P099 12-month immunological changes in patients randomized to switch either to BIC/TAF/FTC or DTG/3TC (DEBATE Study)

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Background and Aim

Dolutegravir/lamivudine (**DTG/3TC**) is recommended either as initial or switch regimen by international guidelines; however, few data exist on the control of inflammation after switching to this regimen. The aim of the present study was to evaluate, in a randomized longitudinal study, the immunological impact of switching to bictegravir/emtricitabine/tenofovir alafenamide (**BFTAF**) or to **DTG/3TC**.

Methods

Open-label, prospective, randomized trial enrolling 66 patients on a triple-drug regimen and with a stable (>12 months) undetectable HIV RNA.

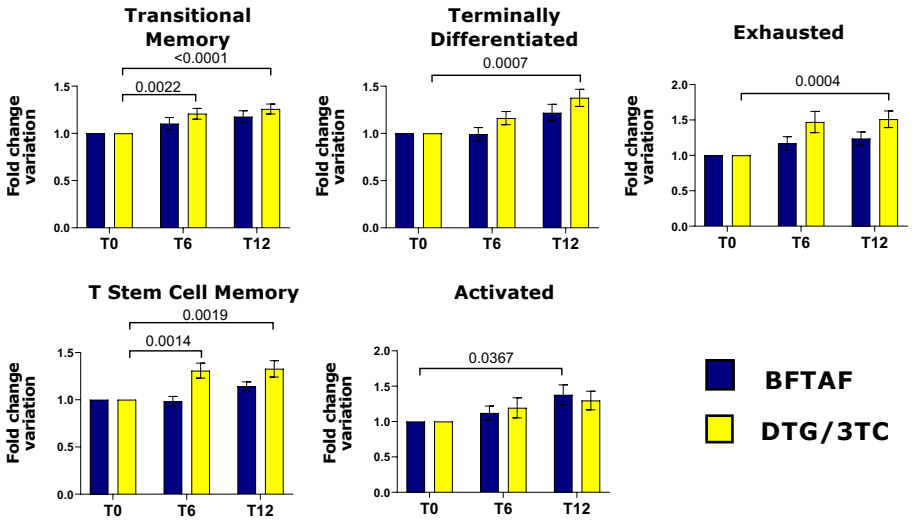
Blood was obtained from patients treated with BFTAF (n=33) or DTG/3TC (n=33) longitudinally studied at time 0, after 6 (T6) and after 12 months (T12).

By polychromatic flow cytometry, we characterized peripheral blood T cells, B lymphocytes and monocytes. Statistical analysis was performed by paired or unpaired Student's t test.

Results

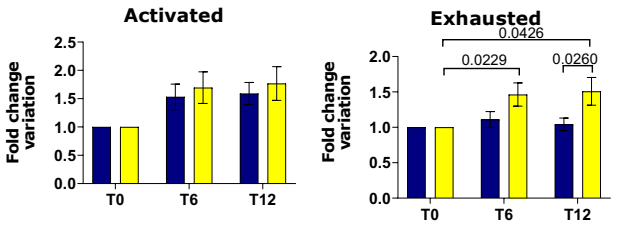
At T12, absolute number of T and B lymphocytes were similar in either group. However, differences were present in $CD4^+$ T cells: the DTG/3TC group (yellow) showed a more marked increase with time in transitional memory lymphocytes (T0 *vs*. T 6: p=0.0022; T0 *vs*. T12: p<0.0001), terminally differentiated T cells (T0 *vs.* T12: p=0.0007), exhausted cells (T0 *vs.* T12: p=0.0004) and T stem cell memory (T0 *vs.* T6: p=0.0014; T0 *vs.* T12: p=0.0019). Activated $CD4^+$ T cells were more represented in BFTAF group (blue, T0 *vs.* T12: p=0.0367).

$CD4^+$



$CD8^+$

Activated $CD8^+$ T cells expressing HLA-DR and CD38 increased similarly in either group, while those with markers of exhaustion were more represented in DTG/3TC group (T0 *vs.* T6: p=0.0029; T0 *vs.* T12: p=0.0426; p=0.0260 between groups at T12).

