Poster PE3/6

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Reversibility of dolutegravir/lamivudine/abacavir FDC neuropsychiatric toxicity after 24 weeks of switching to elvitegravir/cobicistat/emtricitabine/tenofovir-alafenamide. The DREAM Clinical Trial (GESIDA 9016).

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BACKGROUND

To determine in a clinical trial designed to assess if neuropsychiatric adverse events (AEs) observed in some patients after starting dolutegravir (DTG) are due to DTG or to another concomitant conditions.

METHODS

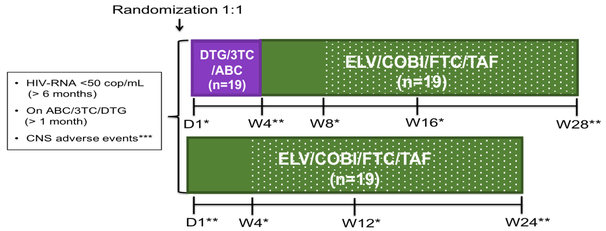
Open-label randomized (1:1) multicenter clinical trial designed to assess reversibility of neuropsychiatric AEs after switching DTG/lamivudine/abacavir (DTG/3TC/ABC) to cobicistat-boosted elvitegravir/emtricitabine/tenofovir alafenamide (ELV/COBI/FTC/TAF).

Study design: Reported in the figure.

Procedures: Headache, insomnia, abnormal dreams, dizziness, fatigue, lack of concentration, nervousness, anxiety, depression and Suicidality, the most common neuropsychiatric AEs reported in DTG/3TC/ABC label and in local clinical experience were documented at each visit and graded in a manner based on the AIDS Clinical Trials Group (ACTG) Division of AIDS scale (2014). To assess the effect of switching DTG/3TC/ABC to ELV/COBI/FTC/TAF on these EAs, a score (DREAM) resulting of adding the grade of these AEs was calculated. In addition to that score, each participant also completed the Hospital Anxiety & Depression Scale (HADs) and the Pittsburgh Sleep Quality Index (PSQI) questionnaires.

Statistics: Raw results on DREAM, HADs and PSQI scores were normalized (0-100) and then changes from baseline were compared at each visit using t-test, McNemar test or generalized estimating equations (for longitudinal linear models). We analyzed differences at week 4 between study arms (primary objective) and changes in the DREAM, HADs and PSQI scores after switching to ELV/COBI/FTC/TAF at weeks 4, 12 and 24 week (secondary objectives).

STUDY DESIGN



* CNS adverse events sleep and mood assessments.
** 3-Tesla brain MRI and CNS adverse events, neurocognitive, sleep and mood assessments.
*** Neuropsychiatric adverse events that appeared or got worse after ABC/3TC/DTG initiation

BASELINE CHARACTERISTICS*

	DTG/3TC/ABC N (19)	ELV/COBI/FTC/TAF N (19)
Age, mean (SD)	40.2 (10.1)	45.6 (8.9)
Gender: Male, n (%)	19 (100)	18 (94.7)
Ethnicity: Caucasian, n (%)	16 (84.2)	18 (94.7)
Illicit drug use, mean (SD)	6 (31.6)	5 (26.3)
Neuropsychiatric comorbidities, n (%)	4 (21.1)	5 (26.3)
Years since HIV diagnosis, mean (SD)	9.4 (9.2)	9 (7.9)
Years of HIV-undetectability, mean (SD)	4.5 (4.2)	5.6 (4.9)
Months on DTG/3TC/ABC, mean (SD)	15.5 (8.8)	19.3 (8.1)
CD4 Nadir, mean (SD)	416 (218)	413 (225.5)
Previous AIDS diagnosis, mean (SD)	1 (5.2)	4 (21.1)
Current CD4 cell count, mean (SD)	772 (402.6)	748.3 (317.6)
Cognitive function: GDS, mean (SD)	0.2 (0.3)	0.4 (0.5)
Neurocognitive impairment, n (%)	5 (26.3)	5 (26.3)
Positive anxiety screen: HADs, n (%)	12 (63.2)	13 (68.4)
Positive Depression screen: HADs, n (%)	6 (31.6)	8 (42.1)
Positive Insomnia screen: PSIQ, n (%)	17 (89.5)	17 (89.5)

