Choice in today’s era of treatment optimization: Leaving nobody behind

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Johannesburg, South Africa
Overview

- Early introduction of Dolutegravir (DTG)
- 2019 update on potential risk of neural tube defects with use of DTG
- Leaving no one behind: Informed choice in adolescent girls and young women living with HIV
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### OPTIMAL ARVs

<table>
<thead>
<tr>
<th>Efficacious</th>
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<tbody>
<tr>
<td>Low toxicity</td>
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<tr>
<td>Well tolerated and easy to take</td>
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<tr>
<td>Durable/High genetic barrier to resistance</td>
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<tr>
<td>Better sequencing/switching</td>
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<tr>
<td>Harmonized across populations (Preg, TB, Peds)</td>
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<td>Reduces cost</td>
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### 2016 WHO Guidelines: ART recommendations for adults and adolescents

<table>
<thead>
<tr>
<th>First-line ART</th>
<th>PREFERRED</th>
<th>ALTERNATIVE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TDF + XTC + EFV</td>
<td>AZT + 3TC + EFV (or NVP)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TDF + XTC + DTG</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TDF + XTC + EFV&lt;sub&gt;400&lt;/sub&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TDF + XTC + NVP</td>
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</tbody>
</table>
Dolutegravir (DTG)

- A “best in class” integrase inhibitor
- Well tolerated
- Low toxicity
- High genetic barrier to resistance
- Once daily dosing
- Small tablet size
- Can be dosed twice daily in patients on TB treatment
- Does not interact with hormonal contraception
- Safe to use during pregnancy*
- Available for adults and adolescents as:
  - 50mg tab
  - TDF/3TC/DTG 300mg/300mg/50mg (aka TLD)
  - ABC/3TC/DTG 600mg/300mg/50mg
TDF/3TC(FTC)/EFV as the preferred first line ARV combination among adults and adolescents and initial shifts towards Dolutegravir (DTG) in low- and middle-income countries (situation as of November 2017)
May 2018: New findings informed DTG safety profile among women of child bearing potential

- Observational study in Botswana, found 4 cases of neural tube defects out of 426 women who became pregnant while taking DTG.

- This rate of approximately 0.9% compares to a 0.1% risk of neural tube defects in infants born to women taking other antiretroviral medicines at the time of conception.
What did this mean for programmatic approaches to introduction of DTG-based regimens?

Adults and adolescents living with HIV

**BOX 3. A WOMAN-CENTRED APPROACH**

Woman-centred health services involve an approach to health care that consciously adopts the perspectives of women and their families and communities. This means that health services see women as active participants in and beneficiaries of trusted health systems that respond to women’s needs, rights and preferences in humane and holistic ways. Care is provided in ways that respect women’s autonomy in decision-making about their health, and services must provide information and options to enable women to make informed choices. The needs and perspectives of women, their families and communities are central to providing care and to designing and implementing programmes and services. A woman-centred approach is underpinned by two guiding principles: promoting human rights and promoting gender equality.

Source: Consolidated guideline on sexual and reproductive health and rights of women living with HIV (3).
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July 2019 Update from Tsepamo: NTD Prevalence by ARV Exposure

As of March 2019, rate of NTDs with DTG at conception lower than initially signaled [1,2].

No significant difference in major external structural malformations with DTG vs non-DTG ART [1,2].

WHO released updated recommendations reconfirming use of DTG-based ART as preferred first-line and second-line therapy [3].

This is a POTENTIAL risk. We are still not sure!

### Outcome

<table>
<thead>
<tr>
<th></th>
<th>At Conception</th>
<th>DTG (n = 1683)</th>
<th>Non-DTG (n = 14,792)</th>
<th>EFV (n = 7959)</th>
<th>DTG in Pregnancy (n = 3840)</th>
<th>HIV Negative (n = 89,372)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NTDs per exposures, n/N</td>
<td></td>
<td>5/1683</td>
<td>15/14792</td>
<td>3/7959</td>
<td>1/3840</td>
<td>70/89372</td>
</tr>
<tr>
<td>Prevalence difference, % (95% CI)</td>
<td>Reference</td>
<td>0.20 (0.01-0.59)</td>
<td>0.26 (0.07-0.66)</td>
<td>0.27 (0.06-0.67)</td>
<td>0.22 (0.05-0.62)</td>
<td></td>
</tr>
<tr>
<td>NTDs per exposures since May 2018, n/N</td>
<td></td>
<td>1/1275</td>
<td>1/3492</td>
<td>0/2172</td>
<td>1/1028</td>
<td>9/23,315</td>
</tr>
</tbody>
</table>

