Real world persistence of E/C/F/TAF vs DTG + ABC/3TC regimens for treatment of HIV in a large Spanish cohort - VACH

Poster P083

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Background

- Persistence and adherence to antiretroviral therapy (ART) for HIV infection have been correlated with improved patient outcomes.
- Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) and dolutegravir + abacavir/lamivudine (DTG+ABC/3TC) are recommended ARTs by current HIV management guidelines[1].
- Persistence of E/C/F/TAF vs DTG + ABC/3TC regimens has been evaluated in clinical trials; however, data from real-world settings are limited.

Objective

- The objective of this analysis was to compare real-world persistence of two commonly used triple therapies, E/C/F/TAF and DTG + ABC/3TC and risk of discontinuation due to virological failure and adverse events in a large Spanish cohort.

Materials and Methods

- A retrospective analysis was performed using data from the VACH cohort - a prospective multicentre Spanish cohort of adult HIV patients.
- All treatment-experienced patients, between 01/08/2016 (introduction of E/C/F/TAF) and 01/06/2017, initiating DTG+ABC/3TC or E/C/F/TAF were included. Unit of analysis was patient-regimen.
- Time to non-persistence was defined as the time from patient-regimen initiation to discontinuation (for any reason), loss-to-follow-up, death or censoring, whichever occurred first. Time to discontinuation due specifically to virological failure and adverse events, as reported by the clinician, were also studied.
- Kaplan-Meier analyses with log-rank test were performed on time to non-persistence, time to virological failure and time to AE.
- Cox proportional hazard models were used to compare regimen groups controlling for: age, gender, HBV diagnosis, HCV diagnosis, AIDS diagnosis, illicit drug usage/abuse, CD4 (<350 cells/µL), number of previous regimens, number of previous virological failures and years on antiretroviral therapy – all at patient-regimen initiation.

Results

Regimens, status and reasons for discontinuation

- E/C/F/TAF: 1279 patient-regimens (643.93 patient-years of follow-up)
- DTG+ABC/3TC: 600 patient-regimens (96% were on DTG/ABC/3TC) (271.3 patient-years of follow-up)
- A significantly higher number of DTG+ABC/3TC regimens were discontinued due to any reason compared to E/C/F/TAF (8.2% vs 4.0%, p<0.001).
- Discontinuation due to AEs was also significantly higher in DTG+ABC/3TC compared to E/C/F/TAF (2.3% vs 0.5%, p<0.001) with AEs accounting for 28.6% of all discontinuations in DTG+ABC/3TC vs 13.7% in E/C/F/TAF.
- No significant difference between the two regimens was found for discontinuations due to VF, or any other reason reported.

Table 1. Summary of study regimen status and reasons for discontinuation

n (%)	DTG+ABC/3TC N=600	E/C/F/TAF N=1279	p value
Remains on treatment	550 (91.7%)	1181 (92.3%)	
Loss to follow up	1 (0.2%)	43 (3.4%)	
Death	0 (0%)	4 (0.3%)	
Discontinued	49 (8.2%)	51 (4.0%)	**<0.001**
Adverse events	14 (2.3%)	7 (0.5%)	**<0.001**
Simplification	8 (1.3%)	7 (0.5%)	0.139*
Avoiding long term toxicity	3 (0.5%)	3 (0.2%)	0.584*
Virological failure	3 (0.5%)	2 (0.2%)	0.379*
Intolerance	1 (0.2%)	2 (0.2%)	1.000*
Drug interactions	0 (0.0%)	2 (0.2%)	0.926*
Other	18 (3.0%)	24 (1.9%)	0.125
Missing	2 (0.4%)	4 (0.4%)	

* Fisher's exact test, otherwise Chi-square test

Demographics

- Baseline patient-regimen characteristics differed in the two groups (**Table 2**). Patients on E/C/F/TAF were younger, and had been less time on ART, although number of previous regimens was similar. The proportion of patients with AIDS and HCV was lower in the E/C/F/TAF group. Remarkably ten patients with HBV had initiated treatment with DTG+ABC/3TC. The percentage of patients with HIV RNA <50 cells/mm3 at treatment initiation was higher with E/C/F/TAF and mean number of previous virological failure (0.7 vs 0.9) was lower with E/C/F/TAF (**Table 2**).

