# Adult third-line ART update

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**SAHCS Conference** 

University of the Witwatersrand

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### Disclosures

- Speaker fees and honoraria from Gilead Sciences, AbbVie, Cipla, Mylan, Aspen, Sanofi, Pfizer and Janssen
- Conference sponsorship from BD, Gilead, Janssen, Merck, Cipla and Mylan
- Part of ART optimisation collaborations
- Funding from USAID, Unitaid, SAMRC and study drug donations from ViiV Healthcare and Gilead Sciences for ART optimisation studies

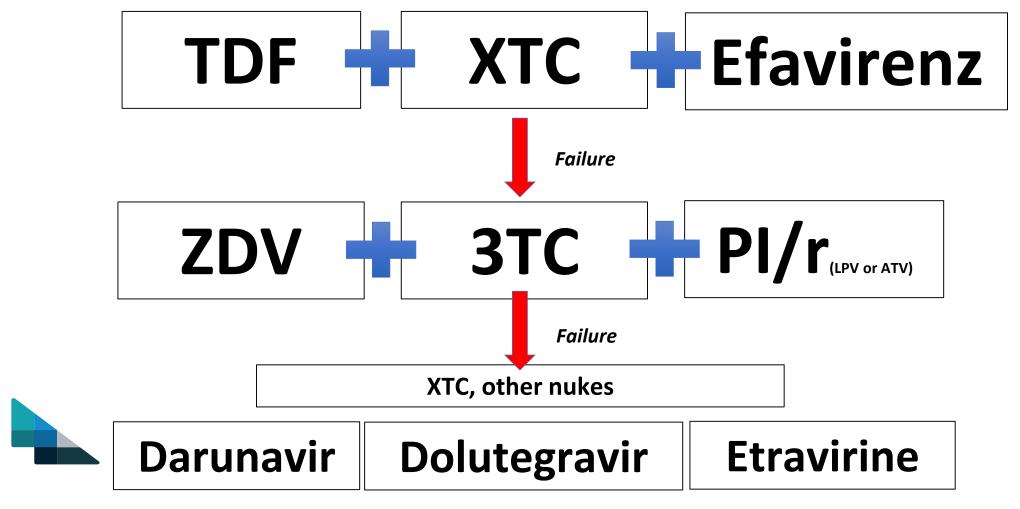




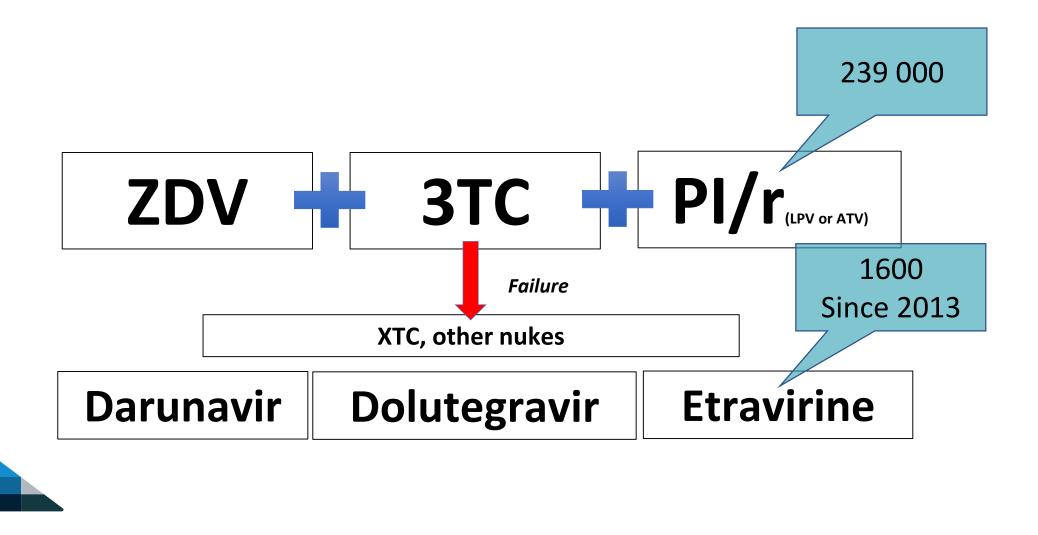




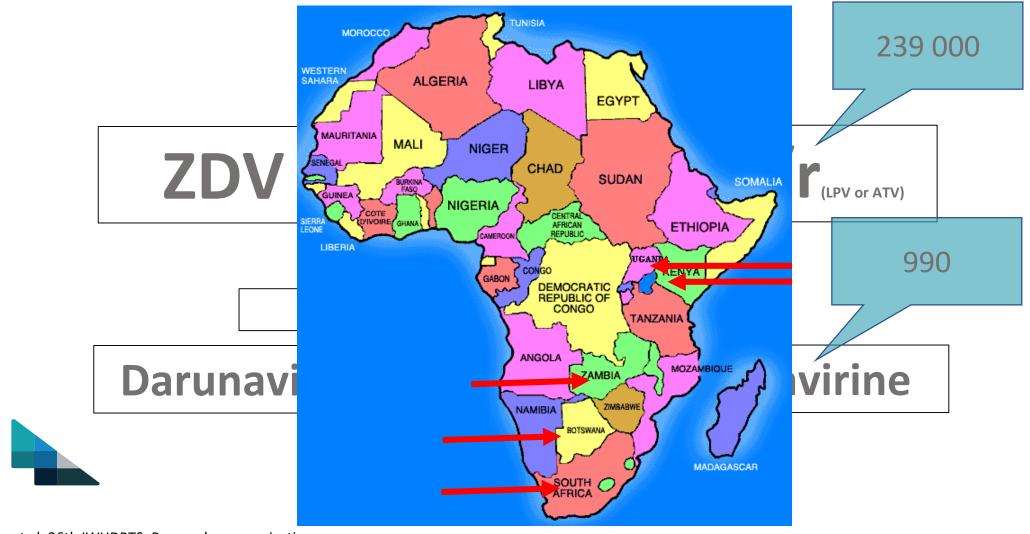
## SA has largest ARV programme: > 5 million



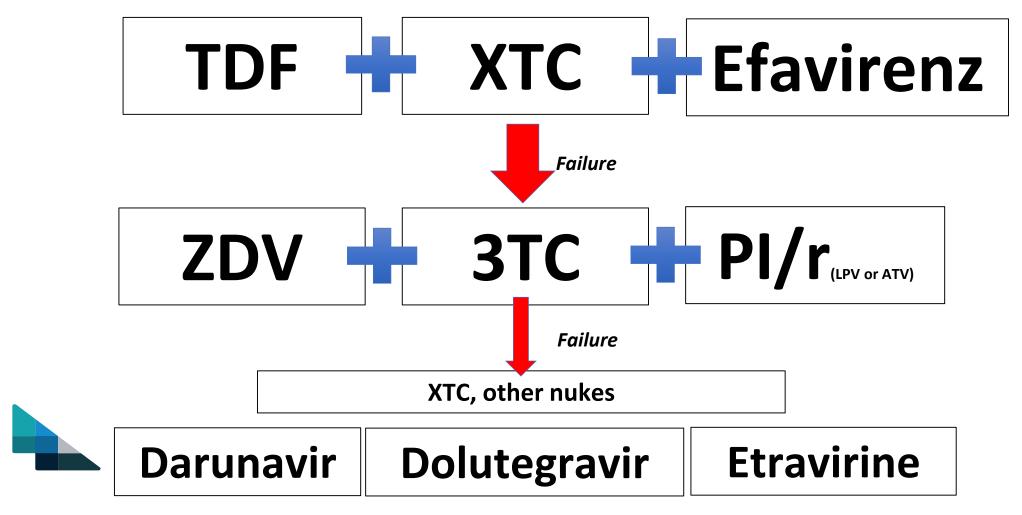
## SA has largest ARV programme: > 5 million



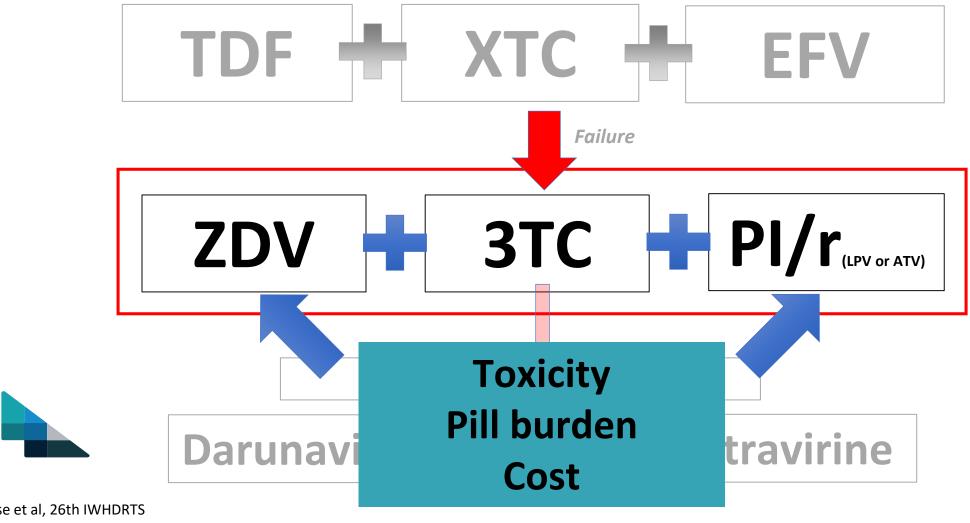
## SA has largest ARV programme: > 5 million