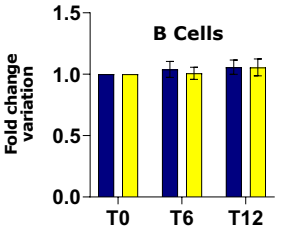


DEBATE Arms

Characteristics	3TC/DTG N= 33	BIC/FTC/TAF N= 33	Total N= 66
Age, years			
Median (IQR)	48 (43, 57)	55 (43, 60)	54 (43, 59)
Sex at birth, n(%)			
Male	29 (87.9%)	28 (84.8%)	57 (86.4%)
Nationality, n(%)			
non-Italian	6 (18.2%)	3 (9.1%)	9 (13.6%)
Mode of HIV transmission, n(%)			
Heterosexual contact	9 (27.3%)	10 (30.3%)	19 (28.8%)
MSM	19 (57.6%)	16 (48.5%)	35 (53.0%)
PWID	2 (6.1%)	6 (18.2%)	8 (12.1%)
OTHER	3 (9.1%)	1 (3.0%)	4 (6.1%)
Lenghth of known HIV infection, years			
Median (IQR)	12 (8, 17)	16 (12, 22)	14 (9, 20)
Lenghth of time with VL below 50 cps/mL, months			
Median (IQR)	98 (73, 139)	120 (71, 170)	101 (72, 161)
HCVAb+, n(%)	6 (19.4%)	4 (12.5%)	10 (15.9%)
Previous AIDS, n(%)	6 (18.2%)	3 (9.1%)	9 (13.6%)
CD4 and CD8 count, Median (IQR)			
CD4 Nadir	303 (183, 413)	268 (208, 354)	296 (197, 375)
CD4 Baseline	709 (543, 927)	857 (657, 1144)	787 (598, 1070)
CD4/CD8 ratio	1.0 (0.7, 1.3)	1.1 (0.8, 1.2)	1.0 (0.7, 1.3)
3rd agent in previous therapy, n(%)			
INSTI	10 (30.3%)	9 (27.3%)	19 (28.8%)
RAL	1 (3.0%)	2 (6.1%)	3 (4.5%)
DTG	5 (15.2%)	4 (12.1%)	9 (13.6%)
EVG	4 (12.1%)	3 (9.1%)	7 (10.6%)
PI/r	0 (0.0%)	5 (15.2%)	5 (7.6%)
ATV	0 (0.0%)	2 (6.1%)	2 (3.0%)
DRV	0 (0.0%)	3 (9.1%)	3 (4.5%)
NNRTI	22 (66.7%)	19 (57.6%)	41 (62.1%)
EFV	8 (24.2%)	3 (9.1%)	11 (16.7%)
NVP	2 (6.1%)	5 (15.2%)	7 (10.6%)
RPV	12 (36.4%)	11 (33.3%)	23 (34.8%)
NRTI	1 (3.0%)	0 (0.0%)	1 (1.5%)
NRTI backbone			
ABC+3TC	8 (24.2%)	9 (27.3%)	17 (25.8%)
FTC+TDF	8 (24.2%)	6 (18.2%)	14 (21.2%)
FTC+TAF	16 (48.5%)	17 (51.5%)	33 (50.0%)
AZT+3TC	1 (3.0%)	1 (3.0%)	2 (3.0%)

Table 1. *Characteristics of study population among patients treated with DTG/3TC or BFTAF. Data are represented as number (n), median and interquartile range (IQR).*

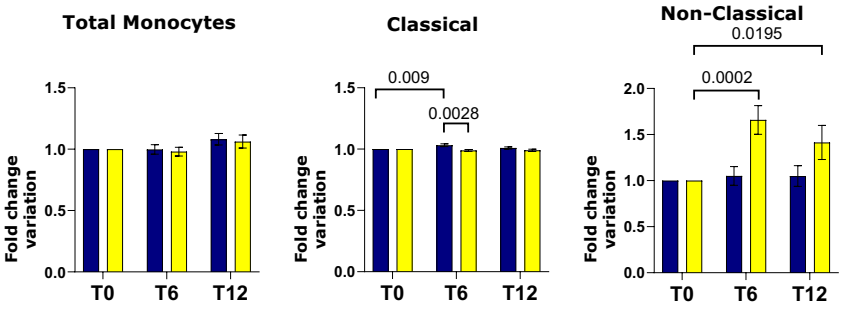
$CD19^+$



No significant changes were seen among B cell populations.

Monocytes ($CD14^+$)

Total monocyte number and percentage did not change with time in either group, but classical monocytes ($CD14^{++}CD16^-$) increased in BFTAF group (T0 *vs.* T6: p=0.009; p=0.0028 between groups at T6), while non-classical monocytes ($CD14^+CD16^{++}$) increased with time in DTG/3TC group (T0 *vs.* T6: p=0.0002; T0 *vs.* T12: p=0.0195).



Conclusions

In this randomized study, **switch to DTG/3TC** was associated after 12 months with an **increase** both in **$CD4^+$** and **$CD8^+$ T lymphocytes** with markers related to **terminal differentiation** and **exhaustion**, and in **non-classical monocytes**, a population of cells that has been recently associated with endothelial dysfunction. Taking into account the importance of endothelial cells in triggering inflammation and in sustaining such process, further studies are need to deepen our findings.