CLINICAL AND LABORATORY OUTCOMES 24 WEEKS AFTER STARTING DTG VERSUS EFV IN ACUTE HIV

Poster 0475

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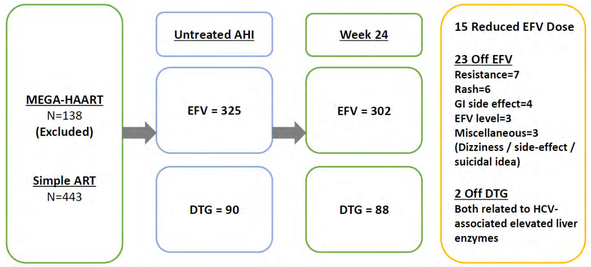
BACKGROUND

- Efavirenz(EFV)- and Dolutegravir(DTG)-based antiretroviral therapy (ART) are the previous and current first line regimens in most ART guidelines.
- Integrase inhibitors, including DTG, lead to higher CD4+ T-cell level recovery than EFV in chronic HIV infection [1] but this has not been examined in acute HIV infection (AHI).
- Both EFV and DTG may give rise to neuropsychiatric side effects.
- This study compared clinical laboratory and mood parameters before and after initiating Efavirenz(EFV)- and Dolutegravir(DTG)-based ART during AHI.

METHODS

- Participants were individuals with AHI (Fiebig I to V) enrolled in the RV254/SEARCH010 cohort in Thailand who initiated ART within days (median=0; IQR 0-1) after diagnosis (EFV + 2NRTI: 2009 to Jan 2017 (denoted as EFV); DTG + 2 NRTI: Feb 2017 onwards (denoted as DTG); other ART only if clinically indicated for intolerance or resistance). Participants who received other ART regimens, including MEGA-ART as part of a sub-study, were excluded (**Figure 1**).
- The current analysis focused on the following endpoints before after 24 weeks of ART:
  - Plasma HIV-1 RNA, blood CD4+ and CD8+ T-cell levels
  - Mood parameters, measured by the 9-item Patient Health Questionnaire (PHQ-9, score 0-27) for depression symptoms and the Distress Thermometer (DT) for anxiety/stress (score 0-10).

Figure 1. Case Selection (2009 – June 2019)



Remarks:
MEGA-ART: DTG+2NRTI+Maraviroc or EFV+2NRTI+Raltegravir+Maraviroc
PHQ-9 Affective: Questions 1, 2, 6, 7, 8, 9; **PHQ-9 Somatic:** Questions 3, 4, 5

SUMMARY OF FINDINGS

- Discontinuation frequency for adverse events or resistance was 7% for EFV and 2% for DTG.
- Rates of plasma HIV-1 suppression at week 24 were 98% and 93% for DTG and EFV respectively.
- At week 24, DTG users showed greater increments in CD4 and CD8 T-cell levels than EFV users. DTG-based ART remained independently associated with greater CD4+ T-cell increment in multivariable analysis (**Table 3 & 4**).
- At week 24, the frequencies of moderate depression symptoms (PHQ-9>9) in the DTG and EFV groups were 15% vs 13% respectively. Both groups had lower PHQ-9 and DT scores at week 24 than at baseline but the scores were similar across the groups.

RESULTS

Table 1. Characteristics of Groups at Baseline

	EFV (n=302)	DTG (n=88)	P-value
Age	26 (22-31)	26 (23-33)	0.668
Sex (Male)	295 (98)	87 (99)	0.689
Fiebig I & II	120 (37)	25 (28)	0.134
Fiebig III-V	205 (63)	65 (72)	
CD4+ T-cell	378 (267-504)	324 (234-434)	0.022
CD8+ T-cell	541 (346-993)	465 (304-778)	0.025
CD4/CD8	0.66 (0.39-1.03)	0.74 (0.47-1.13)	0.299
Blood Log_{10} HIV-1 RNA	5.99 (5.33-6.81)	6.16 (5.12-6.84)	0.580
ARS	256 (79)	64 (71)	0.156
PHQ-9 Total Score*	9 (6-13)	8 (4-13)	0.081
PHQ-9 Affective Subscore*	5 (3-8)	4 (2-8)	0.171
PHQ-9 Somatic Subscore*	4 (2-6)	3 (2-5)	0.064
Distress Thermometer*	5.0 (2.3-7.0)	4.2 (1.8-6.5)	0.104
HIV-1 subtype			0.001
CRF01_AE	238 (78.8)	54 (61.4)	
CRF01_AE/B	41 (13.6)	30 (34.1)	
B	6 (2.0)	0 (0)	
C	1 (0.3)	0 (0)	
Other	2 (0.7)	0 (0)	
Untypable	14 (4.6)	4 (4.6)	