* No significant differences were observed between study groups

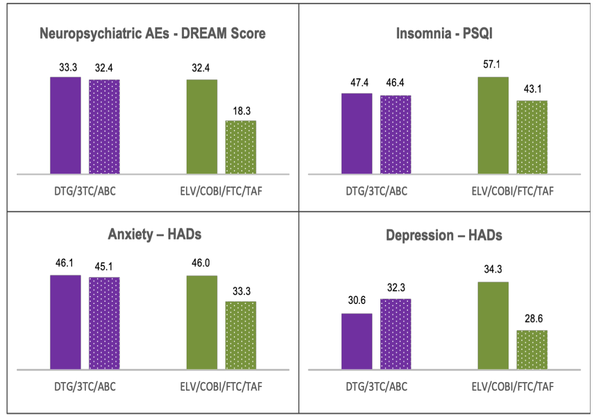
TREATMENT EFFICACY (WEEK 24)

	WEEK 24
HIV RNA <50 cop/mL, n (%)	36 (94.8)
HIV RNA >50 cop/mL, n (%)	0 (0)
HIV RNA missing value, n (%)	1 (2.6)
Treatment discontinuation due to AEs*, n (%)	1 (2.6)

* Drug abuse

PRIMARY OBJECTIVE

We observed significant differences in all neuropsychiatric scores changes, at week 4, among patients switched to ELV/COBI/FTC/TAF and those on DTG/3TC/ABC



SYMPTOMATIC IMPROVEMENTS

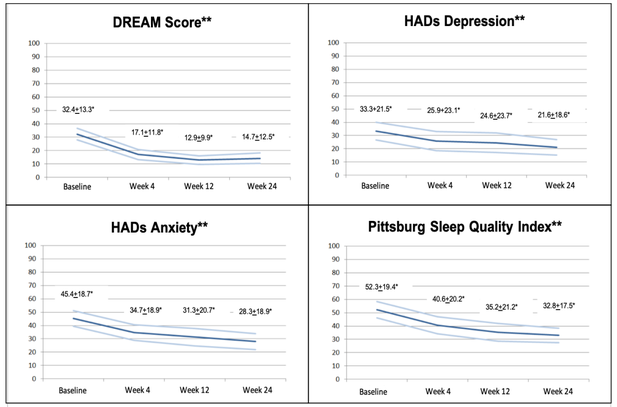
We observed significative improvements after switching to ELV/COBI/FTC/TAF in all neuropsychiatric symptoms recorded in the DREAM Score

	BASELINE (n=38)	WK 4 (n=38)	WK 12 (n=38)	WK 24 (n=37)
Insomnia, (%)	73.7	34.2*	18.4*	8.1*
Abnormal dreams, (%)	31.6	13.2*	5.3*	8.1*
Impaired concentration, (%)	57.9	21.1*	13.2*	16.1*
Nervousness or irritability, (%)	47.4	15.8*	10.5*	10.8*
Asthenia or fatigue, (%)	55.3	26.3*	21.1*	24.3*
Symptoms of anxiety, (%)	42.1	18.4*	7.9*	10.8*
Symptoms of depression, (%)	34.2	18.4*	5.3*	13.5*
Suicidality, (%)	8	0	0	0

* Significant differences from baseline.

SECONDARY OBJECTIVE

We observed significative changes in all neuropsychiatric scores 24 weeks after switching to ELV/COBI/FTC/TAF.



* Significant changes at this timepoint from baseline (all p values <0.0015)
** Significant changes in the longitudinal model (all p values <0.001)

CONCLUSIONS

Our study supports that DTG/3TC/ABC is associated with neuropsychiatric AEs that improve even after switching to another INSTI regimen.

Our study also confirms improvements observed in neuropsychiatric EAs after DTG/3TC/ABC cessation in previous cohorts studies.

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