Cost effectiveness of the introduction of dolutegavir in first- or second-line ART regimens in sub-Saharan Africa

Poster number MOPE0285


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Presented at the 9th IAS Conference on HIV Science — Paris, France

Background

• Generic formulations of dolutegavir may well be introduced in sub-Saharan Africa in the coming years. It is not clear how it can be deployed in the most cost effective way.

• To explore the potential effectiveness and cost effectiveness of various policies involving use of dolutegavir within 1st, or 2nd-line antiretroviral drug regimens in the context of sub-Saharan Africa.

Policies considered

1 No change in policy (1st-line efavirenz/TDF/3TC, 2nd-line atazanavir/3TC/FTC)
2 As 1, except increase in rate of switch to 2nd-line in those with 1st-line failure
3 As 1, except in all ART initiators use dolutegavir instead of efavirenz in 1st line
4 As 1, except that for all on 1st-line move from efavirenz to dolutegavir
5 As 1, except 2nd-line regimen dolutegavir- rather than atazanavir-based
6 As 1, except 2nd-line regimen dolutegavir- rather than atazanavir-based, plus an increase in rate of switch to 2nd-line
7 As 1, except dolutegavir 1st-line regimen for all ART initiators, no switching to 2nd-line in those on dolutegavir, replace atazanavir with dolutegavir in those on 2nd-line already.
8 1st-line dolutegavir/TDF/2TC, 2nd-line dolutegavir/3TC/FTC

Modelling approach

• Individual-based simulation model of HIV transmission, effect of ART, considering specific drugs and resistance mutations

• Model based around southern Africa with multiple potential setting scenarios generated through simulation

• Parameters such as
  - ART adherence profile
  - ART interruption rate
  - Switch rate after first line failure

• For each setting scenario, we compare outcomes of policy options across 20 years from 2016.

• Assumptions on effectiveness of dolutegavir vs efavirenz:*
  - Lower rate of resistance emergence
  - Greater potency
  - Greater tolerability

• Cost effectiveness analysis: health systems perspective, 3% discount rate, cost effectiveness threshold $500.

• Absolute costs and DALI’s relevant for a country of population size of ~10 million adults in 2016

Charateristics of setting scenarios at baseline (2017)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Modelled populations. (Median and 5% - 95% centiles)</th>
<th>Examples of studies with estimates</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV prevalence (age 15-49)</td>
<td>10.0% (0.0% - 20.1%)</td>
<td>Dolutegavir (2016), Tanzania (2014), Malawi (2016), Botswana (2016)</td>
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<tr>
<td>People living with HIV, percent diagnosed</td>
<td>76% (42% - 90%)</td>
<td>Malawi (2016), Tanzania (2014), Botswana (2016)</td>
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<tr>
<td>People living with HIV, percent on ART, diagnosis to death</td>
<td>46% (41% - 83%)</td>
<td>Dolutegavir (2016), Tanzania (2014), Botswana (2016)</td>
</tr>
<tr>
<td>People living with HIV, percent on ART, death to diagnosis</td>
<td>63% (41% - 77%)</td>
<td>Dolutegavir (2016), Tanzania (2014), Botswana (2016)</td>
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<tr>
<td>People on ART with NNRTI resistance exposure, percent with NRTI resistance</td>
<td>42% (20% - 88%)</td>
<td>Dolutegavir (2016), Tanzania (2014), Botswana (2016)</td>
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<tr>
<td>People on ART, percent with VL &gt; 1000 copies/mL</td>
<td>49% (19% - 64%)</td>
<td>World Bank South Africa HIV report 2017, WHO resistance report 2017, Malawi (2016), Tanzania (2014), Botswana (2016)</td>
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<tr>
<td>People on ART, percent with VL &gt; 1000 copies/mL</td>
<td>11% (1% - 17%)</td>
<td>WHO resistance report 2017, Malawi (2016), Tanzania (2014), Botswana (2016)</td>
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<tr>
<td>People on ART, percent with resistance to NRTI drugs</td>
<td>32% (20% - 88%)</td>
<td>WHO resistance report 2017, Malawi (2016), Tanzania (2014), Botswana (2016)</td>
</tr>
<tr>
<td>People on ART, percent with resistance to NNRTI drugs</td>
<td>10% (0% - 41%)</td>
<td>WHO resistance report 2017, Malawi (2016), Tanzania (2014), Botswana (2016)</td>
</tr>
<tr>
<td>People on ART, percent resistance to TDF (in 1st -line ART)</td>
<td>41% (14% - 44%)</td>
<td>Dolutegavir (2016), Tanzania (2014), Botswana (2016)</td>
</tr>
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Preliminary Conclusions

• Based on its known attributes, it is predicted that there would be substantial health benefits from introduction of dolutegavir (greatest if all people on first line are moved to dolutegavir) and that this may well be cost saving compared with current approaches, especially since the cost of dolutegavir is likely to be substantially lower than the $44 assumed.

• It is uncertain whether the most cost effective role for dolutegavir is replace efavirenz as a first line regimen or to replace boosted PIs in 2nd-line regimens, or to replace both with a single regimen approach.

• Further data are needed to inform this, particularly on the virologic efficacy of dolutegavir-based regimens when there is resistance to 3TC/TFC and possible additional resistance to TDF (in 1st-line) or zidovudine (in 2nd-line)