## With continued ARV scale up...

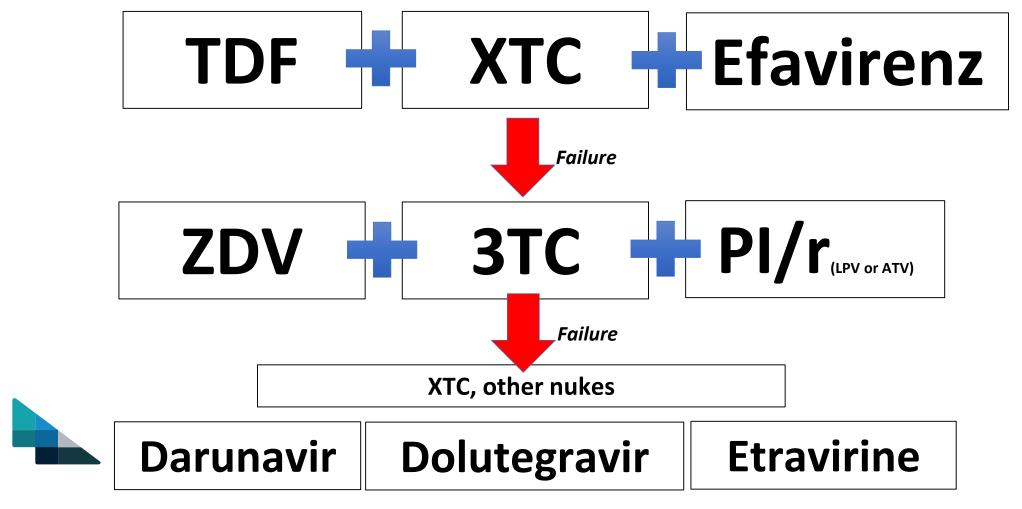


### Second-line

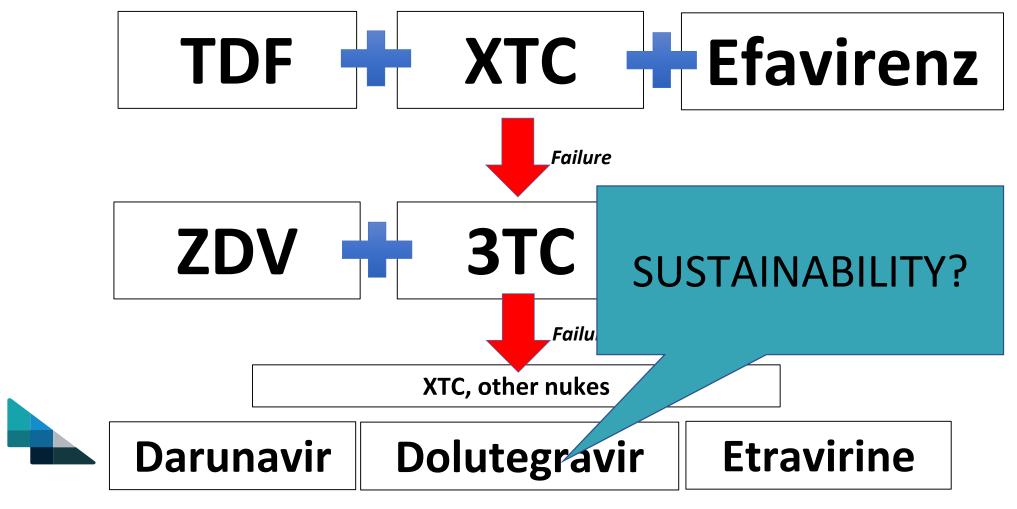


Moorhouse et al, 26th IWHDRTS

## As more patients fail PI/r regimens...

