P 172

THE EFFECTS OF SWITCHING FROM DOLUTEGRAVIR/ABACAVIR/LAMIVUDINE TO BICTEGRAVIR/EMTRICITABINE/ TENOFOVIR ALAFENAMIDE IN VIROLOGICALLY SUPPRESSED PEOPLE LIVING WITH HIV ON NEUROPSYCHIATRIC SYMPTOMS: PRELIMINARY FINDINGS FROM A RANDOMIZED STUDY

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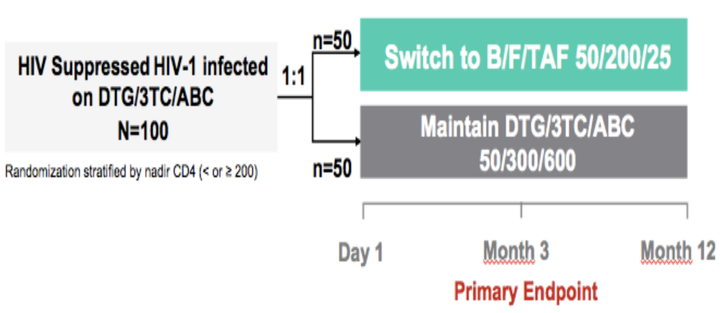
Introduction

- Central nervous system (CNS) adverse events (AE) occur with various antiretroviral regimens (ART), and have been a cause of discontinuation of dolutegravir-containing ART, especially when used in combination with abacavir.
- The main aim of this study was to evaluate whether the switch to bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF arm) is associated with a reduction in severity and incidence of neuropsychiatric symptoms compared to continued dolutegravir/abacavir/lamivudine (DTG/ABC/3TC arm).

Study Design

Fig.1 Study design



Methods

- DOBINeuro is an ongoing, 12-month, randomized, multi-center, interventional trial, enrolling PLWH treated with DTG/ABC/3TC for >6 months and with HIV-1 RNA <50 cps/ml for >12 months.
- Exclusion criteria include previous AIDS events, active alcohol intake or substance abuse, major psychiatric disorders, history of virological failure with InSTI, HBsAg+.
- At baseline (BL), PLWH are randomized to continue DTG/ABC/3TC (arm A) or switch to B/F/TAF (arm B).
- The main endpoint is to analyse differences in the evolution of neuropsychiatric symptoms at 3 months (3M).
- The secondary endpoints are to evaluate quality of life, suicide risk, cognitive impairment, other self-reported symptoms (using validated questionnaires) at 3M.
- Here, we describe preliminary findings at 3M in the first enrolled patients.

Results

Tab.1 Baseline characteristics (n=34)

	Overall	Arm A n=17 DTG/ABC/3TC	Arm B n=17 B/F/TAF	Comparison between arms p
Age, years (median, IQR)	51.1 (37.4-57.7)	50.4 (41.8-56.8)	51.8 (30.0-58.1)	0.718
Male gender, n (%)	25 (73.5)	12 (70.6)	13 (76.5)	1.000
Non Italian born, n (%)	8 (23.5)	3 (17.6)	5 (29.4)	0.688
Caucasian ethnicity, n (%)	27 (79.4)	15 (88.2)	12 (70.6)	0.398
Behavior, n (%)				0.308
Heterosexual contact	12 (35.3)	8 (47.1)	4 (23.5)	
MSM	15 (44.1)	6 (35.3)	9 (52.9)	
Injection Drug Use	1 (2.9)	1 (5.9)	0	
Other/Unknown	6 (17.6)	2 (11.8)	4 (23.5)	
Years from HIV diagnosis (median, IQR)	10.3 (5.3-21.0)	10.7 (4.9-21.5)	9.9 (5.4-19.0)	0.796
Time from first ART, years (median, IQR)	9.8 (4.8-18.8)	9.8 (4.7-21.5)	9.8 (4.7-14.8)	0.570
Nadir CD4, cells/mmc (median, IQR)	302 (140-467)	299 (123-420)	334 (138-516)	0.796
Zenith viral load, log_{10} cp/mL (median, IQR)	4.87 (3.89-5.59)	4.88 (4.17-5.63)	4.54 (3.43-5.62)	0.541
Years on 3TC/ABC/DTG (median, IQR)	4.6 (3.5-5.1)	4.6 (3.2-4.9)	4.6 (3.6-5.2)	0.399
Years from last HIV-1 RNA >50 cp/mL (median, IQR)	6.1 (4.2-10.2)	6.2 (3.7-8.2)	6.0 (4.2-11.7)	0.419
Diabetes mellitus, n (%)	2 (5.9)	1 (5.9)	1 (5.9)	1.000
Arterial Hypertension, n (%)	3 (8.8)	2 (11.8)	1 (5.9)	1.000
Weight in kg (median, IQR)	73.0 (58.0-84.0)	73.5 (62.0-87.0)	73.0 (53.5-82.5)	0.576
CD4 cells count, cells/mmc (median, IQR)	693 (511-1091)	613 (457-995)	784 (522-1288)	0.296
CD4/CD8 ratio (median, IQR)	0.92 (0.47-1.47)	0.99 (0.77-1.39)	0.84 (0.42-1.65)	0.692
eGFR by CK-EPI, mL/min (median, IQR)	79 (67-98)	78 (67-94)	81 (64-100)	0.970
Total cholesterol, mg/dL (median, IQR)	196 (180-226)	200 (174-231)	196 (180-218)	0.984
HDL cholesterol, mg/dL (median, IQR)	46 (42-56)	46 (42-56)	50 (42-56)	0.850
LDL cholesterol, mg/dL (median, IQR)	122 (99-144)	131 (112-147)	120 (91-142)	0.277
Triglycerides, mg/dL (median, IQR)	139 (91-215)	135 (72-188)	141 (97-287)	0.346

- Overall, 14.7% of PLWH showed cognitive impairment at baseline (def. global Z score ≤-1) with no difference between arms

- At 3 months:
  - No significant differences were observed between and within arms regarding self-reported adherence, quality of life assessment and suicide risk.
  - **At 3M, only in the B/F/TAF arm, being depressed (mean score 0.81 vs 1.25, p=0.029) and having muscle aches (mean score 0.63 vs 1.50, p=0.017) were less frequently reported than at BL**
  - HIV-RNA was confirmed <50 cp/mL for all participants in both arms

Safety

- Two non-serious adverse events were reported
  - 1 grade 3 increase of triglycerides with DTG/ABC/3TC
  - 1 self-limited episode of abdominal pain with B/F/TAF, not treatment-related
- Neither led to drug discontinuation

Conclusion

- Switch to B/F/TAF in virologically suppressed PLWH was associated with improvement in two reported symptoms compared to continued DTG/ABC/3TC.
- Further data from the 12-months study follow-up are required to evaluate the potential impact on the incidence and severity of neuropsychiatric symptoms of treatment switch to B/F/TAF compared to continued dolutegravir.

DOBINeuro study group

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