



Outcomes of the DTG rollout in first- and second-line ART

AWACC, 30 October 2025

Dr Yukteshwar Sookrajh

eThekweni Municipality: Primary Health Care Services Directorate; yukteshwar.sookrajh@durban.gov.za

Dr Jennifer Brown

CAPRISA & University of Oxford; jennifer.brown@caprisa.org



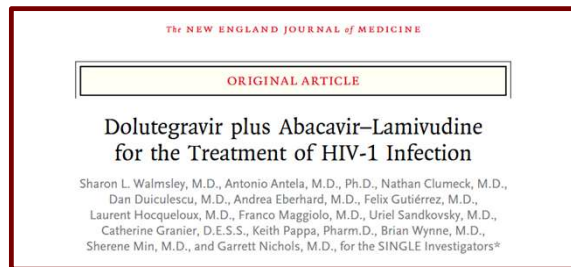
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Presentation Overview

- Recap of RCT evidence of DTG in first-line ART
- Real-world outcomes on DTG in first-line ART in KZN
- Recap of RCT evidence of DTG in second-line ART
- Real-world outcomes of DTG in second-line ART in KZN
- DTG and cardiovascular events in South Africa
- Conclusion

Recap: DTG in first-line ART



SINGLE

Among 833 ART-naïve adults, **ABC/3TC/DTG was superior to TDF/FTC/EFV600 in terms of 48-week viral suppression** to <50 copies/mL (88% vs 81%) and time to viral suppression, with less discontinuation.



ADVANCE

Among 1053 adolescents and adults not taking ART in the previous 6 months, **TAF/FTC/DTG (84%) and TDF/FTC/DTG (85%) were non-inferior to TDF/FTC/EFV600 (79%) in terms of 48-week viral suppression** to <50 copies/mL. DTG-based ART led to less discontinuation, but more weight gain (especially with TAF).



NAMSAL

Among 613 ART-naïve adults, **TDF/3TC/DTG was non-inferior to TDF/3TC/EFV400 in terms of 48-week viral suppression** to <50 copies/mL (74.5% vs 69.0%).

Timelines of the DTG rollout

Jul 2018	WHO recommends DTG-based ART (with restricted use among women)
Dec 2019	South African National Department of Health recommends DTG-based first- and second-line ART
Jun 2021	Risk concerns for women removed



Protests for access to DTG at AIDS 2018, Amsterdam

The SHAPE project

Strengthening Health systems through Audit & Programmatic data Evaluation

Aim:

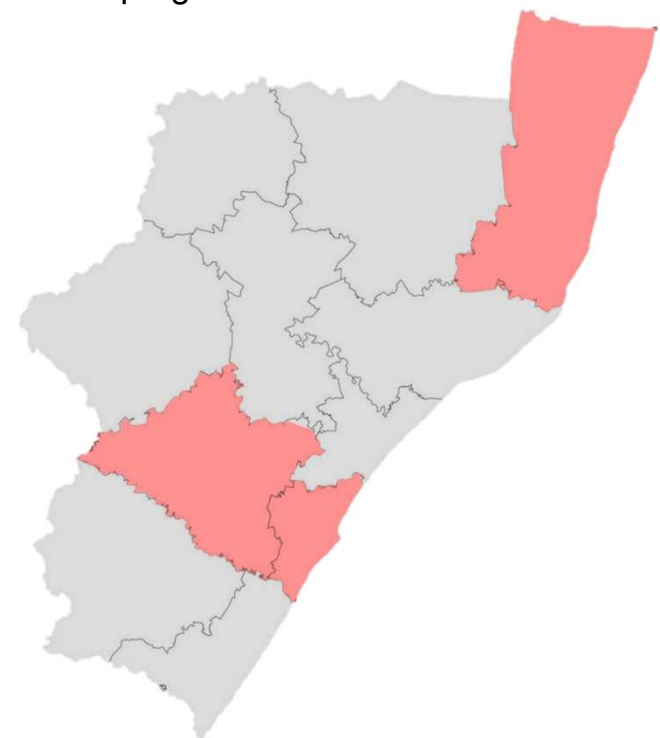
To evaluate key components of the South African HIV/TB programme to guide improvements in programmatic implementation and policy

Study design:

- Analysis of routinely collected, de-identified primary care data (mainly TIER.Net)
- >450,000 people on ART, approx. 120 clinics
- Complemented by qualitative work and audits

Data management:

- Further data de-identification (e.g. dates shifted by random number)
- Cleaning of clear systematic errors (e.g. start dates after end dates)
- Rules to identify obvious capture errors
- Personal identifiable information not included