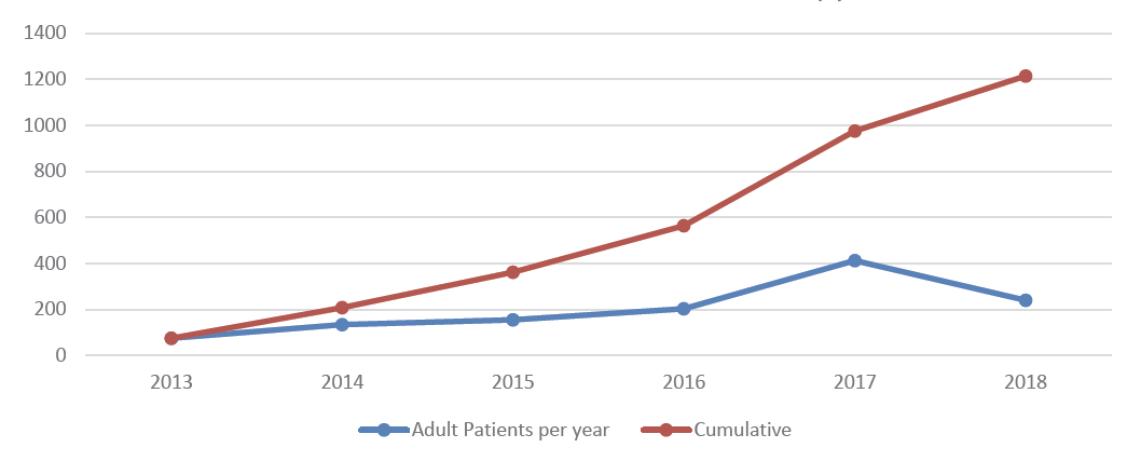


## As more patients fail PI/r regimens...



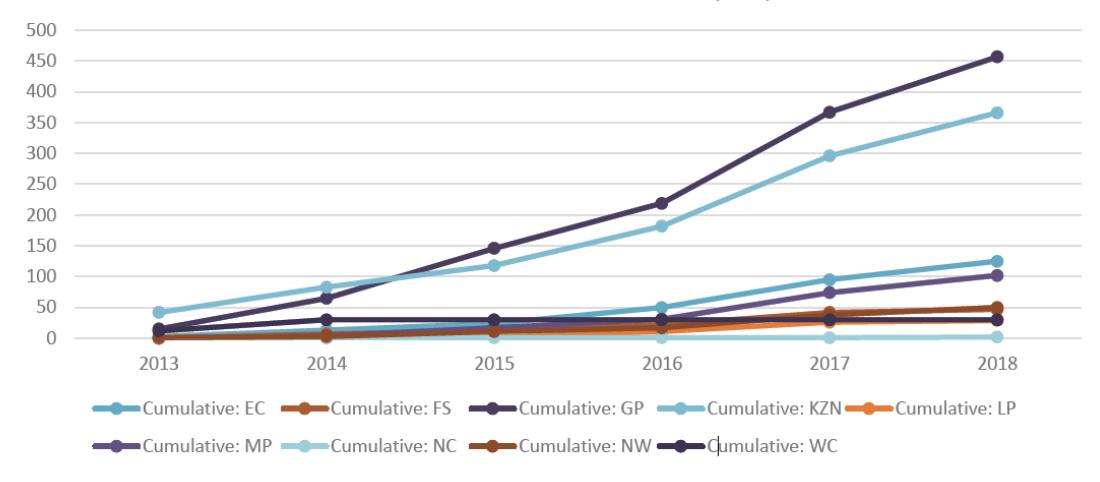
# So how many adults failing PI/r-based ART are accessing third-line ART?