Table 2. Patient and clinical characteristics at patient-regimen initiation

	DTG+ABC/3TC N=600	E/C/F/TAF N=1279	P-value
Age (years), Mean (SD)	49.6 (10.5)	46.2 (10.8)	***<0.001***
Gender, % Male	73.0%	76.9%	0.064
AIDS diagnosis, % Yes	25.0%	19.9%	***0.011***
HCV, % Yes	34.2%	26.9%	***0.001***
HBV, % Yes	1.6%	8.0%	***<0.001***
eGFR, % <60 min/ml/1.73m²	5.9%	4.3%	0.206
CD4 count at treatment initiation, % < 350 cells/microL	14.7%	11.6%	0.203
VL at treatment initiation, % <50 cells/mm³	79.1%	84.6%	***0.003***
Number of previous ART regimens, Mean (SD)	4.22 (3.3)	4.03 (3.6)	0.245
Duration of ART regimens (years), Mean (SD)	12.2 (7.4)	10.1 (7.4)	***<0.001***
Previous VF, Mean (SD)	0.9 (1.4)	0.7 (1.5)	***0.007***

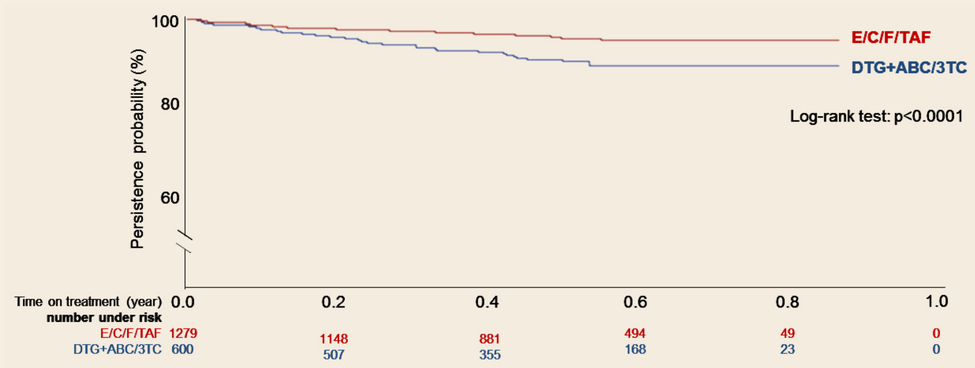
ART: anti-retro viral treatment, VF: virological failure VL: viral load

Results (cont'd)

Persistence

- Time to discontinuation due to any reason was significantly shorter in patients in DTG+ABC/3TC than in E/C/F/TAF (p<0.0001) (**Figure 1**). After controlling for demographic and clinical characteristics, the likelihood of discontinuation was 2.08 times higher in DTG+ABC/3TC vs E/C/F/TAF (95% CI for hazard ratio 1.41-3.13; p=0.0002) (**Figure 4**)