SHAPE Team

Collaborators

- CAPRISA
- eThekwini Municipality Primary Health Care Services Directorate
- University of Oxford
- uMgungudlovu District Health
- Bethesda Hospital
- Mseleni Hospital
- Desmond Tutu HIV Centre, University of Cape Town

Approvals

- Biomedical Research Ethics Committee, UKZN
- Provincial Health Research Ethics Committee
- uMkhanyakude District Health Research Committee
- uMgungudlovu District Health Office
- eThekwini Municipality Primary Health Care Services Directorate Research Committee

Uptake and outcomes with first-line DTG



Dr Jienchi Dorward

Research questions

- How did gender affect uptake of DTG?
- How did use of DTG affect subsequent treatment outcomes of 12-month retention in care and viral suppression?

Eligibility

- Adults (≥ 15 years) in 59 clinics in eThekweni – all clinics from eThekweni Municipality
- Initiation cohort: initiating ART between Dec 2019 and Feb 2022
- Transition cohort: taking non-DTG-based first-line ART in Dec 2019 and eligible to transition to first-line DTG-based ART (i.e., no viral load ≥ 1000 copies/mL in last 12 months)

Uptake and outcomes with first-line DTG

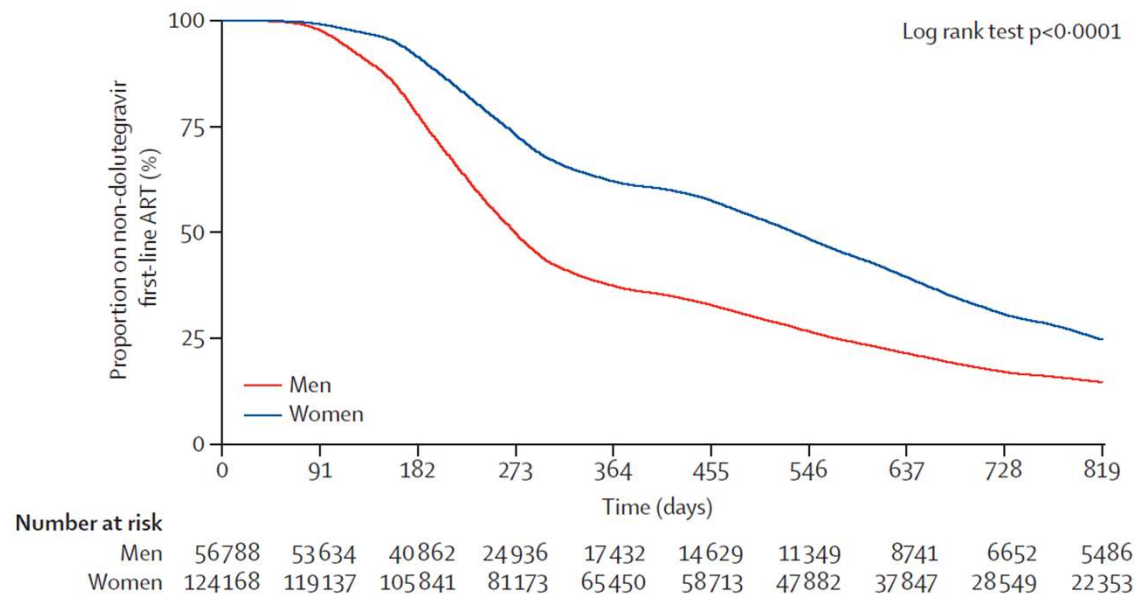
Uptake results – initiation cohort

- 45,392 ART initiations (36.7% men, 52.8% non-pregnant women, 10.5% pregnant women)
- **Non-pregnant** (69.9%; RR 0.78 [95% CI 0.74–0.82]) **and especially pregnant women** (46.9%; RR 0.57 [0.49–0.66]) **were less likely than men** (82.3%) **to receive DTG**, particularly:
 - early in the rollout (Dec 2019 – Feb 2020: RR 0.29 [0.23–0.38]; Sep – Nov 2021: RR 1.00 [0.98–1.03])
 - among women of childbearing age (15-24 years: RR 0.73 [CI 0.69–0.77]; age ≥55 years: RR 0.97 [0.90 –1.03])

Uptake and outcomes with first-line DTG

Uptake results – transition cohort

- 180,956 people (68.6% women)
- By February 2022, 67.0% had transitioned to first-line DTG
- **Lower hazard of transition to DTG among women (HR 0.56, 95% CI 0.56–0.57)**



