Pregnancy and infant outcomes among HIV-positive women on dolutegravir versus efavirenz-based antiretroviral therapy: week 48 analysis of the ADVANCE trial

Nomathemba Chandiwana¹, Godspower Akpomiemie¹, Andrew Hill², Matthew Chersich¹, Simiso Sokhela¹, Nonkululeko Mashabane¹, Celicia Serenata¹, Masebole Masenya¹, Lee Fairlie¹, Bronwyn Bosch¹, Francois Venter¹, Michelle Moorhouse¹

1 Wits Reproductive Health and HIV Institute (Wits RHI), University of the Witwatersrand, Johannesburg, South Africa
2 Liverpool University, Pharmacology, Liverpool, United Kingdom

INTEREST 2019, 16 May 2019, Accra, Ghana
Disclosure slide

This study has been supported by USAID and Unitaid, with study drugs donated by Gilead Sciences and ViiV Healthcare

The U.S. Agency for International Development (USAID) invests in OPTIMIZE through its support of a global consortium, led by Wits RHI, that includes ICAP at Columbia University, Mylan Laboratories, the University of Liverpool and the Medicines Patent Pool. USAID is a key implementing agency of the U.S. President’s Emergency Plan for AIDS Relief (PEPFAR) and is responsible for over half of all PEPFAR programs with activities focused in 35 priority countries and regions, mainly in sub-Saharan Africa and Asia. For more information, please visit: www.usaid.gov

Unitaid finds new and better ways to prevent, test and treat HIV, tuberculosis and malaria quickly and more affordably. It takes game-changing ideas and turns those into practical solutions that can help accelerate the end of the three diseases. Established in 2006 by Brazil, Chile, France, Norway and the United Kingdom, Unitaid plays an important part in the global effort to defeat HIV, tuberculosis and malaria. For more information, please visit: www.unitaid.org
Background

- Dolutegravir holds considerable advantages over other ARVs in terms of resistance profile, tolerability and cost [1]
- Findings from an observational cohort study in Botswana reported concerning raised levels of NTDs following DTG exposure in early pregnancy [2]
- The ramifications of this finding have been immense
  - Particularly in SSA, where most PLHIV are WOCBP
  - Threatening the possibility of a universal regimen for all, by creating parallel ART programmes
- Yet there are inadequate data on DTG’s safety in pregnancy.
Methods

- To describe pregnancy outcomes in the ongoing ADVANCE trial (NCT03122262)
- Phase 3 clinical trial with 1053 patients randomised to
  - DTG-TAF-FTC, or DTG-TDF-FTC or EFV-TDF-FTC
- All women completed week 48, were on ART before conception
- Gestational age assessment and congenital foetal anomaly screen
- Women on dolutegravir were switched to alternative regimens if < 8 weeks gestation
- Infant HIV status at birth and birth defects were also assessed

<table>
<thead>
<tr>
<th>Pregnancy/infant outcomes</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous abortion</td>
<td>Non-induced expulsion of an embryo or foetus &lt; 20 weeks gestation</td>
</tr>
<tr>
<td>Elective termination</td>
<td>Voluntary termination of pregnancy &lt; 13 weeks gestation</td>
</tr>
<tr>
<td>Preterm birth</td>
<td>Live birth &lt; 37 weeks gestation</td>
</tr>
<tr>
<td>Small for gestational age</td>
<td>&lt; 10th percentile of weight for gestational age</td>
</tr>
<tr>
<td>Stillbirth</td>
<td>Foetal death at or after 28 weeks gestation</td>
</tr>
<tr>
<td>Neonatal death</td>
<td>Death during the first 28 days of life</td>
</tr>
</tbody>
</table>
Results

- Annual pregnancy rate 12.5% (78/623)
- Median age at conception 31.6 years
- Two thirds (50/78) occurred in women on a DTG-based regimen
- 3 infants had minor birth defects
- No HIV transmissions occurred
Conclusions

• Our study adds to important evidence on outcomes of InSTI use before conception
• Women who initiated DTG-based ART before conception did not have higher rates of adverse pregnancy outcomes
• However, it is important to pool data on stillbirths and infant deaths across similar trials, on the safety of DTG as well as newer ARVs
• Urgent need for prospective pharmacovigilance during pregnancy and breastfeeding is required for African settings
Acknowledgements

• Thank you to our participants
• ADVANCE team and our collaborators
• USAID (PEPFAR) and Unitaid
• Gilead and Viiv

Poster #15