Introduction of dolutegravir and the early viral response seen in South African children and adolescents

T. Mafora, N. Van Dongen, T. Ferreira, K Gunter-Technau, G Sorour
Rahima Moosa Mother and Child Hospital

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Introduction

- HIV => significant burden of disease in South Africa.
- Southern African region => majority of global HIV infections.
- 38.4 million people living with HIV globally - 1.8 million children
- South Africa - largest ART programme in the world
- Dolutegravir (DTG) introduced in November 2019
- Mainstay of both adult and paediatric first and second line regimens
- Unfortunately little data on DTG effects on viral suppression in the paediatric population, particularly from routine implementation

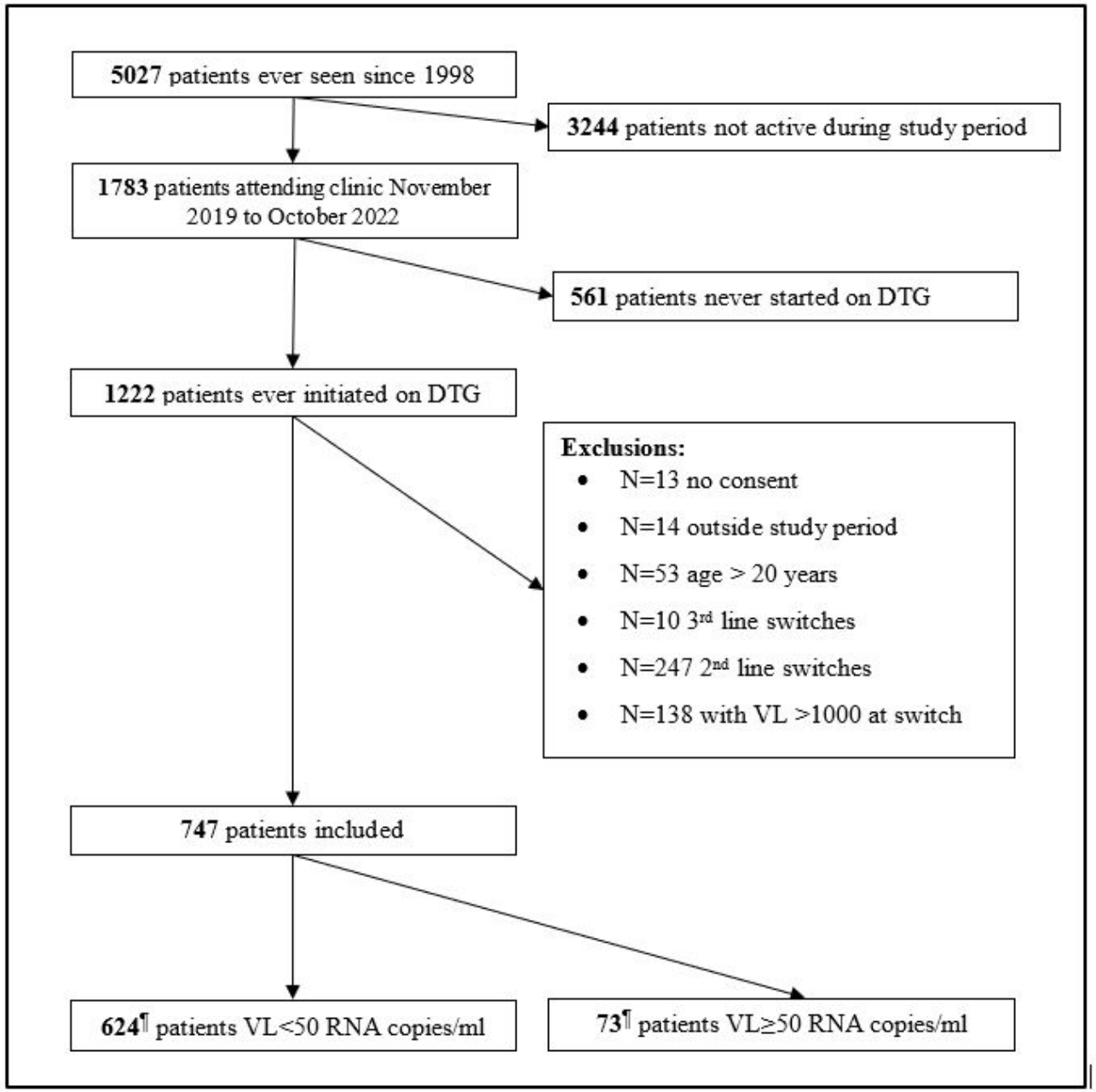
Aim

- This study evaluated the viral response of ART-experienced children and adolescents who transitioned to first-line DTG-based regimen between November 2019 and October 2022, in the first 36 months of their DTG containing regimen