Uptake and outcomes with first-line DTG

Outcome results – initiation cohort

- N = 45,392
- **12-month retention was slightly higher with DTG- (65.4%) than with non-DTG-based ART (62.0%; aRR 1.09, 95% CI 1.04–1.14), but low in both groups**
- Among 12,911 with a 12-month VL, **viral suppression was slightly higher with DTG- (83.0%) than non-DTG-based ART (81.4%; aRR 1.09, 95% CI 1.04–1.14)**

Outcome results – transition cohort

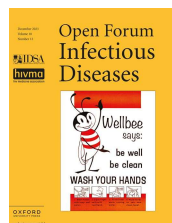
- 46,159 people who transitioned to DTG were matched with 46,159 controls who had not transitioned at the same time point
- **12-month retention was slightly higher with DTG- (93.5%) than with non-DTG-based ART (90.9%; aRR 1.03, 95% CI 1.02–1.03)**
- Among 72,219 with a 12-month VL, **viral suppression was slightly higher with DTG- (95.5%) than with non-DTG-based ART (89.7%; aRR 1.01, 95% CI 1.00–1.02)**

Uptake and outcomes with first-line DTG

Key points

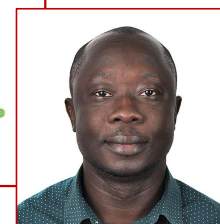
- Initially lower uptake of DTG among women, then equalization
- Slightly higher 12-month retention with DTG, though generally low retention within 12 months after ART initiation
- Slightly higher viral suppression with DTG

Resuppression after viraemia with TLD or TEE



Clinical Outcomes After Viremia Among People Receiving Dolutegravir vs Efavirenz-Based First-line Antiretroviral Therapy in South Africa

Kwabena Asare,^{1,2,3} Lara Lewis,^{1,3} Johan van der Molen,¹ Yukteshwar Sookraj,³ Thokozani Khubone,³ Pravikrishnen Moodley,⁴ Richard J. Lessells,^{1,5,6} Kogieleum Naidoo,^{1,6,7} Phelelani Sosibo,³ Nigel Garrett,^{1,2,6} and Jienchi Dorward^{1,7,8}



Dr Kwabena Asare

Research questions

After initial viraemia while taking DTG- or EFV-based first-line ART,

- how guideline-compliant was clinical management of viraemia?
- how did the first-line regimen affect 12-month retention in care and viral suppression (<50 copies/mL)?

Eligibility

- Adults receiving first-line TDF/3TC/DTG (TLD) or TDF/FTC/EFV (TEE)
- First viraemia (≥ 50 copies/mL) in Jun to Nov 2020
- 59 clinics in eThekweni

Resuppression after viraemia with TLD or TEE

Results – clinical management of viraemia

- 9,657 people with viraemia: 78.7% TEE and 21.3% TLD
- 42.1% in the TEE group and 42.2% in the TLD group received a 3-month VL
- Among people with virological failure (sustained viraemia $\geq 1,000$ copies/mL) in the TEE group (n= 328), 31.7% were switched to second-line ART within 12 months

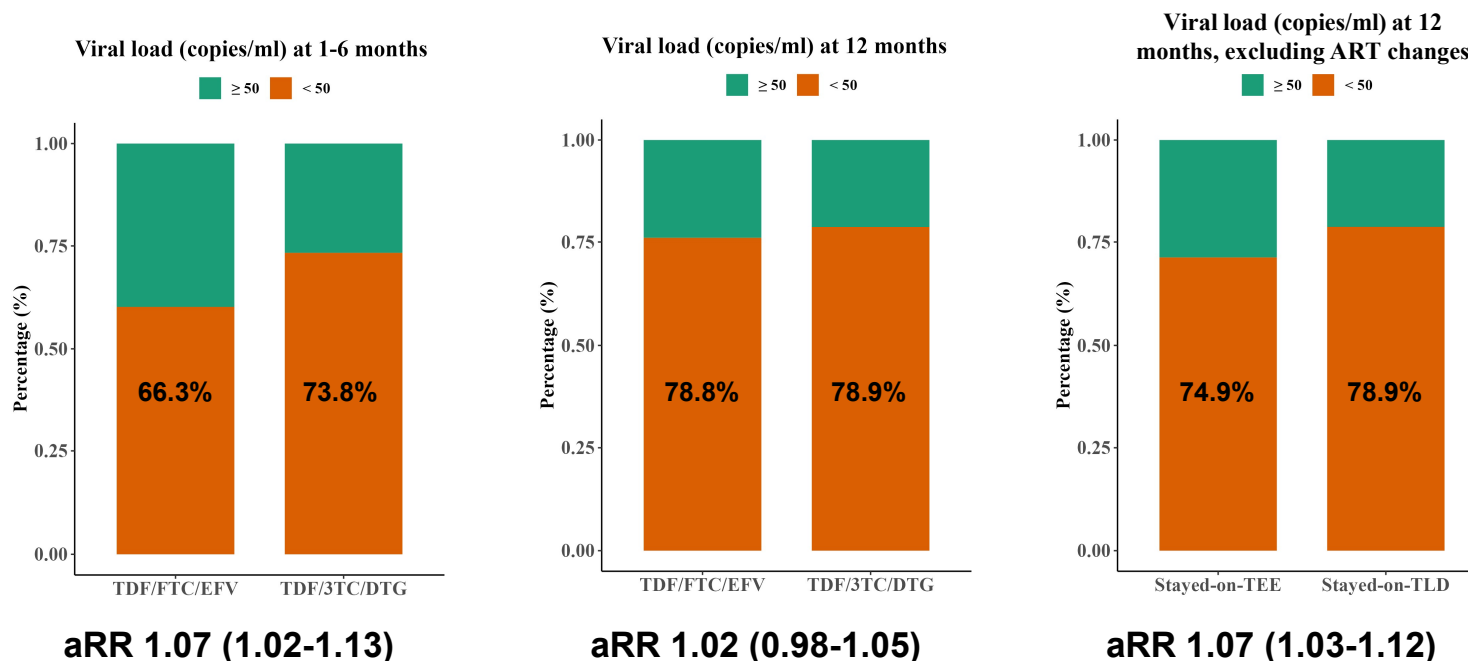
Results – retention in care after viraemia