### July 2019 WHO Update

#### Preferred and alternative first-line ART regimens

<table>
<thead>
<tr>
<th></th>
<th>4 weeks – 10 years (infants and children)</th>
<th>&gt;10 yrs and 30kg (adolescents)</th>
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<tbody>
<tr>
<td><strong>Preferred</strong></td>
<td>ABC + 3TC + DTG&lt;sup&gt;d&lt;/sup&gt;</td>
<td>TDF + 3TC (or FTC) + DTG&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Alternative</strong></td>
<td>ABC + 3TC + LPV/r</td>
<td>TDF + 3TC + EFV&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>ABC + 3TC + RAL&lt;sup&gt;e&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TAF&lt;sup&gt;f&lt;/sup&gt; + 3TC (or FTC) + DTG</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> TDF: tenofovir disoproxil fumarate; EFV: efavirenz

<sup>b</sup> Effective contraception should be offered to adult women and adolescent girls of childbearing age or potential. DTG can be prescribed for adult women and adolescent girls of childbearing age or potential who wish to become pregnant or who are not otherwise using or accessing consistent and effective contraception if they have been fully informed of the potential increase in the risk of neural tube defects (at conception and until the end of the first trimester). If women identify pregnancy after the first trimester, DTG should be initiated or continued for the duration of the pregnancy (Box 2).

<sup>c</sup> LPV/r-based ART should not be used in settings with national estimates of pretreatment resistance to EFV of 15% or higher. If LPV/r-based ART is preferred, and if EFV is unavailable, a boosted PI-based regimen should be used. The choice of PI/r depends on programmatic characteristics.

<sup>d</sup> TAF may be considered for people with established osteoporosis and/or impaired kidney function.

<sup>e</sup> For age and weight groups with approved DTG dosing.

<sup>f</sup> RAL should be used as an alternative regimen only if LPV/r solid formulations are not available.

<sup>g</sup> For age and weight groups with approved TAF dosing.

<sup>h</sup> EFV should not be used for children younger than three years of age.

<sup>i</sup> Neonates starting ART with an RAL-based regimen should transition to an LPV/r solid formulation as soon as possible.
Effective contraception should be offered to adult women and adolescent girls of childbearing age or potential. DTG can be prescribed for adult women and adolescent girls of childbearing age or potential who wish to become pregnant or who are not otherwise using or accessing consistent and effective contraception if they have been fully informed of the potential increase in the risk of neural tube defects (at conception and until the end of the first trimester). If women identify pregnancy after the first-trimester, DTG should be initiated or continued for the duration of pregnancy.
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What did this mean for programmatic approaches to introduction of DTG-based regimens?

- Adults and adolescents living with HIV
  - Men and women NOT of childbearing potential
    - TLD
  - Women and adolescent girls of childbearing potential
    - On contraception
      - TLD
    - Not on contraception
      - TLE
What does this mean for programmatic approaches to introduction of DTG-based regimens?

Adults and adolescents living with HIV

- Men and women NOT of childbearing potential
  - TLD

- Women and adolescent girls of childbearing potential
  - Informed choice

Informed choice about sexual reproductive health options
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How do we support adolescent girls and young women to make informed choices?

- An adolescent-friendly approach is needed to support AGYW to make informed choices about:
  - HIV treatment
  - Sexual Reproductive Health
Decision making in young people

- Accept information from people they trust and in language they understand
- Favor their own experiences and anecdotal evidence over information about statistics
- Influenced by peers and social media
- View occasional health threatening acts as less risky
  - May misperceive independent risks as cumulative (i.e. I won’t fall pregnant if I only have sex once in a while)
What do AGYW need to support choice of HIV treatment options

• Adolescent-friendly health care workers!
• Information in language they can understand- and give honest answers to their questions
• Provide information that is positive- not just fearful
• Correct misperceptions they may have heard or explain why guidance has changed if they ask
• Continue the discussion over time to answer additional questions, ensure understanding, provide any new information and be supportive if there is a change in choice
A few additional thoughts about supporting choice in AGYW choices about sexual reproductive health

• Adolescent girls are eligible for all methods of contraception
  – Long acting reversible contraception may be preferable for adherence reasons

• Adolescents are less tolerant of side effects
  – May need to additional support to choose or switch forms of contraception

• Rates of STI’s are disproportionately high
  – U=U is a message that has spread but emphasize that dual protection (i.e. condoms) protect their health

• Fertility intentions and choice to use contraception may change over time
Thank you!

• There is reassuring evidence that the potential risk of NTD’s with use of DTG is lower than previously believed- but there is still uncertainty
• If there really is a risk- it is LOW
• DTG for women and girls of childbearing potential should be based on informed choice NOT use of contraception
• AGYW may need a different approach to make a truly informed choice about both HIV treatment options and SRH but lets not leave them behind