Why is South Africa important?

• Almost a fifth of global HIV-positive population
• Almost 5 million people on ART (95% on TDF/FTC (or 3TC)/EFV); about 170 000 second; 3rd line 4000
• Procurement giant: SA=PEPFAR=Global Fund for ART generics
• Sustainable programme – mostly funded off SA tax base
• Almost halving of incidence in last 5 years in some demographics – HSRC, July 2012
Figure 3.1: Number of registered deaths by year of death, 1997–2016*

*Data for 1997–2015 have been updated with late registrations/delayed death notification forms processed in 2016/2017.
Current ART in SA

- Tenofovir + FTC + Efavirenz

Failure >1000 copies/ml

- AZT (zidovudine) + 3TC + LPV/r

  (ATV/r if not tolerated)

Failure, genotyping

XTC, other nukes

- Darunavir
- Dolutegravir
- Etravirine
Challenges for SA - HIV

- Re-entry to system – drive NNRTI resistance – and is most patients initiating 1st line!
- Large numbers – drug storage
- Stockout of singles
- Lots of pregnancies
- Patients getting older – increased co-morbidities
- (very small numbers of paeds)
% of HIV+ adults at different levels of engagement in HIV care

- Undiagnosed
- Diagnosed, ART-naïve
- Previously on ART
- Total on ART

Thembisa version 4.1
What about reproductive health and the NTDs?

- >60% of ART programme female, most of child-bearing potential
- Freely available broad choices of contraception and termination
- Massive contraception stock outs
- ≈50% of pregnancies are unplanned (not the same as unwanted!)
- EFV drug interactions with hormonal contraception
Changing disease severity over time

Adjusted proportion of patients started ART by CD4 category

**Source:** Consolidated National report covering monthly and quarterly ART data to end March 2014

**Thanks:** Andrew Boulle
Changing disease severity over time

Adjusted proportion of patients started ART by CD4 category

TB less of an issue – key for discussion re DTG

Thanks: Andrew Boulle

Source: Consolidated National report covering monthly and quarterly ART data to end March 2014
Confidential data – Lucas Hermans, submission

• Analysed >95 000 patients in NHLS database
• 34.9% (1 273/3 649) were switched to second-line ART. Patients were switched after a median of 58 weeks
• Young adults and men highest risk for viraemia
• 45% re-suppressed on NNRTI – huge implications for DTG
DTG history in SA

• Discussions started in 2013 – based on small tablet size
• ADVANCE – DTG vs EFV started 2017, results due 2019
• In meantime, costs of TLD modelled to be lower than TLE
• Appetite for transition within DoH up when cost savings demonstrated
• Alignment with registration, tenders and guidelines begun
• NTD signal huge complication
CLINICAL UPDATE

Cutting the cost of South African antiretroviral therapy using newer, safer drugs

W D F Venter,1 FCP (SA), MMed; B Kaiser,2 MPH, PharmD, BCPS; Y Pillay,3 PhD; F Conradie,4 MB BCh; G B Gomez,5 PhD; P Clayden,6 M Matsoalo;7 C Amole,8 BA; L Rutter,7 BA; F Abdullah,9 M Barnhart,10 MD, MPH; A Pillay,11 PhD; A Pozniak,11 M Moorhouse,1 MB BCh; M Chersich,1 MB BCh, PhD; C:

1Wits Reproductive Health and HIV Institute, University of t
2Formerly UNITAID, Geneva, Switzerland
3HIV/AIDS, TB and Maternal, Child and Women’s Health i
“Dolutegravir in first line therapy has by far the highest impact in getting to the last 90 for South Africa”

Professor Gesine Meyer-Rath - Boston University/HE²RO
Combining full UTT with TLD for all reduces infections by 19%, deaths by 8%, and cost by 10% by 2037/38, with cost savings from the first year on.

TLD for men + women > 55 halves TLD’s impact on new infections and cost savings.

Thanks Gesine Meyer-Rath; IAS July 2018
SA possible scenarios post-NTD signal

• Stay with TEE (or TLE) or go with DTG (with small number on TLE)
• Or hybrid – messy, but may be only way forward
• Implement observational cohorts urgently
Initial planning scenarios would have allowed for earlier adoption of TLD however registration delays have made full-scale April 2019 most likely option.

<table>
<thead>
<tr>
<th>Supplier (Products)</th>
<th>2017</th>
<th>2018</th>
<th>2019</th>
</tr>
</thead>
</table>

A supplementary tender launched in August to the two anticipated approved suppliers would enable the introduction of TLD to selected cohorts by the end of September/October.

A national tender launched in Q1 2019 could have as many as nine suppliers approved and would enable the introduction of TLD by the end of March/April.

<table>
<thead>
<tr>
<th>Actual or expected filing mo.</th>
<th>Anticipated MCC approval dates (filing + 12 mo.)</th>
<th>Earliest mo. with 9 month stability data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blue</td>
<td>Green</td>
<td>Orange</td>
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</tbody>
</table>
But...

• What about switching? Big headache if stable and happy – new side effects

• Balance several issues:
  • Stability of supply (big issue for DoH)
  • Current side effects? New side effects?
  • TB, desire for pregnancy
Changes in D4T, AZT & TDF use – often FAST

Between 2 to 4 million people using AZT containing regimen in 2012

WHO AMDS database, 2014 (preliminary data)
What are the options treatment for programmes in a DTG era?

- TDF/3TC/DTG likely to replace a large chunk 1st line and a big chunk of 2nd line in 2019
- Switch patients are a headache – fix what isn’t broken?
- PI based patients –
  - move to TLD if suppressed on TDF/FTC/PI
  - ?same if suppressed on AZT/3TC/PI
- Women of child bearing age?
  - Sensible to support EFV till more data
  - Do NOT change if pregnant
  - If want DTG, reinforce effective contraception
- Treatment option for people initiating ART with active TB
  - Use existing efavirenz regimen
  - Double dose DTG (50mg BD/100mg daily) (con: needs singles); possible future with 50mg FDC
Conclusion

• Probably Q2 introduction – with EFV for TB, intolerance and ?what % of women?
• What do we do with 4-odd million people on TLE and most happy?
• What will be the impact of demand creation?
• Complexity of two first line regimens is huge – especially for training
Thank you
27th International Workshop on HIV Drug Resistance and Treatment Strategies

Monday, 22 October to Tuesday, 23 October 2018
Gallagher Convention Centre, Midrand,
Johannesburg, South Africa

www.hivresistance2018.co.za

4th Southern African HIV Clinicians Society Conference 2018

Wednesday, 24 October to Saturday, 27 October 2018
Gallagher Convention Centre, Midrand,
Johannesburg, South Africa

www.sahivsoc2018.co.za