Methods

- Secondary analysis - existing prospectively followed cohort based at Rahima Moosa Mother and Child Hospital
- Children and adolescents already on first line ART who switched to DTG (between November 2019 and October 2022)
- Baseline characteristics (at DTG switch): age, weight, gender, viral load (VL), CD4, and pre-switch regimen
- Past ART exposure and past viraemic periods (years VL >1000 copies/ml) assessed
- Group based outcomes created i.e., suppressed vs not suppressed based on VL at 6 months (3-9 months), 12 months (9-15 months) , 24 months (16 – 27 months) and last VL
- VL suppression rates (< 50 copies/ml) calculated at 6, 12 and 24 months post-switch
- De-identified data analysed using SAS (Version 9.4, SAS Institute Inc., Cary, NC, USA)

Figure 1: Study population with inclusion and exclusion criteria.



Results

- 747 participants switched to DTG
  - 724 (97%) qualified for a VL
  - 697 (96%) had at least one VL done after switch
- Overall, 83% (450/543) were suppressed at 6 months, 86% (434/504) at 12, 91% (487/534) at 24 months
- At a median of 637 days after switch, 90% (624/697) were suppressed at their last VL
- Factors associated with not being suppressed at the last VL included
  - missing a follow-up visit by more than 90 days post-switch to DTG,
  - switching to DTG with a VL of 50-1000 rather than <50 copies/ml,
  - having the blood test done during July-December,
  - exposure to viraemia ≥1000 copies/ml > two years before DTG switch.

Table 1: Baseline characteristics of study population stratified by virological outcome (N=747

Characteristic	Total	Suppressed[§]	Unsuppressed	P-value
Regimen pre-DTG				
NNRTI	549 (73)	470 (75)	55 (75)	1.0
PI	198 (27)	154 (25)	18 (25)	
Age at ART start, median years (IQR)	1.6 (0.5-4.2)	1.6 (0.5-4.2)	2.0 (0.9-4.9)	0.19
Time on ART pre-DTG, median years (IQR)	10.8 (7.8-13.1)	10.9 (8.1-13.1)	11.6 (6.7-13.3)	0.46
Age at DTG start, median years (IQR)	13.3 (11.1-15.7)	13.4 (11.2-15.7)	13.7 (11.4-16)	0.83
ART exposure per drug, n (%), median years (IQR)[∂]				
NRTI pre-DTG				
d4T	4.9 (3.3-6.9)	4.8 (3.2-6.7)	5.5 (3.5-8.3)	0.14
AZT	3.2 (1.1-5.1)	3.3 (1.0-5.7)	2.1 (0.9-2.4)	0.21
ABC	6.8 (4.4-8.7)	7.1 (4.6-8.7)	5.8 (3.4-8.5)	0.036
TDF	0.5 (0-1.3)	0.5 (0-1.3)	0.0 (0-1.3)	0.99
NNRTI pre-DTG				
EFV	6.3 (4.1-9.7)	6.4 (4.3-9.6)	6.0 (3.2-9.8)	0.51
Any PI pre-DTG	7.2 (4.5-9.3)	7.3 (4.6-9.3)	7.0 (3.9-9.8)	0.44
VL pre-DTG switch [£]				
0------<50	657 (89)	557 (90)	58 (81)	0.012
50------1000	81 (11)	60 (10)	14 (19)	
Viraemia time before switching to DTG, median years (IQR)				
VL above 50 copies/ml	3.4 (1.9-5.0)	3.4 (2.0-4.8)	3.8 (1.9-5.7)	0.11
VL above 1000 copies/ml	0.6 (0.1-1.4)	0.6 (0.1-1.3)	0.7 (0.2-1.7)	0.36

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Table 2: Six, twelve, 24 month and last virological outcomes of patients after switching to DTG

