Dolutegravir Exposure Testing Accurately Targets Integrase Resistance and Reduces Laboratory Monitoring Costs

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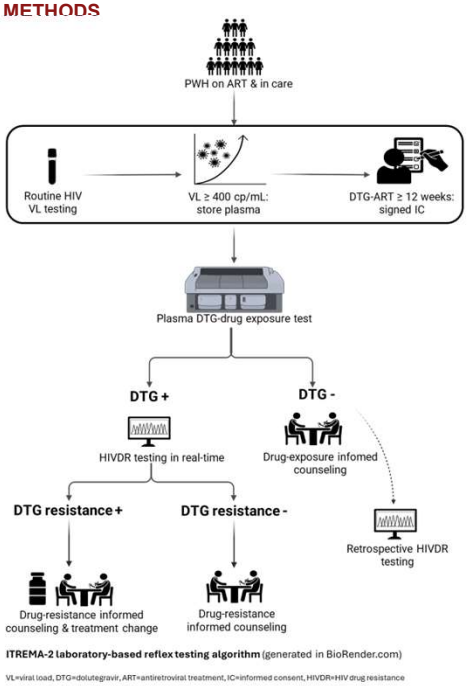
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BACKGROUND

- **DTG resistance** is emerging among treatment-experienced people with HIV in low- and middle-income countries.
- Guidelines **restrict resistance testing** to cases of prolonged viremia, assuming most DTG-associated viremia stems from **suboptimal adherence** rather than viral resistance.
- This conservative approach **risks delaying detection of resistance.**
- We implemented and evaluated a **laboratory-initiated reflex testing strategy (ITREMA-2)** that uses plasma DTG exposure levels to **optimize resistance testing timing** in routine clinical care in 2 clinics in Johannesburg.

METHODS



ITREMA-2 laboratory-based reflex testing algorithm (generated in BioRender.com)

VL=viral load, DTG=dolutegravir, ART=antiretroviral treatment, IC=informed consent, HIVDR=HIV drug resistance

Laboratory-initiated **plasma DTG reflex testing** offers an objective, scalable and cost-efficient screening approach to **target resistance testing** to those **at highest risk of DTG resistance**, while supporting adherence management in others.

This strategy is being implemented by the South African Department of Health, demonstrating its **feasibility for large-scale public-sector roll-out**.

POPULATION BASELINE CHARACTERISTICS

56 %

Age 43 years (SD +/- 12)

3.8 $\log_{10}$ cp/mL (IQR: 3.0-4.9)

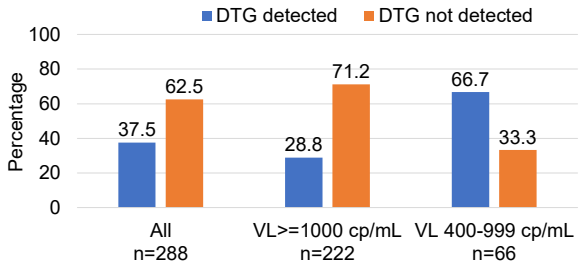
TDF-3TC-DTG (84%)
ABC-3TC-DTG (13%)
AZT-3TC-DTG (1%)
2 NRTI+DTG+DRV/r (2%)

82% prior ART exposure

88 months on ART (IQR: 51-148)

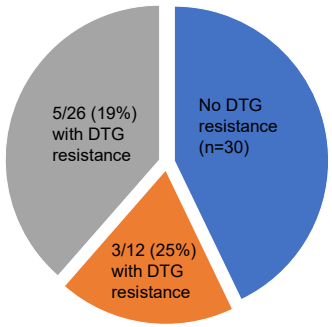
13 months on DTG (IQR: 6-28)

PLASMA DTG EXPOSURE TESTING



Single VL≥ 1000 cp/mL (aOR 0·39, 95% CI:0·18-0·86, p=0·019)
No VL in the last 12m (aOR 0·02, 95% CI:0·01-0·38, p=0·002)
were associated with **undetectable plasma DTG**

70 individuals with ≥1 viremic episode



DTG RESISTANCE

- **DTG resistance** detected in 13/103 (**12.6%**) individuals with detectable plasma DTG
- **All** 13 individuals had **prior exposure to non-DTG regimens**
- **Detectable plasma DTG** (OR 10.62, 95% CI: 2.36-47.85, p=0.002) and the presence of **(N)NRTI mutations** were associated with **DTG resistance**

NEGATIVE PREDICTIVE VALUE OF PLASMA DTG

- **134/137 (98%)** of individuals with **undetectable plasma DTG** had **no DTG resistance**

COST MODELING

- This **laboratory reflex strategy** (no resistance testing if plasma DTG is undetectable) **reduced laboratory costs by 22%** compared to current South African testing guidelines.

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In case of viral rebound, measuring DTG levels in the blood helps identify those most likely to have resistance and who would benefit from resistance testing. Implemented as an automatic laboratory response, it enables earlier access to resistance testing, avoids expensive unnecessary tests, and identifies those who may benefit more from additional adherence counseling.