Median (IQR) and, n (%) are shown accordingly; *EFV=294; DTG= 88

Table 2. Week 24 Outcomes by ART

	EFV	DTG	P-value
CD4+ T-cell	585 (481-704)	631 (517-817)	0.050
CD8+ T-cell	584 (456-760)	630 (490-875)	0.026
CD4/CD8	1.00 (0.77-1.30)	0.93 (0.77-1.28)	0.469
HIV-1 RNA < 50	274 (93)	85 (98)	0.124
PHQ-9 Total*	4 (2-8)	4 (2-8)	0.939
PHQ-9 Affective*	2 (0-4)	2 (0-5)	0.765
PHQ-9 Somatic*	2 (1-3)	2 (1-3)	0.827
Distress Thermometer*	2.0 (1.0-4.0)	1.5 (1.0-3.2)	0.271

Median (IQR) and, n (%) are shown accordingly; *EFV=292; DTG= 87

Table 3. Interval Change of Various Parameters by ART Regimen

	EFV-based	DTG-based	p-value
ΔCD4	+205 (105 to 314)	+286 (174 to 435)	<0.001
ΔCD8	+19 (-333 to 241)	+169 (-42 to 331)	<0.001
ΔCD4/CD8	+0.29 (0.03 to 0.61)	+0.19 (0 to 0.46)	0.106
ΔPHQ-9	-4 (-1 to -8)	-3 (0 to -7)	0.122
ΔAffective	-3 (0 to -5)	-2 (0 to -5)	0.252
ΔSomatic	-1 (0 to -3)	-1 (0 to -2)	0.086
ΔDistress Thermometer Score	-1.8 (0 to -4)	-1.4 (0 to -3.4)	0.392

Median (IQR) and, n (%) are shown accordingly
Δparameter = Week24 parameter – Week0 parameter

Table 4. Factors Associated with CD4 Changes

	Univariable	Multivariable	
	p-value	mean difference (95% CI)	p-value
Sex	0.490	-	-
Age	0.332	-	-
Baseline CD4+ T-cell	<0.001	-0.22 (-0.12 to -0.33)	<0.001
Baseline CD8+ T-cell	<0.001	-0.05 (-0.02 to -0.08)	<0.001
CD4/CD8	0.855	-	
Plasma HIV-1 RNA	<0.001	27.5 (10.4 to 44.6)	0.002
Fiebig I and II	0.566	-	-
ARS	<0.001	72.8 (41.1 to 117.2)	0.001
ART regimen (DTG)	<0.001	79.2 (41.1 to 117.2)	<0.001

Δparameter = W24 parameter – W0 parameter
Factors with p<0.05 in univariate analysis were included into multivariable analysis

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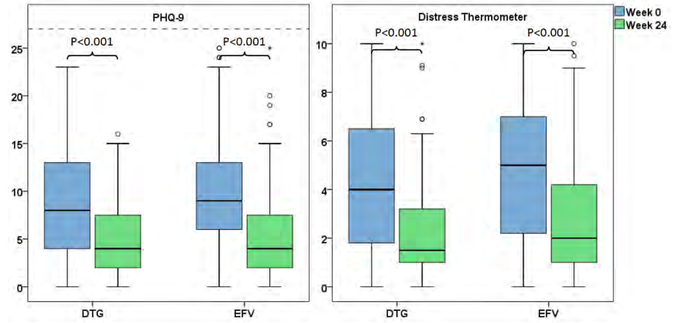
Figure 2.



LIMITATIONS

- Individuals with major psychiatric illness were excluded in the parent protocol.
- The DTG group had lower baseline CD4 and CD8 T-cell levels and higher rates of Fiebig III and CRF01 AE/B recombinant subtype than the EFV group (p<0.05).

CONCLUSIONS

- Compared to EFV, initiating DTG-based ART at AHI was associated with a greater gain in CD4 T-cell level and a higher absolute CD4 count at week 24.
- Self-reported depression and distress symptoms were statistically similar between the 2 ART regimens at week 24, suggesting that mood and stress symptoms observed at AHI improved with ART regardless of the ART regimen.
- DTG discontinuation was not attributed to any AE.

FOLLOW-UP PLAN

- To compare any new and persistent differences in clinical and neuropsychiatric parameters between the two regimens at week 96

References

[1] Edwards, J. K., Cole, S. R., Hall, H. I., Mathews, W. C., Moore, R. D., & Mugavero, M. J. (2018). Virologic suppression and CD4 cell count recovery after initiation of raltegravir-or efavirenz-containing HIV treatment regimens. AIDS (London, England), 32(2), 261.

Disclaimers

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