Adults on third-line antiretroviral therapy



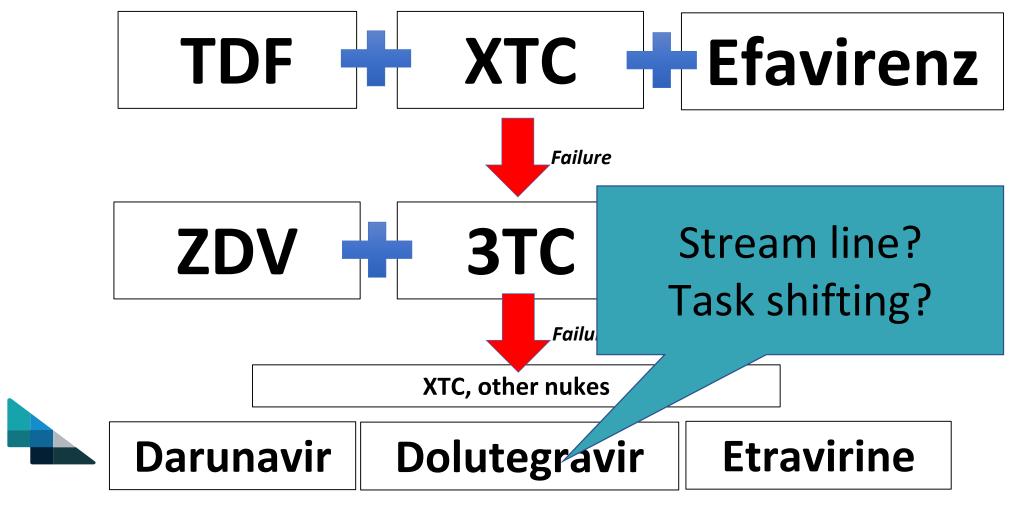
## Provincial spread

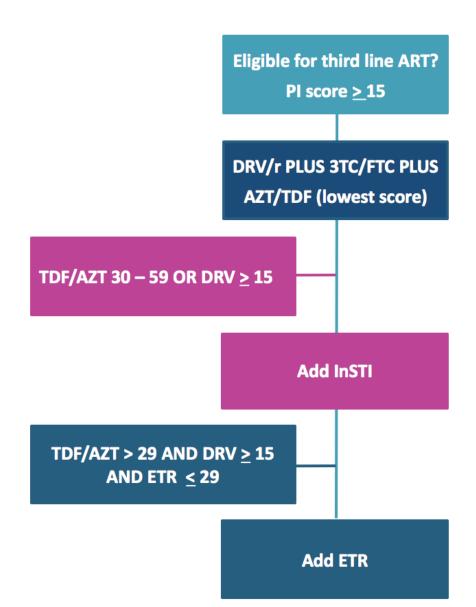
Cumulative adults on third-line ART\* per province



WC numbers do not increase from 2014, as third-line ART was decentralised to province was decentralised to province

## As more patients fail PI/r regimens...

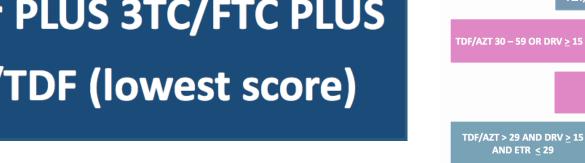






**Eligible for third line ART? PI score > 15** 

DRV/r PLUS 3TC/FTC PLUS **AZT/TDF** (lowest score)



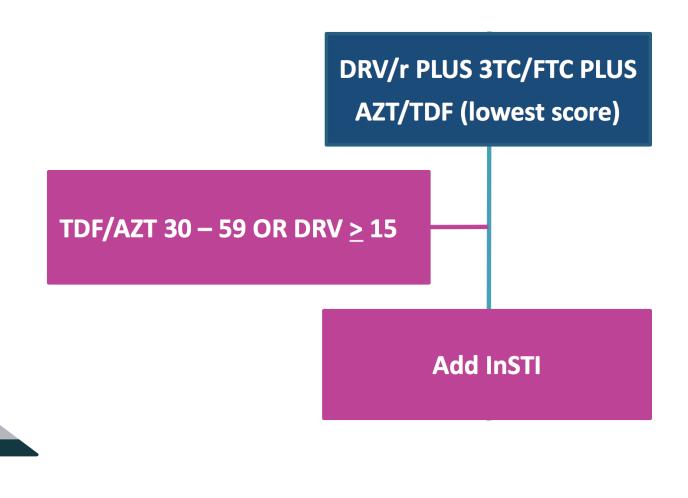
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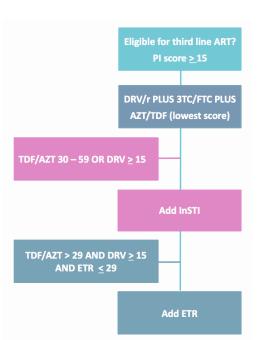
DRV/r PLUS 3TC/FTC PLUS **AZT/TDF (lowest score)** 

