1</td>
<td></td>
<td></td>
<td>3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Total              | 40             | 3       | 6        | 1         | 11       | 2         | 17           |
FDCs approved in 2003-2012

<table>
<thead>
<tr>
<th>Year</th>
<th>Ingredients</th>
<th>Trade name</th>
<th>Sponsor</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>Abacavir/Lamivudine</td>
<td>Epzicom</td>
<td>GSK</td>
</tr>
<tr>
<td>2004</td>
<td>Tenofovir/Emtricitabine</td>
<td>Truvada</td>
<td>Gilead</td>
</tr>
<tr>
<td>2006</td>
<td>Efavirenz/Emtricitabine / Tenofovir</td>
<td>Atripla</td>
<td>BMS / Gilead</td>
</tr>
<tr>
<td>2011</td>
<td>Rilpivirine/Emtricitabine / Tenofovir</td>
<td>Complera / Eviplera</td>
<td>Janssen/Gilead</td>
</tr>
</tbody>
</table>
25 single products in 6 “classes” & still counting, but key questions remain…

- Tolerability
- Resistance
- Convenience
- Special Populations
- Cost

Focus of research: to overcome limitations of current regimens
Improving Tolerability …

- new product development
- reformulation

NRTI Class – Tenofovir is preferred product today

Reformulation – Tenofovir Alafenamide (TAF)

- similar safety and efficacy to Tenofovir DF
- Improved bio availability
- potentially reduced side effects.

[CROI 2013]

25 mg dose selected for development as single agent
10 mg dose in FDC with cobicistat (PK booster)

Ongoing studies: co-formulations of TAF, FDC with Darunavir
Dosage Optimisation Studies

Reducing dose of ARVs in current use

Efavirenz
AZT
d4T
Atazanavir/Ritonavir

+ Cost reduction through reduction in API

? Role for EDCTP in treatment optimisation research
Special Populations

Children
  Appropriate formulations
  Product approval for children
  ? Dolutegravir /Abacavir/Lamivudine

HIV TB co-infection
  Rifabutin + Boosted PIs & Intergrase Inhibitors

Women of child bearing age

Post registration surveillance

? Role for EDCTP: include post registration surveillance
Clinical Trial Capacity in Africa

- suitable sites with trained personnel
- sufficient resources & infrastructure
- appropriate regulatory & ethical oversight

Consolidation of clinical trial capacity building started in EDCTP 1
Diagnostic tests

- Toxicity
  - Haematology, Renal function, Lipids & Glucose

- Diagnosis of Co-infections – HepB, HepC

- Efficacy – CD4, Viral Load

- Resistance testing

? Role of EDCTP in development and implementation of POCs
HIV Cure Research

Eradication of the “HIV Reservoir”

- Lack of assays to quantify the reservoir
- Products very experimental

- More clarity within next 10 years

- Africa should participate
  ANRS : studies in children & early treatment studies in adults aimed

? EDCTP as a partner in HIV Cure Research Strategy
Questions

How can EDCTP best enhance the HIV treatment product pipeline for developing countries?

- A role for EDCTP in post marketing research
  e.g. dosage - optimisation, reformulation, co-formulation how can this be effected?

- Would it be better to focus on the needs of special populations?

How can EDCTP consolidate contribution to clinical trial capacity building, so African sites to participate in HIV treatment development? What is the best model for this capacity building?

There is a role for EDCTP in the development validation and establishment of diagnostic tests for viral load, CD4, antiviral toxicities and important co-infections, to monitor efficacy and safety of HIV treatment. – how can this be defined?

Future research in HIV Cure: should EDCTP remain open to this field?