Efficacy and Inflammatory Markers After 144 Weeks of Switch to DTG/3TC in a Randomized Trial

663

Evy E. Blomme[1], Evelien De Smet[1], Elianne Burg[1], Loïc Schrooyen[1], Sophie Degroote[2], Sophie Vanherrewege[2], Els Caluwe[2], Linos Vandekerckhove[1,2], Sarah Gerlo[1,3], Marie-Angélique De Scheerder[2]

[1]HIV Cure Research Center, Department of Internal Medicine and Pediatrics, Ghent University, Ghent, Belgium, [2]Department of Internal Medicine, Ghent University Hospital, Ghent, Belgium
[3]Department of Biomolecular Medicine, Ghent University, Ghent, Belgium

BACKGROUND

Reducing the number of active compounds for lifelong HIV treatment is of interest, especially to reduce potential long-term side effects. **The Rumba study** is the first randomized clinical trial evaluating the impact on the **viral reservoir, inflammation and metabolic parameters** of switch from a 2nd generation integrase inhibitor (INSTI)-based triple ART regimen towards DTG/3TC vs. B/F/TAF. Results at 48 weeks confirm the effectiveness and safety of switch to DTG/3TC. Here, we quantified the mean change in inflammatory markers and immune cell counts between baseline and week 144 as an **exploratory objective**.

METHODS

Phase 4 prospective controlled switch trial:
✓HIV-1 RNA<50 copies/ml plasma
✓ 3 months on any stable 2nd generation INSTI-based triple ART

Participants were randomized 2:1 to switch to DTG/3TC (N=89) or to switch or stay on B/F/TAF (N=45).

B/F/TAF
bictegravir/
emtricitabine/
tenofovir alafenamide



DTG/3TC
dolutegravir/
lamivudine

Quantification

Plasma
- Viraemia: Cobas AmpliPrep-Cobas TaqMan HIV-1 test
- D-dimers: immunoturbidimetry
- Cytokines: Meso Scale Discovery (sCD14, sCD163 R-plex, TNF-α S-plex, others U-plex)

Whole blood
- Immune cells: Sysmex XN-1000, flow cytometer FACS Canto II

Statistical analysis: linear regression on natural log-transformed data, adjusted for baseline responses, CD4/CD8 ratio, smoking status and age.

Switch to DTG/3TC does not have a negative impact with regard to viral suppression, inflammatory markers and immune cell counts.

RESULTS

Table 1: Baseline characteristics of the Rumba study population. Data are expressed as numbers or medians with interquartile range. VL= viral load. *p<0.05

Randomized participants	Total N=134		B/F/TAF N=45		DTG/3TC N=89	
Intention-to-treat-exposed (ITT-E) population	n=130		n=43		n=87	
Sex (M/F)	118/12		39/4		79/8	
Ethnicity (European/African/other)	102/14/14		32/5/6		70/9/8	
Smoking status (never/ex/current smoker)	57/24/49		24/6/13		33/18/36	
Age (y)	47	(37;55)	46	(38;52)	48	(40;56)
CD4 at screening (cells/µl)	689	(548;926)	603	(519;765)	690	(525;926)
CD4 nadir (cells/µl)	302	(200;459)	256	(130;332)	309	(155;449)
CD4/CD8 ratio	1,02	(0,7;1,38)	1,02	(0,78;1,32)	0,96	(0,64;1,38)
Peak viral load (copies/ml plasma)	97647	(26380;332504)	80670*	(17951;193505)	190546*	(57544;436516)
Time on ART (y)	7,2	(4,6;10,8)	6	(4,35;8,95)	8,6	(5,2;11,5)
Time from start ART to undetectable VL (y)	0,3	(0,2;0,4)	0,3	(0,2;0,7)	0,3	(0,2;0,4)
Total HIV-1 DNA copies/10^6 CD4+ T cells	485	(228;1110)	58	(10;203)	43	(12;98)
Intact HIV-1 DNA copies/10^6 CD4+ T cells	44	(12;111)	485	(232;1443)	579	(297;1191)

- Baseline characteristics were well balanced between the treatment groups, except for peak viral load.
- At W144 data were available for 103 participants (73 DTG/3TC; 30 B/F/TAF), no discontinuation was reported due to virological failure.
- Virological success was high, with all participants having a viral load <50 copies/ml at W144.

Table 2: Immunological changes after 144 weeks in the ITT-E population. The estimated geometric mean ratio of the groups' (3DR/2DR) relative change from baseline (W144/D1) is reported with 95% CI.

	3DR/2DR Treatment ratio			B/F/TAF (3DR) W144/D1 visit ratio			DTG/3TC (2DR) W144/D1 visit ratio		
Endpoint	Estimate	95% LCL	95% UCL	Mean	95% LCL	95% UCL	Mean	95% LCL	95% UCL
sCD14	1.03	0.95	1.12	0.90	0.83	0.97	0.87	0.83	0.91
sCD163	0.97	0.88	1.08	1.00	0.91	1.09	1.03	0.97	1.09
VCAM-1	0.97	0.86	1.09	0.98	0.88	1.10	1.01	0.95	1.09
TNF-α	0.98	0.88	1.10	0.98	0.89	1.08	1.00	0.93	1.06
CXCL1	1.00	0.77	1.29	0.95	0.75	1.21	0.95	0.82	1.11
IL-21	1.02	0.74	1.40	1.21	0.88	1.65	1.19	0.98	1.43
IP-10	1.10	0.90	1.35	1.07	0.89	1.30	0.97	0.87	1.09
IL-8	1.02	0.89	1.18	1.08	0.95	1.23	1.06	0.97	1.15
IL-10	0.91	0.54	1.52	1.33	0.83	2.11	1.46	1.10	1.95
D-dimer	0.96	0.73	1.27	0.96	0.74	1.23	0.99	0.84	1.17
CRP	0.89	0.58	1.38	0.97	0.65	1.44	1.08	0.84	1.39
CD4	1.00	0.89	1.13	0.97	0.87	1.08	0.97	0.91	1.03
CD8	1.00	0.86	1.17	0.88	0.77	1.01	0.88	0.81	0.96
Monocytes	1.04	0.94	1.16	1.08	0.98	1.19	1.04	0.97	1.10

The relative changes from baseline of the investigated inflammatory markers did not differ between the treatment groups, both in the complete case and multiple imputation (MICE, n=50) analyses. sCD14 decreased by 13% [CI 9-17%] in DTG/3TC and 10% [3-17%] in B/F/TAF. Furthermore, we observed no significant differences between the groups for CD4, CD8 and monocyte counts/µl whole blood.

CONCLUSIONS

The Rumba W144 data confirms that switch to DTG/3TC does not have a negative impact with regard to viral suppression, inflammatory markers and immune cell counts. **We did not observe significant differences** in these exploratory outcomes between B/F/TAF and DTG/3TC.

ADDITIONAL KEY INFORMATION

Correspondence: evy.blomme@ugent.be
We thank all study participants.
The study is supported by ViiV Healthcare
ClinicalTrials.gov ID NCT04553081

HIV CURE Research center
GHENT UNIVERSITY