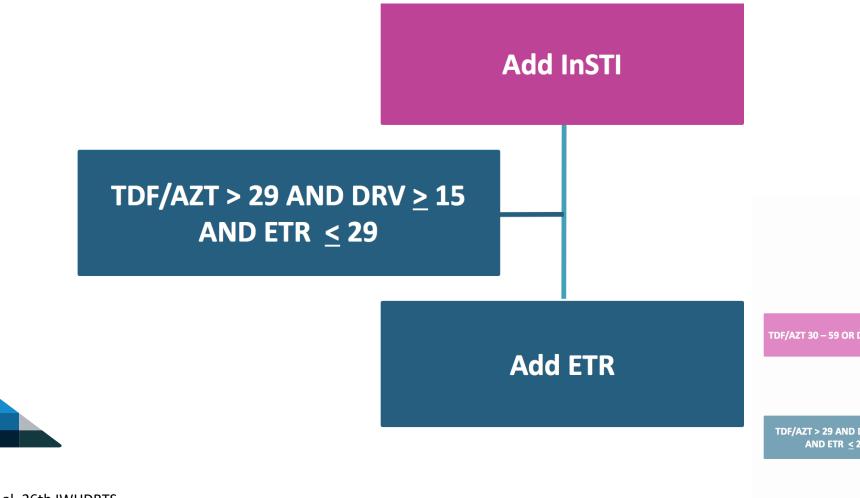
Add InSTI

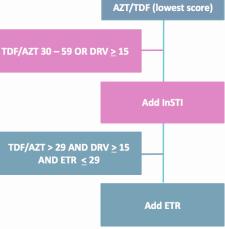
Add ETR











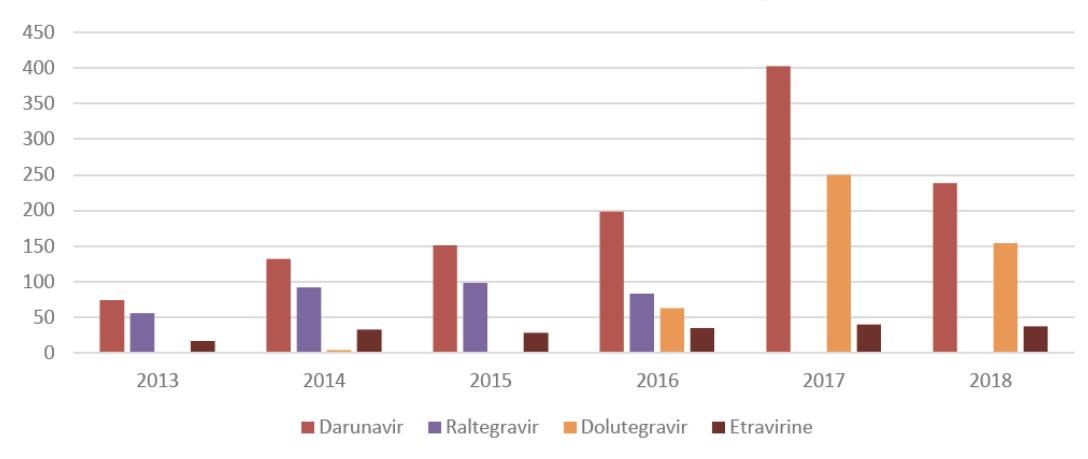
Eligible for third line ART?

PI score > 15

DRV/r PLUS 3TC/FTC PLUS

## Drugs used in third-line ART (adults)

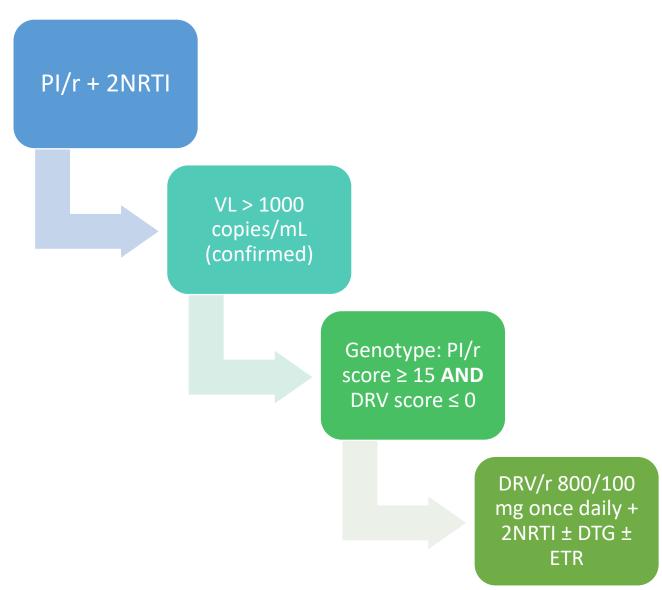
### Adult third-line antiretroviral usage



