UPTAKE AND OUTCOMES OF FIRST-LINE DOLUTEGRAVIR IN A LARGE SOUTH AFRICAN COHORT

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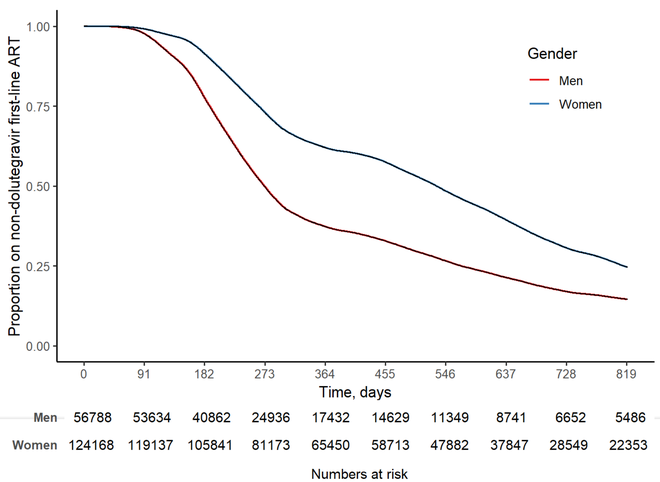
BACKGROUND

- Since 2018 the WHO has recommended dolutegravir-based first-line antiretroviral therapy (ART), due to clinical trial evidence of increased efficacy compared to the previously recommended efavirenz.
- Initially, safety concerns regarding a potential increased risk of neural tube defects led the WHO to recommend restricted use among women of child-bearing potential. However, new findings led WHO to remove these restrictions in July 2019.
- We aimed to determine dolutegravir uptake in women, and the impact of dolutegravir on clinical outcomes in routine care in South Africa

METHODS

- We analyzed de-identified, routine data from 59 primary care clinics in eThekwini Municipality, South Africa, from DTG introduction in Dec 2019 to Feb 2022.
- We used Poisson regression, Cox proportional hazards models, and time dependent propensity score matching to assess initiation and transition to dolutegravir-based ART by gender, and associations with 12-month retention-in-care and viral suppression <50 copies/mL.

Figure 1. Kaplan Meier curve of transition to dolutegravir among people already receiving non-dolutegravir based first-line ART in December 2019



In this study of over 220,000 people in South Africa, women were less likely to receive first-line dolutegravir than men. Among those who did receive dolutegravir, subsequent 12-month retention and viral suppression were better compared to those receiving efavirenz.
The benefits of dolutegravir were strongest among people receiving concurrent tuberculosis treatment when initiating ART, and among people transitioned to dolutegravir with most recent viral load at baseline ≥200 copies/mL.

RESULTS

- Of 45,392 adults initiating ART, 28,725 (63·3%) were women, median age was 31 years (IQR 26,38), and 31,264 (69·9%) initiated dolutegravir. Dolutegravir initiation was lower in non-pregnant (risk ratio [RR] 0·78 [0·74, 0·82]) and pregnant women (RR 0.57 [0·49, 0·66]) versus men. At 12-months, retention-in-care (adjusted RR 1.09 [1.04,1.14)) and viral suppression (aRR 1·04 [1·01, 1·06]) was higher in dolutegravir initiators.
- Among people with tuberculosis, 316/774 (40·8%) were initiated on dolutegravir. In this group, the association between dolutegravir and viral suppression was stronger (aRR 1·14 [1·07, 1·22]) than among those without tuberculosis (aRR 1·03 [1·01, 1·06], Wald test for interaction p= 0·006, **Table 1**).
- Among 180,956 adults receiving first-line ART in December 2019, median age was 38 years (32,45), 124,168 (68·6%) were women and 98·6% received efavirenz. By February 2022, 121,210/158,999 (76·2%) of those in care were transitioned to first-line dolutegravir. Transition was lower in women (hazard ratio 0·56, [0·56,0·57]). Among 92,318 propensity score matched people, 12-month retention-in-care (aRR 1·03 [1·02, 1·03]) and viral suppression (aRR 1·0.1 [1·00, 1·02]) were slightly higher in the dolutegravir versus non-dolutegravir group.

Table 1: Viral suppression among people initiated on dolutegravir versus non-dolutegravir ART, by tuberculosis status*, n = 12, 911

	Proportion with viral suppression <50 copies/mL		
TB status at ART initiation	**Non-dolutegravir regimen (n/N)**	**Dolutegravir regimen (n/N)**	**aRR (95% CI)**
No TB	5000/6083 (82·2%)	5032/6054 (83·1%)	1·03 (1·01-1·06)
Known TB	327/458 (71·4%)	257/316 (81·3%)	1·14 (1·07-1·22)

RESULTS cont.

- In sensitivity analysis with an interaction term between dolutegravir use and baseline viral load, dolutegravir was only associated with improved viral suppression among people with baseline viral load ≥200 copies/mL (e.g. 200-399 copies/mL, aRR 1.15 [1.05, 1.26], 400-999 copies/mL, aRR 1.25 [1.13, 1.38], **Table 2**).

CONCLUSIONS

- In this large South African cohort study, women were less likely to receive dolutegravir than men, and people receiving dolutegravir had better retention-in-care and viral suppression compared to efavirenz.
- While this study is limited by being unable to assess adverse events such as weight gain, the benefits of dolutegravir on clinical outcomes support the ongoing dolutegravir rollout.

ADDITIONAL KEY INFORMATION

The authors have no conflicts of interest to declare.

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Table 2 Poisson regression models of viral suppression among people transitioned to dolutegravir versus those not transitioned, by baseline viral load

	Proportion with viral suppression		
Baseline VL (copies/ml)	**Dolutegravir (n/N)**	**Non-dolutegravir (n/N)**	**aHR (95% CI)**
<50	31414/34477 (91·1%)	29843/32921 (90·7%)	1·01 (1·00-1·01)
50-199	1082/1301 (83·2%)	997/1239 (80.5%)	1·03 (1·00-1·07)
200-399	265/329 (80·5%)	275/394 (69·8%)	1·15 (1·05-1·26)
400-999	255/309 (82·5%)	221/335 (66·0%)	1·25 (1·13-1·38)
Missing	407/504 (80·8%)	312/410 (76·1%)	1·06 (0·97-1·16)