Neuropsychiatric Outcomes in Adults with HIV and TB on Twice daily BIC/FTC/TAF with Rifampicin

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BACKGROUND

Integrase strand transfer inhibitors (INSTIs), such as dolutegravir and bictegravir, have known association with neuropsychiatric symptoms in people living with HIV. Due to drug-drug interactions during co-treatment with rifampicin-based TB treatment, the dose of the INSTI is often doubled. However, the neuropsychiatric outcomes during double dose bictegravir exposure has not been evaluated.

METHODS

- We conducted a secondary analysis of the INSIGHT study (NCT04734652) and assessed neuropsychiatric outcomes in participants randomized to receive bictegravir, emtricitabine, tenofovir alafenamide (BIC arm) or dolutegravir, lamivudine, tenofovir (DTG arm).
- Bictegravir regimen or dolutegravir were dosed twice daily during TB treatment and once daily thereafter.
- Participants underwent regular follow-up, including neuropsychiatric assessments, at baseline and weeks 4, 8, 12, 24, 32,40 and 48 (Table 1).
- Self-reported anxiety, depression and sleep were assessed using the General anxiety disorder screener (GAD-7),Patient Health Questionnaire (PHQ-9) and a study modified Global Sleep Assessment Questionnaire (GSAQ), respectively.

RESULTS

- A total of 122 adults with HIV and TB were enrolled, 80 in the BIC arm and 42 in the DTG arm.
- Median age was 35 years, 65% were male, and 60% had baseline CD4 < 200 cells/µl.
- Mild anxiety and depression were observed in 1% and 9% of individuals on BIC, and 7% and 12% on DTG (Table 1).
- Moderate depression was observed in 1% and 5% of BIC and DTG groups, respectively.
- Most neuropsychiatric symptoms noted at follow up were present prior to INSTI initiation.
- Self-reported sleep disruption was reported in 59% of individuals in the BIC arm and 74% in the DTG arm.

Neuropsychiatric AEs were uncommon in the study, most were mild or moderate and similar pre and post INSTI initiation

BIC/FTC/TAF twice daily was not associated with more neuropsychiatric events than twice daily dolutegravir in PWH and TB on Rifampicin

Table 1: Baseline and follow up Neuropsychiatric assessment per arm

Neuropsychiatric characteristic	Modified Intention-to-Treat N = 120			
	Baseline Assessment		Follow up Assessment	
	BIC arm N = 80[1]	DTG arm , N = 42[1]	BIC arm N = 78[1]	DTG arm N = 42[1]
Anxiety Categories				
None (score 0)	42 (53%)	21 (50%)	42 (54%)	23 (55%)
Minimal (score 1-4)	36 (45%)	20 (48%)	34 (44%) #23	16 (38%) #13
Mild (score 5-9)	2 (2%)	1 (2%)	#1 (1%)	3 (7%)
Moderate (score 10-14)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Severe (score ≥ 15)	0 (0%)	0 (0%)	*1 (1%)	0 (0%)
Depression categories				
None (score 0-4)	71 (89%)	36 (86%)	69 (88%)	35 (83%)
Mild (score 5-9)	8 (10%)	6 (14%)	7 (9%) #4	5 (12%) #4
Moderate (score 10-14)	1 (1%)	0 (0%)	#1 (1%)	2 (5%)
Moderately Severe (score 15-19)	0 (0%)	0 (0%)	*1 (1%)	0 (0%)
Severe (score 20-27)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Sleep disruption	**N=80**	**N=42**	**N=78**	**N=42**
Sleep score ≥6 (Tool range 5-20)	49 (61%)	30 (71%)	46 (59%)	31 (74%)
Mean (SD)	7 (2)	7 (2)	7 (2)	7 (2)
Median (IQR)	6 (5,8)	6 (5,7)	6 (5,8)	6 (5,7)
Range	5,16	5,14	5,16	5,12

[1] n (%), # Symptoms since baseline, *Same individual,
BIC=Bictegravir, DTG=Dolutegravir, IQR=Interquartile Range, N=number, SD=Standard Deviation

RESULTS

- One event of severe anxiety and depression occurred two days into treatment in the BIC arm, with full symptom resolution after five days with no drug intervention or study treatment discontinuation.

CONCLUSIONS

In this study, double-dose bictegravir was associated with a similar number of neuropsychiatric events as double-dose dolutegravir, and none of the identified events required neuropsychiatry interventions, treatment disruption or dose modifications. Neuropsychiatric events were similar pre and post INSTI initiation.



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