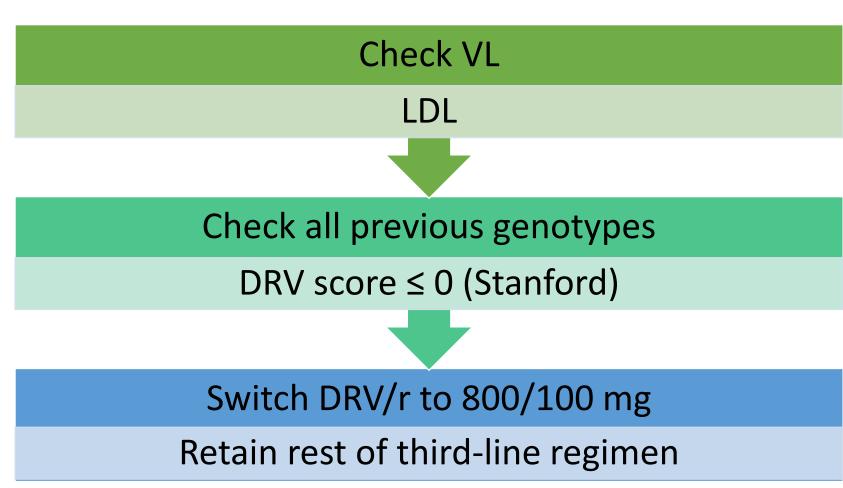
## DRV 400 mg is now available in SA

- Currently patients on DRV in third-line receive DRV/r 600/100 mg bid
- A small proportion of third-line patients have no DRV RAMs, and in such patients it may be possible to use DRV/r 800/100 mg daily instead of DRV/r 600/100 mg bid to, reducing pill burden, dosing frequency and side effects
- Patients initiating third-line ART: if DRV score (Stanford) is zero on all genotypes, may initiate DRV 800/100 mg daily
- Switching patients already on third-line: the patient's VL must be LDL, AND the DRV score (Stanford) MUST be zero on all genotypes the patient has had done

## Initiating third-line ART



# On DRV/r based third-line ART (600/100 mg bid)



### What is new in third-line?

JAIDS Journal of Acquired Immune Deficiency Syndromes Publish Ahead of Print DOI: 10.1097/QAI.0000000000001883

> Third-line antiretroviral therapy programme in the South African public sector: cohort description and virological outcomes

Michelle Moorhouse MBBCh (Wits), DA (SA), FRSPH<sup>1</sup>, Gary Maartens, MBChB, MMed<sup>2</sup> Willem Daniel François Venter, MBBCh, MMed, FCP (SA), DTM&H, Dip HIV Man (SA)<sup>1</sup>, Mahomed-Yunus Moosa, MBChB, FCP (SA), PhD<sup>3</sup>, Kim Steegen, BSc, MSc, PhD<sup>4</sup>, Khadija Jamaloodien, BPharm, BCom (Law), MSC Clin Epi<sup>5</sup>, Matthew P Fox, DSc, MPH<sup>6</sup>, Francesca Conradie, MBBCh, DTM&H, Dip HIV management



### Non-linear Uptake of Third-line Antiretroviral Therapy

### Non-linear Uptake of Third-line Antiretroviral Therapy among Adult Patients in the South African Public Sector

Authors: M. Moorhouse<sup>1</sup>, M. Rassool<sup>2</sup>, Y. Fernandez<sup>3</sup>, MP. Fox<sup>4</sup>, R. Lancaster<sup>5</sup>, M. Fox, G. Maartens<sup>6</sup>

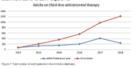
### Background

South Africa has the largest antiretroviral therapy (ART) programme globally, and is one of few sub-Saharan African countries with access to third-line ART (TLART) in its public sector. Nith continued scale-up of ART, the number of patients falling first line, with its low genetic barrier, and subsequently second-line ART, with its higher pill burden, twice daily dosing and poor tolerability, is likely to increase. On account of this, TLART was introduced into South Africa's public sector in September 2013. Here we describe the uptake of adult TLART since its introduction.

TLART is accessed through a centralised national committee in the public sector in South Africa. The patient's clinician submits at application to the committee, and the committee assesses third-line eligibility, making regimen recommendations for each case. Thirdline eligibility criteria include: at least one year of professe inhibitorbased ART, with virologic failure despite adherence optimisation. and a resistance genotype showing protease inhibitor resistance. The regimen is then sent directly to the patient's facility on a named-patient basis. We reviewed the adult TLART database to assess third-line uptake since 2013.