Figure 1. Kaplan Meier estimator curves for discontinuation due to any reason

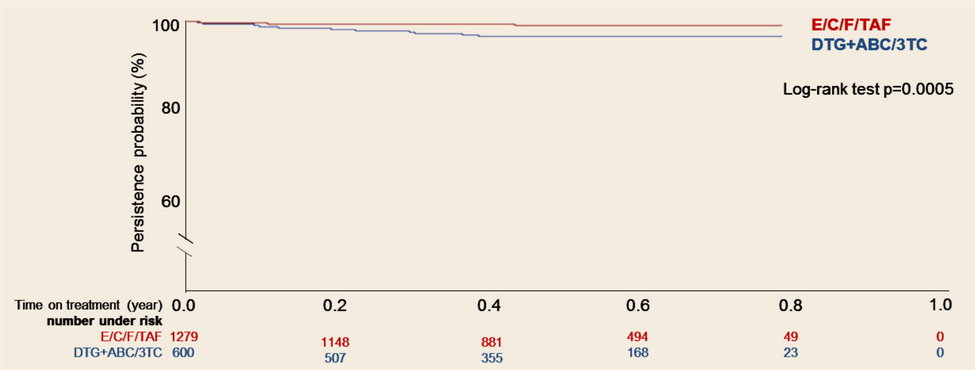


* Fisher's exact test, otherwise Chi-square test

Toxicity

- Time to discontinuation due to AEs was significantly shorter in patients in DTG+ABC/3TC than in E/C/F/TAF (log-rank test, p=0.0005) (**Figure 2).** After controlling for demographic and clinical characteristics, the likelihood of discontinuation was 3.33 times higher in DTG+ABC/3TC vs E/C/F/TAF (95% CI for hazard ratio 1.64-7.14; p=0.001) (**Figure 4**)

Figure 2. Kaplan Meier estimator curves for discontinuation due to an adverse event



Efficacy

- No difference in time to virological failure was detected between DTG+ABC/3TC and E/C/F/TAF in the unadjusted or adjusted analyses (**Figures 3 and 4**).

Figure 3. Kaplan Meier estimator curves for discontinuation due to virological failure

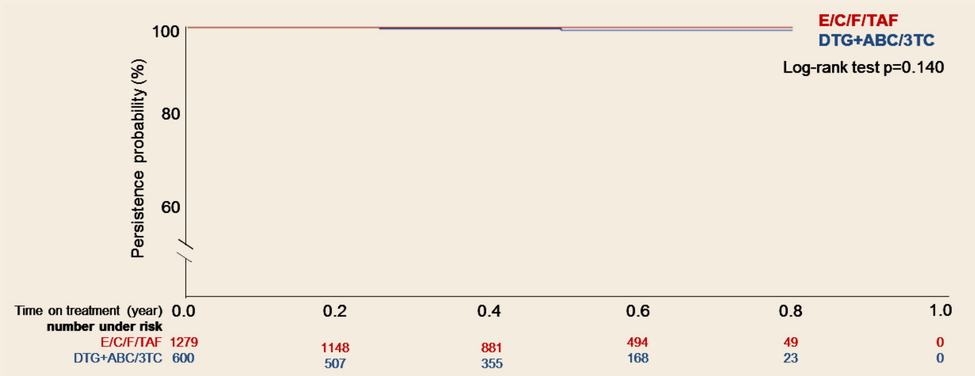
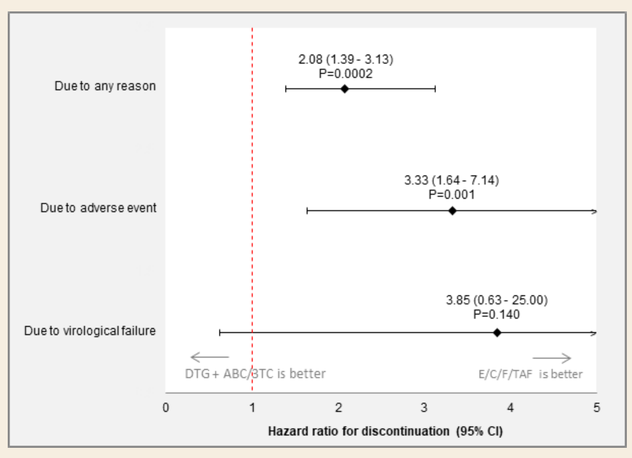


Figure 4. Cox proportional hazard models for time to discontinuation



Results are given as hazard ratio (95% confidence interval boundaries of hazard ratio) and p-value for the hazard ratio

Hazard ratios over one indicate that the likelihood of discontinuation is higher for DTG+ABC/3TC than for E/C/F/TAF

Conclusions

In this real world analysis in a large Spanish cohort, persistence was higher in patients on E/C/F/TAF vs DTG+ABC/3TC, with no difference in time to discontinuation due to virological failure but a three-fold higher probability of discontinuation due to AEs in DTG+ABC/3TC.

Reference

1. European AIDS Clinical Society (EACS) Guidelines Version 9.0 October 2017 www.eacsociety.org/guidelines/eacsguidelines/eacs-guidelines.html

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