Poster 0440

Neuropsychiatric Outcomes Before and After Switching to Dolutegravir(DTG)-based Therapy

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BACKGROUND

- Neuropsychiatric adverse events (NP-AEs) have been reported with DTG but NP symptoms have not been systemically quantified using structured scales.
- This study examined mood and cognitive parameters before and after a planned transition from a non-DTG to a DTG-based regimen within a longitudinal study.

METHODS

Participants

- RV254/SEARCH010 cohort participants who initiated cART immediately after AHI diagnosis

Selection Criteria

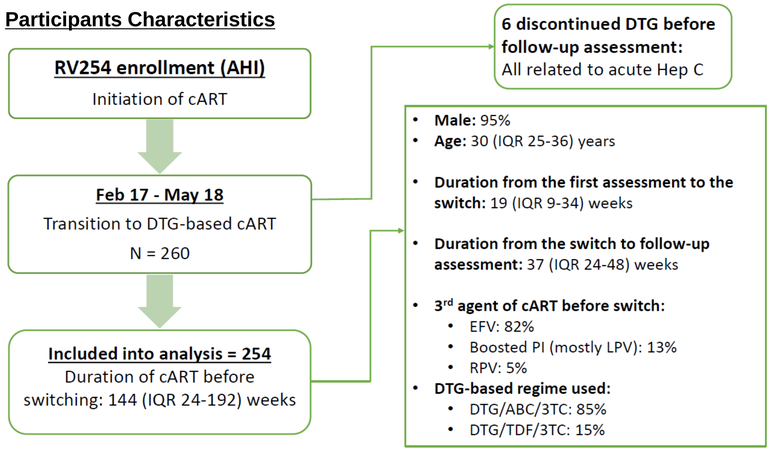
- After at least 24 weeks of non-DTG-based cART
- Clinically stable with undetectable or declining plasma HIV-1 RNA (<500copies/ml)
- Without elevated liver enzymes or unstable liver disease

Examined Parameters

Laboratory	Neuropsychiatric	Cognition tests
CD4+ & CD8+ T-cell levels	Distress thermometer (DT)	Fine motor speed and dexterity Grooved Pegboard test (GPB)
Plasma HIV-1 RNA	^2Q-Depression screening	Psychomotor speed Color Trails 1 , Trail Making A
	Patient Health Questionnaire-9 (PHQ-9)	Executive functioning/set shifting Color Trails 2

^The 2Q-Depression includes one question about mood and another question about loss of interest or pleasure in daily activities [1].

Participants Characteristics



RESULTS

Table 1. Parameters Before and After Transition to Dolutegravir (N=254)

	Pre-switch**	Post-switch**	P value
CD4+ T-cells (cells/ul)	624 (512-783)	662 (530-833)	< 0.001
CD8+ T-cells (cells/ul)	578 (449-787)	618 (482-796)	0.155
CD4/CD8	1.09 (0.85-1.41)	1.12 (0.87-1.43)	0.026
NPZ-4	0.70 (0.31-1.10)	0.88 (0.37-1.19)	< 0.001
Color Trails 1 z-score	1.15 (0.59-1.56)	1.30 (0.64-1.74)	0.001
Color Trails 2 z-score	0.61 (0.14-1.11)	0.86 (0.40-1.22)	< 0.001
Grooved Pegboard Test z-score	0.54 (-0.20-1.05)	0.64 (-0.09-1.10)	0.149
Trail Making A z-score	0.75 (0.14-1.15)	0.80 (0.07-1.33)	0.037
PHQ-9 score	5 (1-7)	5 (2-8)	0.009
Moderate Depression (PHQ-9≥10), n(%)	24 (10)	40 (16)	0.006
Moderate-severe Depression (PHQ-9≥15), n(%)	8 (3)	8 (3)	1.000
^ PHQ-9 Somatic Sub-score	2 (0-3)	2 (1-3)	0.007
# PHQ-9 Cognitive/Affective Sub-score	2 (0-4)	2 (0-5)	0.064
2Q-Depression Screening, n(%)	2 (1)	3 (1)	1.000
Distress Thermometer (DT) Score	2 (1-5)	2 (1-4)	0.898
*Viral Suppression, n(%)	244 (96)	250 (98)	0.070

**Median (IQR) is presented unless specified; Wilcoxon and McNemar Test were used accordingly.
^ Questions 3, 4, 5; # Questions 1, 2, 6, 7, 8, 9.
* Defined as plasma HIV RNA < 50 copies/ml.
Abbreviations: NPZ-4 = Composite z-score of the 4 neuropsychiatric tests; PHQ-9 = Patient Health Questionnaire-9.

Table 2. Factor Correlation with PHQ-9 Changes after DTG*

	Univariable		Multivariable	
	PHQ-9 mean difference (95% CI)	P-value	PHQ-9 mean difference (95% CI)	P-value
Age	-0.05 (-0.01 to 0.008)	0.096		NS
Sex (male)	0.64 (-1.4 to 2.70)	0.537		
CD4, every 100 cells/ul	-0.03 (-0.2 to 0.2)	0.713		
Viral suppression	-3.4 (-5.7 to -1.2)	0.003	-3.2 (-0.9 to -5.4)	0.006
PHQ-9 ≥ 10 before DTG	-2.8 (-4.3 to -1.3)	<0.001	-2.7 (-1.2 to -4.2)	<0.001
PHQ-9 ≥ 15 before DTG	-6.2 (-8.6 to -3.7)	<0.001		
EFV use before DTG	0.11 (-1.1 to 1.3)	0.859		

*PHQ-9 change = PHQ-9 at 2nd assessment minus PHQ-9 at 1st assessment
Statistical method: Linear regression with PHQ-9 change as dependent variable
Abbreviations: NS = not significant; PHQ-9 = Patient Health Questionnaire-9.

SUMMARY OF FINDINGS

- There was no DTG discontinuation due to NP-AEs after a median duration of 37 weeks.
- While the proportion of participants with moderate depression (PHQ-9≥10) increased after DTG, the median total PHQ-9 score and the percentage of participants with moderate-severe depression (PHQ-9≥15) remained unchanged. Scores on the DT and the 2Q-Depression were similar after DTG.
- Both somatic and affective/cognitive components in the PHQ-9 worsened after DTG, but the magnitude of change was only statistically significant for the somatic subscale.
- A pre-existing viral suppression and high PHQ-9 scores were associated with a lower PHQ-9 score after DTG in multivariable analysis.
- There was no decline in neurocognitive tests performance after DTG-based cART.

LIMITATIONS

- Participants are mostly young males without medical problems other than HIV-1 infection with relatively high CD4 nadirs.
- Individuals with major psychiatric illness were excluded in the parent protocol.
- There is a lack of a control group comprised of individuals who did not switch to DTG.

CONCLUSION

- Transition to a DTG-based regimen in cART-experienced individuals does not appear to significantly increase the risk for mood disturbance or neurocognitive impairment.
- The modest increase in somatic complaints observed in this study correspond to reports of insomnia and related symptoms in prior clinical observations.

References

[1] Kongsuk T, Supanya S, Kenbubpha K et al. Services for depression and suicide in Thailand. WHO South East Asia J Public Health 2017; 6:34-38.

Acknowledgements

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Disclaimers

The views expressed are those of the authors and should not be construed to represent the positions of the U.S. Army or the Department of Defense. The investigators have adhered to the policies for protection of human subjects as prescribed in AR 70–25.