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Efficacy of Dolutegravir Based Single Tablet Regimen in People with HIV who Inject Drugs

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Introduction

- People with HIV who inject drugs (PWHID) often experience unscheduled antiretroviral therapy (ART) interruptions (USTI) and are at increased risk of developing ART resistance (1, 2).
- PWHID present particular challenges for HIV treatment and have been under-represented in, or generally excluded from, prospective trials of antiretroviral therapies.
- Dolutegravir (DTG) has a high genetic barrier to resistance and is available as a single tablet regimen (STR) with abacavir (ABC) and lamivudine (3TC) (3, 4).
- We aimed to assess the efficacy, tolerability of, and adherence to ABC/3TC/DTG in PWHID.

Methods

- **Design:** A multicenter, prospective, single-arm, open label 96-week observational clinical trial' (*The TAISTR Study',* EudraCT: 2016-000087-42).
- **Population:** Adult people with HIV with a history of injection drug use (IDU) as the principal HIV transmission risk factor or with current or recent (past 12 months) history of IDU, who are either ART-naïve or experienced.
- **Intervention:** PWHID were started on ABC/3TC/DTG once daily.
- **Assessments:** Subjects attended 11 clinical visits over 96 weeks. Clinical and safety, assessments were performed at all study visits. Adherence was determined at 4, 24, 48 and 96 weeks.
- **Combined primary endpoint** included percentage of participants with suppressed HIV viral load (VL) (VL<40 copies/mL (cps/mL)) and adherence, assessed as medication possession ratio (MPR), at week 48 (W48), USTI over 96 weeks and safety.

Intent to treat (ITT) analysis included participants who received ≥1 dose of ABC/3TC/DTG.

**MPR was calculated as total number of ART doses dispensed divided by the number of days between visits, with MPR ≥0.8 considered adequate adherence.*

Results

Of 45 enrolled, 33 contributed to the analysis (8 screen failure, 4 lost to follow-up after screening).

Baseline characteristics:

- Of 33 included in the analysis, 24 (73%) were male, 33 (100%) Caucasian with median (IQR) age 43 (40, 47) years.
- Active IDU was reported in 21 (64%) participants, 28 (85%) were current smokers, 21 (64%) unemployed and 11 (33%) were not in stable accommodation.
- Median (IQR) time since HIV diagnosis was 10 (4, 13) years. At baseline (BL), 31 (94%) were ART experienced (97% on protease inhibitors) and 19 (59%) had VL<40 cps/mL.
- Half of the participants reported history of musculoskeletal and nervous system disorders, infections (Tuberculosis/AIDS defining/other) and gastrointestinal/liver disease.

In People with HIV who inject drugs,

switch to ABC/3TC/DTG STR improved rates of viral suppression, demonstrated adequate adherence and remained effective after unscheduled treatment interruptions

VL SUPRESSION:

82% participants at week 96

Of 41% not suppressed at BL:

16% suppressed at W48

29% suppressed at W96

80% subjects who re-initiated ART (12 of 15) after ART interruption

ADHERENCE

61% participants interrupted ART

Median duration of ART Interruption 12 (5, 33) weeks

MPR 0,84 over 48 weeks

SAFETY

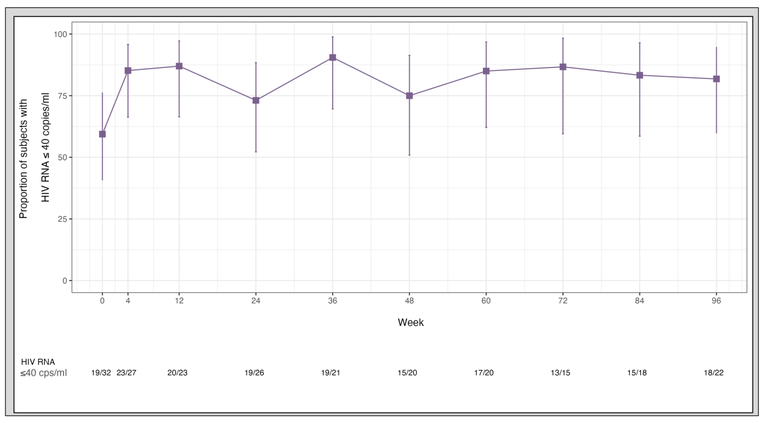
39% participants reported SAE

3% SAE drug related

15% USTI due to AEs

Results

Figure 2. Proportion of participants with suppressed VL (VL<40 cps/mL) over 96 weeks



The proportion of participants with VL<40 cps/mL increased from 59% BL to 75% at W48 (p=0.03) and persisted to W96 (82%) (Fig. 2). Analysis restricted to ART-experienced participants yielded similar results (63% at BL, 74% at W48, and 81% at W96).

Table 1. Summary of AE by system organ and plausible relation to study drug

AE by system organ class	N (%)	Plausible related to drug
Any AE	31 (94%)	25 (76%)
Infections and infestations	23 (70%)	3 (9%)
Gastrointestinal disorders	19 (58%)	14 (42%)
Blood and lymphatic disorders	18 (55%)	5 (15%)
Metabolism and nutrition disorders	16 (49%)	6 (18%)
Psychiatric disorders	14 (42%)	9 (27%)
Nervous system disorders	12 (36%)	9 (27%)
Respiratory, thoracic and mediastinal disorders	8 (24%)	1 (3%)
Injury, poisoning and procedural complications	7 (21%)	-
Investigations*	7 (21%)	3 (9%)
Renal and urinary disorders	7 (21%)	1 (3%)
Skin, subcutaneous tissue disorders	6 (18%)	2 (6%)
Musculoskeletal and connective tissue disorders	6 (18%)	1 (3%)
General disorders and administration site conditions	5 (12%)	1 (3%)
Hepatobiliary disorders	2 (6%)	1 (3%)
Neoplasms benign, malignant and unspecified	2 (6%)	-
Cardiac disorders	1 (3%)	-
Endocrine disorders	1 (3%)	-
Reproductive system and breast disorders	1 (3%)	-
Vascular disorders	1 (3%)	-
Uncoded (cramps, sweating)	2 (6%)	-

** AE Investigations: weight increased, alanine aminotransferase increase, C-reactive protein increase, Helicobacter test positive, liver function test increase*

Conclusion

In the TAISTR trial, we showed that switch to ABC/3TC/DTG STR in PWHID improved rates of viral suppression, demonstrated adequate adherence and remained effective even after unscheduled ART interruptions.

References and Acknowledgements

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