Timing of VL	
6 Months	
Median days to VL (IQR)	180 (164-252)
Qualified for VL§, N (%)	724 (97)
VL done¶, N (%)	543 (75)
< 50 copies/ml	450 (83)
50-1000 copies/ml	85 (16)
>1000 copies/ml	8 (1)
Median VL (IQR)	19 (1-31)
Median VL log (IQR)	1.3 (0-1.5)
12 Months	
Median days to VL (IQR)	364 (342-427)
Qualified for VL§, N (%)	680 (91)
VL done¶, N (%)	504 (74)
< 50 copies/ml	434 (86)
50-1000 copies/ml	53 (11)
>1000 copies/ml	17 (3)
Median VL (IQR)	1 (1-22)
Median VL log (IQR)	0 (0-1.3)
24 Months	
Median days to VL (IQR)	665 (588-728)
Qualified for VL§, N (%)	623 (83)
VL done¶, N (%)	534 (86)
< 50 copies/ml	487 (91)
50-1000 copies/ml	31 (6)
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Last VL	
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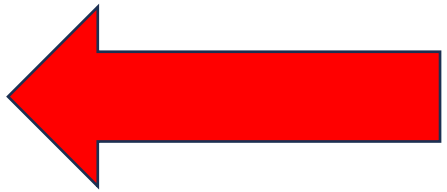

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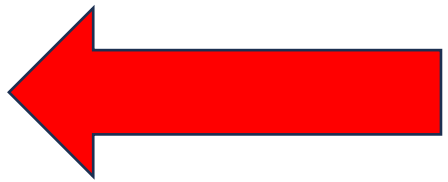

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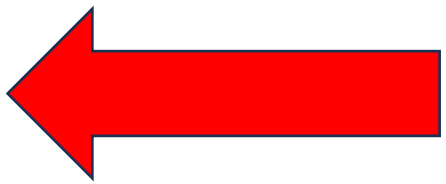

Table 3: Multiple logistic regression model for the outcome of a last viral load >50 RNA copies/ml (N=686)

Characteristic	Total	Unadjusted OR and 95% CI	p	Adjusted OR and 95% CI	p
Viraemia time >1000 copies/ml pre-DTG					
<0.5 years	290	REF		REF	
0.5-1 year	157	**1.1 (0.6-2.1)**	**0.83**	**1.1 (0.5-2.1)**	**0.84**
1-2 years	136	**1.2 (0.6-2.3)**	**0.66**	**1.3 (0.6-2.5)**	**0.53**
>2 years	103	**2.0 (1.0-3.9)**	**0.038**	**1.9 (0.9-3.7)**	**0.071**
VL pre-DTG switch					
0-------<50	612	REF		REF	
50------1000	74	**2.2 (1.2-4.2)**	**0.014**	**2.0 (1.1-3.9)**	**0.041**
Late for visit during follow-up (>90 days)					
Yes	45	**3.1 (1.5-6.4)**	**0.0025**	**3.2 (1.5-6.8)**	**0.0026**
No	641	REF		REF	
Timing of VL test during the year					
January-June	328	REF		REF	
July-December	358	**2.0 (1.2-3.3)**	**0.010**	**2.0 (1.2-3.4)**	**0.011**

Summary

- Since 2019 more than 80% of all the children and adolescents currently in care at this treatment site were switched to DTG
- Most of the population switched were in the adolescent age group and the majority were on NNRTI based regimens at the time just before switching
- On average, patients that were switched to DTG had more than 10 years ART experience
- Despite this, 90% of patients achieved virological suppression at last VL

Strengths and Limitations

- The strengths of the study were that it was a relatively large cohort and patients were followed up for long enough to assess the viral response more effectively, at least over the first 24 months
- The limitations and weaknesses were that CD4 count and clinical staging were not considered and this could have potentially been important in those that did not maintain suppression

Conclusion

- Similar to other studies, VL suppression was effectively maintained in the majority of patients after switching to DTG.
- Caution is needed in children and adolescents with missed visits and extensive prior viraemia.
- Effects of a switch to a DTG-based regimens need to be monitored closely in the paediatric population - a lifetime of ART ahead of them
- Further research
  - understand the implications on long term outcomes of prior regimens
  - exposure to viraemia in children and adolescents
  - how to best design guidelines in the future

Acknowledgements

- Data team at RMMCH, Empilweni
- The dedicated families, children and adolescents of the clinic
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Thank you

Any questions???