- **12-month retention was slightly higher with TLD (84.9%) than TEE (80.8%; aRR 1.03, 95% CI 1.00–1.06)**

Resuppression after viraemia with TLD or TEE

Results – viral suppression after viraemia

- Viral suppression was higher with TLD at 3 months, and similar at 12 months
- When excluding people who changed ART during follow-up (mostly from TEE to first-line TLD), 12-month suppression was higher with TLD



Resuppression after viraemia with TLD or TEE

Key points

- Only around 42% received a 3-month VL after initial viraemia
- Only 31.7% were switched to second-line ART after virological failure with TEE
- 12-month retention was slightly higher after viraemia with TLD than with TEE
- Viral resuppression was higher after viraemia with TLD than with TEE at 3 months and to a lesser degree at 12 months

Recap: DTG in second-line ART

Dolutegravir versus ritonavir-boosted lopinavir both with dual nucleoside reverse transcriptase inhibitor therapy in adults with HIV-1 infection in whom first-line therapy has failed (DAWNING): an open-label, non-inferiority, phase 3b trial

Michael Aboud, Richard Kaplan, Johannes Lombard, Fajie Zhang, Just A Hladik, Elvira Mamedova, Maralee H Leno, Florentien Chetsotsoiki, Carlos Brito, Jing Tan, Doreen Brown, Judy Hopling, Mark Undersander, Maria Claudia Neocoms, Yegor Pundak, Martin Gantland, Kimberly Smith

DAWNING

Among 624 adults with failing first-line NNRTI-based ART, switching to **DTG plus two NRTIs (84%) was superior to LPV/r plus two NRTIs (70%) in terms of 48-week viral suppression to <50 copies/mL**. DTG also had a favourable safety profile with fewer adverse events.

THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Dolutegravir or Darunavir in Combination with Zidovudine or Tenofovir to Treat HIV

Nicholas I. Paton, M.D., Joseph Musazi, M.Sc., Cissy Kityo, Ph.D., Stephen Walimbwa, M.D., Anne Hoppe, Ph.D., Apolo Balyegisawa, M.D., Arvind Kaimal, M.D., Grace Mirembe, M.Med., Phionah Tukamushabe, R.N., Gilbert Ategeka, M.D., James Hakim, F.R.C.P., Henry Mugerwa, M.D., Abraham Siika, M.Med., Jesca Asienzo, B.P.L.M., Barbara Castelnuevo, Ph.D., Agnes Kiragga, Ph.D., and Andrew Kambugu, M.Med., for the NADIA Trial Team*

NADIA

In a two-by-two factorial trial among people switching to second-line ART after failure of first-line NNRTI-based ART containing tenofovir, **DTG (90.2%) was non-inferior to DRV/r (91.7%) and recycling tenofovir (92.3%) was non-inferior to zidovudine (89.6%) in terms of 48-week viral suppression to <400 copies/mL**.

THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Second-Line Switch to Dolutegravir for Treatment of HIV Infection

Loice A. Ombajo, M.B., Ch.B., M.Med., Jeremy Penner, M.D., Joseph Nkuranga, M.B., Ch.B., Jared Mecha, M.B., Ch.B., M.Med., Margaret Mburu, M.P.H., Collins Odhiambo, Ph.D., Florentius Ndirya, M.B., Ch.B., M.Med., Rukia Aksam, M.B., Ch.B., Richard Njenga, B.Sc., Simon Wahome, M.Pharm., Peter Muiruri, M.B., Ch.B., Sheila Eshiwani, M.B., Ch.B., Maureen Kimani, M.B., Ch.B., Catherine Ngugi, M.B., Ch.B., and Anton Pozniak, M.B., Ch.B., M.D.

2SD

Among 791 people taking ritonavir-boosted PI-based ART with viral suppression, **transition to DTG (5.0%) was non-inferior to continuing ritonavir-boosted PI-based ART (5.1%) in terms of 48-week viraemia ≥ 50 copies/mL**, with similar occurrence of adverse events.

Uptake and outcomes with second-line DTG



Clinical outcomes with second-line dolutegravir in people with virological failure on first-line non-nucleoside reverse transcriptase inhibitor-based regimens in South Africa: a retrospective cohort study

Kwabena Asare, Yuktेशwar Sookrajh, Johan van der Molen, Thokozani Khubone, Lara Lewis, Richard J Lessells, Kogieleum Naidoo, Phelani Sosibo, Rosemary van Heerden, Nigel Garrett, Jienchi Dorward



Dr Kwabena Asare



Uptake and 24-month Outcomes of Dolutegravir- Versus Lopinavir-based Second-line Antiretroviral Therapy for People With HIV in South Africa: A Retrospective Cohort Study and Emulated Target Trial

Jennifer Anne Brown,^{1,2} Lara Lewis,^{1,2} Yuktेशwar Sookrajh,^{3,4} Lungile Hobe,⁴ Thulani Ngwenya,⁵ Johan van der Molen,¹ Kwabena Asare,^{1,6} Kwena Tihaku,^{1,7,8} Mlungisi Khanyile,¹ Thokozani Khubone,⁹ Christian Bottomley,^{6,9} Nigel Garrett,^{1,2,9} and Jienchi Dorward^{1,2,9}



Dr Jennifer Brown

Research questions

- How did gender affect uptake of second-line DTG?
- How did the second-line regimen – i.e. AZT/XTC/LPV/r, AZT/XTC/DTG, or TDF/XTC/DTG – affect 12- and 24-month non-retention and viraemia?

Eligibility

- Adults (≥ 15 years)
- Treatment failure (2 VLs ≥ 1000 copies/mL)
- Switch from TDF/XTC/NNRTI to an above-mentioned second-line regimen after Dec 2019
- 59 clinics in eThekweni (12-month outcomes¹) / 108 clinics in eThekweni and uMgungundlovu (uptake and 24-month outcomes²)

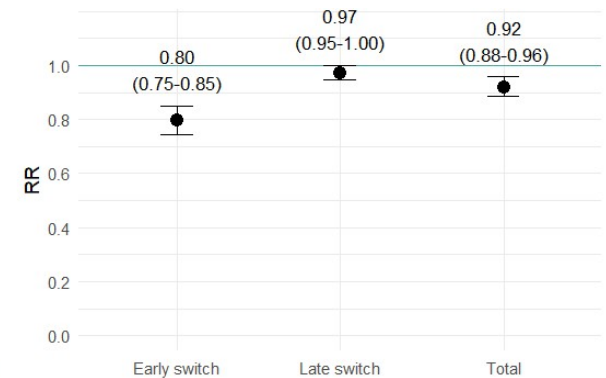
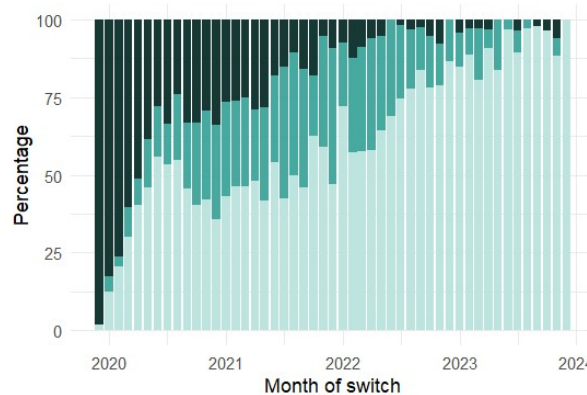
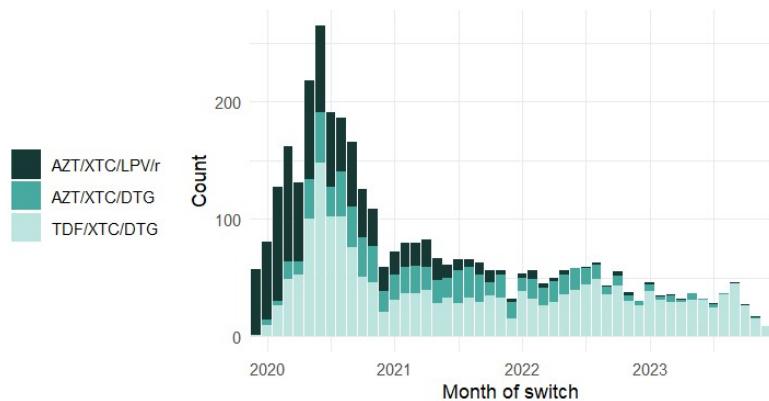
1. Asare et al., Lancet Glob Health, 2024. doi: 10.1016/S2214-109X(23)00516-8.

