Discontinuation of DTG, EVG/c, and RAL due to toxicity in a prospective cohort.

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Background / Objectives: The rates of discontinuation (D/C) due to adverse events (AEs) of the integrase strand transfer inhibitors (INSTI) dolutegravir (DTG), raltegravir (RAL) and cabozantinib-boosted elvitegravir (EVG/c) have been very low in the majority of clinical trials. However, some real-world retrospective series have reported unexpectedly high rates of D/C due to AEs, particularly with DTG. We aimed to compare the D/C rates due to AEs of the three INSTIs in a prospective multicenter cohort.

Methods: The PISCIS Cohort is an ongoing observational study that includes about 2200 HIV-infected patients aged ≥ 16 years from hospitals in Catalonia (Spain) and 3 in the Balearic Islands (Spain) since January 2013 as long as they are continuous or non-continuous patients. Of the 2200 patients included, 689 had started one of the five regimens including DTG/abacavir/lamivudine (ABC/3TC) or tenofovir/famata/entecavir/tenofovir (TDF/TAF), RAL with ABC/3TC or TDF/TAF, or the co-formulation EVG/c/TDF/TAF. D/C due to AEs was defined as the withdrawal of one or more AEs. The incidence rate and 95% CI of D/C due to toxicity was estimated as the ratio of the number of discontinuations per 100 patient/year (py) of follow-up (FU). Adjusted hazard ratios (HR) and their 95% CI were obtained from multivariate Cox models, adjusted for gender, age, transmission group, origin, treatment-naive and hepatitis B/C infection.

Results: 2021 subjects were included, 114 (57%) starting the INSTI as a switch/implication strategy. Neurocognitive AEs included identified: anxiety, depression, insomnia, dizziness, nightmares, paresis, somnolence, tremor and vertigo. The rates of D/C due to any toxicity (2.8-5.5 per 100 py of FU) or for neurocognitive toxicity (0.9-2.8 per 100 py of FU) were low, without significant differences among the 5 regimens. Toxicities were rarely grade 3-4, had been commonly seen before the initiation of the INSTI, and resolution was often seen after drug withdrawal. All results shown in the Tables.

Conclusions: In this prospective cohort study, we did not find significant differences in the rate of D/C due to any toxicity (either related with all the regimen or specifically with the INSTI) among the 5 regimens studied with DTG, RAL or EVG/c, either in naive or in switch. There was a significantly higher rate of D/C due to neurocognitive AEs with DTG vs either RAL or EVG/c. EVG/c was associated with higher rates of D/C due to neurocognitive AEs. Rates of D/C due the AEs were low, but most subjects discontinuing DTG/ABC/TDF did so due to neurocognitive AEs. Why this was not seen with DTG + TDF/FTC merits further investigation.

Funding: This work received an unrestricted grant from VW Healthcare.