### Results

As of 30 June 2018, there are 1214 adults on TLART. The Initial uptake increase was gradual, with a sharp increase in applications seen from 2016 to 2017 (figure 1).

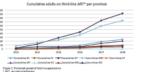


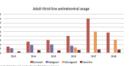
The initial slow uptake is probably due to lack of awarenes ability of TLART, as well as regarding the it. The sharp increase most likely reflects

of third-line: increased access to genotype idensianding of the TLART access process:

### Results Cont.

2018, showing a continuing increase in applications. Consistenti more applications are from KwaZuiu-Natal and Gauteno provinces even in these three provinces, there has been an increase in the number of TLART applications year-upon-year (figure 2). All TLART patients receive ritionavir-boosled darunavir (DRV/ir), and so the increase in DRV/ir use mirrors that of the increase in applications (floure 3). Due to a change from raitegravir to dolutegravir in Jul 2016, the integrase inhibitor uptake is harder to interpret. Of note, the proportion receiving etravirine has declined - the exact reason for this is uncertain.





The uptake of TLART has seen a non-linear increase since 2013. There is a spread of applications across the provinces with greatest numbers from KwaZulu-Natal and Gauteng, Increasing NNETI resistance is noted in the declining number of TLAST patients eligible to receive etravirine as part of their regimen

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### Third-line Antiretroviral Therapy Algorithm

### nm to Determine Appropriate Third-line Antiretroviral Regimens Failing Protease Inhibitor-based Regimens in Resource-limited

F Conradie<sup>2</sup>, G Maartens<sup>3</sup>, WDF Venter<sup>1</sup>, M Moosa<sup>4</sup>, K Jamaloodien<sup>5</sup>, and MP Fox<sup>6</sup>

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lobal Health, Boston University School of Public Health, MA, USA; Department of Epidemiology, Boston University ealth, MA, USA; Health Economics and Epidemiology Research Office, Department of Internal Medicine, School of aculty of Health Sciences, University of the Witwatersrand, Gauteng, South Africa

### Results

pest antiretroviral therapy (ART) programme in the world. It paran African countries with access to third-line ART for led both first-line non-nucleoside reverse transcriptase ART and second-line ritonavir-boosted protease inhibit Hine was first available in SA in September 2013 and is ntralised national committee in the public-sector. With the it is likely that the number of patients failing first-line ART and-line will increase. Second-line PW-based ART has a twice daily dosing and is less tolerable than first-line. I rowce daily occuring and is less tolerable with missions, orgamme grows, more patients will fall second-line and sing numbers accessing third-line will impact sustainability I third-line process. With a view to streamlining, and the i-shifting the third-line approval process, an algorithm to hird-line regimens was developed.

mittee assesses third-line eligibility, making regime ach case. Third-line eligibility criteria include: at least one pinavir or atazanavir), ART with virologic failure despite n, and a resistance genotype showing PI resistance one ≥ 15 on Stanford Database). By examining patterns or sent regimens selected, the third-line committee developed ne appropriate third-line (Figure 1).

tients evidenced by a Stanford score ≥ 15 to their Plin

resistance to DRV/r (score ≥ 15) is present, or if there is intermediate or high-leve resistance (score > 29) to the selected NRTI (TDF or AZT), an integrase inhibito (InSTI) is added to the regimen. If there is both DRV/r resistance (score ≥ 15) and intermediate or high (score > 29) level resistance to the selected NRTI, ther etravirine (ETR) in addition to an InSTI is added, providing the ETR score is s 29.

Rattogravir was the InSTI used initially, until dolutegravir became available in SA
(July 2018). The third-line committee introduced the algorithm to determine thirdline in 2014. Introducing the algorithm has significantly streamlined the third-line



Figure 1: Third-line antiretroviral therapy algorithm

### Conclusion

Developing an algorithm to determine appropriate ART regimens for patients failing Plir-based ART has streamlined the third-line process signi algorithmic approach simplifies third-line, facilitating decentralisation



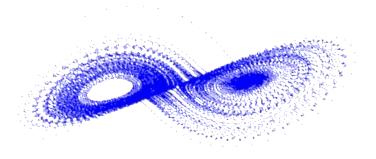






## Final thoughts

- Third-line applications have increased in a non-linear trajectory since 2013
- Quality of applications
- What impact will the introduction of dolutegravir-based regimens have on second- and third-line ART?



## Acknowledgements

















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