2. Brown et al., Open Forum Infect Dis, 2025. doi: 10.1093/ofid/ofaf530.

Uptake and outcomes with second-line DTG

Results – uptake:

- 3,649 eligible people switched between Dec 2019 and Dec 2023; 63% were women
- **Women were slightly less likely than men to switch to DTG-based second-line ART (RR 0.92, 95% CI 0.88–0.96)**



Uptake and outcomes of second-line DTG

Results – treatment outcomes

- 12-month analysis: 1,214 switches (57% AZT/XTC/LPV/r, 18% AZT/XTC/DTG, 25% TDF/XTC/DTG)
- 24-month analysis: 2,321 switches (39% AZT/XTC/LPV/r, 18% AZT/XTC/DTG, 43% TDF/XTC/DTG)

	AZT/XTC/LPV/r	AZT/XTC/DTG	TDF/XTC/DTG	AZT/XTC/DTG – AZT/XTC/LPV/r	TDF/XTC/DTG – AZT/XTC/LPV/r	TDF/XTC/DTG – AZT/XTC/DTG
Death, LTFU or TFO						
12 months (crude)	25%	14%	23%	p=0.012	p=0.73	p=0.60
24 months	36%	33%	38%	aRD -2% (-8, 5)	aRD 3% (-2, 8)	aRD 5% (-2, 11)

- **Similar non-retention (death, loss to follow-up, or transfer out);** slightly lower with AZT/XTC/DTG than with AZT/XTC/LPV/r at 12 months

Uptake and outcomes of second-line DTG

Results – treatment outcomes

- 12-month analysis: 1,214 switches (57% AZT/XTC/LPV/r, 18% AZT/XTC/DTG, 25% TDF/XTC/DTG)
- 24-month analysis: 2,321 switches (39% AZT/XTC/LPV/r, 18% AZT/XTC/DTG, 43% TDF/XTC/DTG)

	AZT/XTC/LPV/r	AZT/XTC/DTG	TDF/XTC/DTG	AZT/XTC/DTG – AZT/XTC/LPV/r	TDF/XTC/DTG – AZT/XTC/LPV/r	TDF/XTC/DTG – AZT/XTC/DTG
Viraemia >50 c/mL						
12 months (crude)	53%	41%	39%	p=0.0093	p<0.0001	p=0.62
24 months	50%	40%	39%	aRD -10% (-19, -2)	aRD -11% (-18, -5)	aRD -1% (-9, 8)

- **Higher viraemia with AZT/XTC/LPV/r than with either DTG-based regimen**

Uptake and outcomes of second-line DTG

Results – treatment outcomes

- 12-month analysis: 1,214 switches (57% AZT/XTC/LPV/r, 18% AZT/XTC/DTG, 25% TDF/XTC/DTG)
- 24-month analysis: 2,321 switches (39% AZT/XTC/LPV/r, 18% AZT/XTC/DTG, 43% TDF/XTC/DTG)

	AZT/XTC/LPV/r	AZT/XTC/DTG	TDF/XTC/DTG
Death, LTFU or TFO			
12 months (crude)	25%	14%	23%
24 months	36%	33%	38%
Viraemia >50 c/mL			
12 months (crude)	53%	41%	39%
24 months	50%	40%	39%

- **Similar non-retention, (death, loss to follow-up or transfer out);** lower with AZT/XTC/DTG than with AZT/XTC/LPV/r at 12 months, otherwise similar after adjustment
- **Higher viraemia with AZT/XTC/LPV/r than with either DTG-based regimen**

Uptake and outcomes of second-line DTG

Key points

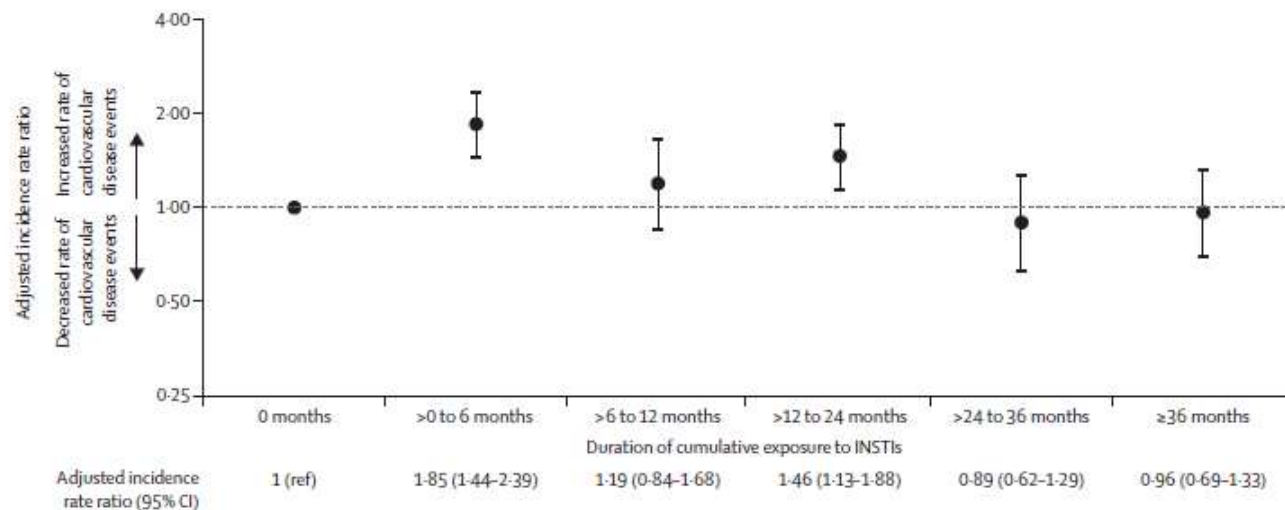
- Uptake of second-line DTG was initially lower among women than men and later equalised
- Death and loss to follow-up were similar across second-line regimens
- 12- and 24-month viraemia were lower with either DTG-based second-line regimen than with AZT/XTC/LPV/r
- High viraemia after switch to second-line ART with all regimens

DTG and cardiovascular events in South Africa

Background

- Clinical trials in Africa have found higher weight gain with DTG than EFV, especially among women^{1,2}
- One observational study in European and Australian cohorts found an increased risk of major adverse cardiovascular events (MACEs) in the first 24 months of INSTI use³, but findings from other observational studies have been mixed³⁻⁶

Adjusted incidence rate ratio of cardiovascular disease composite endpoint by cumulative exposure to INSTIs



1. Kouanfack et al., N Engl J Med, 2019
2. Venter et al. Lancet HIV, 2020

3. Neesgaard et al., Lancet HIV, 2022
4. Surial et al., Clin Infect Dis, 2023

5. Rein et al., Lancet HIV, 2023
6. Brennan et al., Eclinicalmedicine, 2023

DTG and cardiovascular events in South Africa

medRxiv

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Risk of major adverse cardiovascular events with dolutegravir versus efavirenz-based antiretroviral therapy: emulated target trials using routine, de-identified data from South Africa

 Jienchi Dorward,  Xolani Masombuka,  Lara Lewis,  Claudia Pastellides,  Johan van der Molen,  Kwabena Asare,  Kwena Tihaku,  Jennifer Anne Brown,  Christian Bottomley,  Dave Jacobs,  Shirley Collie,  Nigel Garrett



Dr Jienchi Dorward

Research questions

How does the 3-year risk of major adverse cardiovascular events (MACEs) differ between first-line TEE and TLD?

Eligibility

- De-identified data from a South African managed healthcare organisation (Discovery)
- Initiation cohort: initiation of TEE or TLD between Apr 2020 and Dec 2023
- Transition cohort: receiving TEE in Apr 2020 and eligible for transition to TLD
- Private sector outpatient and inpatient claims for prescriptions, laboratory investigations (including results), hospitalisations and diagnostic codes

DTG and cardiovascular events in South Africa

Results – initiation cohort

- 7310 people initiated TLD (n=3711) or TEE (n=3599)
- 57.0% women; median age 38 years (IQR 32-44)
- 18 MACEs with TLD; 28 with TEE
- After adjustment: **similar 3-year risk with TLD as with TEE**

Initiation cohort	3-year risk (95% CI)	Risk difference (95% CI)	Risk ratio (95% CI)
TLD	0.78% (0.37 to 1.32)	-0.18% (-0.82 to 0.50)	0.81 (0.35 to 1.59)
TEE	0.96% (0.60 to 1.40)		

DTG and cardiovascular events in South Africa

Results – transition cohort:

- 22,338 people were receiving TEE in Apr 2020 and eligible for TLD
- 61.7% women; median age 41 years (IQR 36-47)
- 2,837 were transitioned to TLD while not viraemic
- 255 (1.1%) experienced a MACE
- After adjustment: **similar 3-year risk with TLD as with TEE**

Transition cohort	3-year risk (95% CI)	Risk difference (95% CI)	Risk ratio (95% CI)
TLD	1.09% (0.48 to 1.99)	-0.12% (-0.75 to 0.75)	0.90 (0.41 to 1.64)
TEE	1.21% (1.05 to 1.41)		

Uptake and outcomes of second-line DTG

Key points

- We did not observe evidence for an increased risk of MACEs with TLD compared with TEE
- This holds true both among people newly initiating or already established on ART
- However, confidence intervals were wide

SHAPE outlook

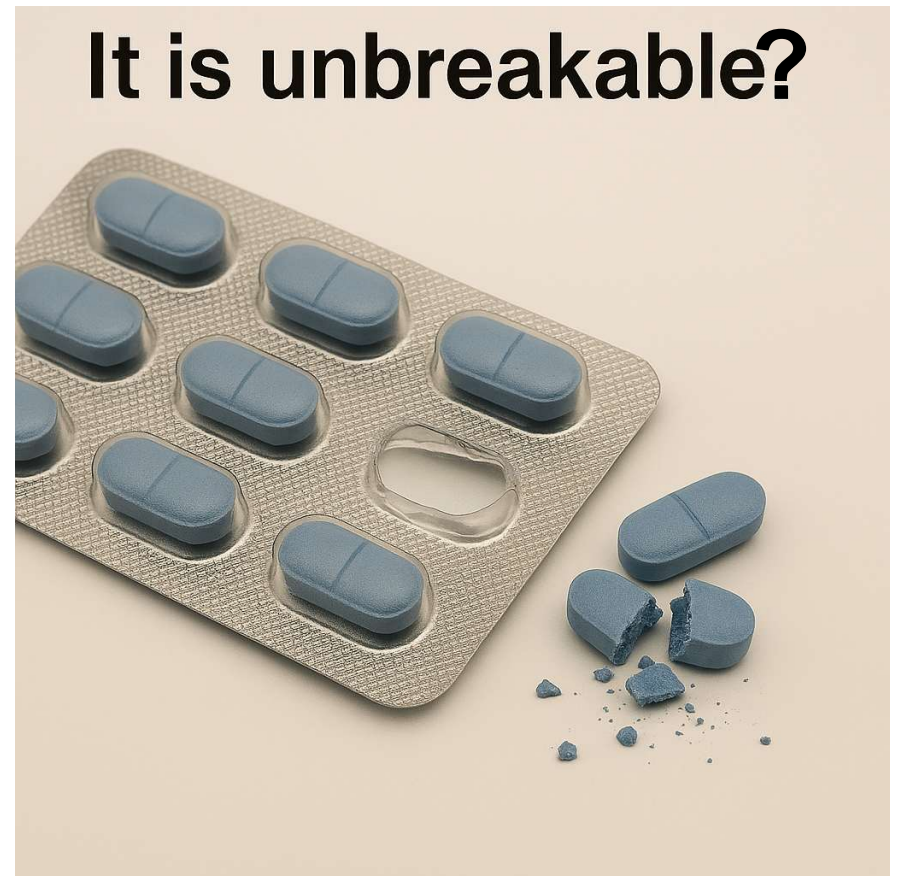
- Assessing the effect of the paediatric transition to DTG
- Assessing the uptake and effect of earlier VL testing that is possible with DTG
- SHAPE cohort suitable for broader analyses on uptake and effect of new treatment modalities (e.g. ongoing work on decentralised ART)



Strengthening Health systems through
Audit & Programmatic data Evaluation

Conclusions

- Encouraging overall outcomes with first- and second-line DTG compared with the prior standard of care among adults, supporting current clinical guidelines
- High disengagement from care in first year after ART initiation
- Substantially more viraemia after switch to second-line ART than in RCTs
- No evidence for increased risk of MACEs with first-line DTG compared with EFV



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Mlungisi Khanyile

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Thokozani Khubone
Phelelani Sosibo
Rose van Heerden

Thulani Ngwenya
Lungile Hobe

Discovery Health:

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Xolani Masombuka
Claudia Pastellides
Dave Jacobs

University of Oxford:

Jienchi Dorward
Jennifer Brown

LSHTM:

Christian Bottomley
Kwabena Asare

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