Impact of NRTI mutations on virological efficacy of antiretroviral regimens containing elvitegravir: an ARCA-ECCO cohort study

Robertta Gaglardi1,2, Sara Modica1, David Redi1, Emanuela Giombini1, Antonia Beacenek1, Domenico Di Carlo1,2, Franco Maggiolo1, Francesca Lombardi1, Alberto Borghetti1, Anna Paola Callegaro1, Anna Rita Gismundo1, Manuela Colagá1,2, Gaetana Sterrantino3, Andrea Costantino3, Sergio Ferrara3, Stefano Ruscio3, Simona Di Giambenedetto3, Maurizio Zazzi3, Andreas De Luca4,5,6, Barbara Rossotti1,2, Nicola Gianotti1,2

Background
Integrate inhibitor-based regimens are recommended by current guidelines as first-choice antiretroviral (ARV) therapy. ARV drug resistance mutations remain a major cause of treatment failure. Very recently, first results of GS-US-292-1824 study showed full virological suppression in experienced patients harboring M184V/I mutation, but results are pending for patients with M184V/I TAM.

The aim of this study was to evaluate the effect of drug mutations on virological efficacy of elvitegravir-containing ARV regimens in naïve and treatment-experienced HIV-1 infected patients in a real life setting.

Material and methods
From the ARCA and ECCO databases we selected naïve and treatment-experienced HIV-1 infected patients starting tenofovir disoproxil fumarate or tenofovir alafenamide/emitricitabine/elvitegravir/cobicistat (from June 2012 to December 2017), with at least one pre-baseline PR/RT resistance genotype and at least 1 HIV-RNA during follow up. Patients with previous detection of mutation to INSTI or previous virological failure with a NRTI including regimen without a following genotype were excluded.

NRTI resistance mutations were defined as the detection of at least one mutation among those included in IAS list (2017).

Primary endpoint:
✓ virological failure (VF, defined as an HIV-RNA > 1,000 copies/ml or 2 consecutive values of >50 cps/ml after week 24 for naïve and treatment experienced with baseline VL >50 copies/ml and at any time for treatment experienced with baseline values of >50 copies/ml).

Secondary endpoint:
✓ predictors of virological failure

Results
During a median observation time of 8 months (4-17), 33 VF occurred (2 in naïve patients, 31 in experienced).

Experienced patients
Virological outcome stratified by NRTI mutation is shown in Figure 1. The estimated probability of being free from VF at 12 months was 89% (95% CI 77-101) in patients with any NRTI major mutation vs 89% (84-94) among those without (log rank 0.478). At multivariate analysis adjusting for any NRTI mutation and HCV serostatus, a longer duration of HIV infection, higher peak of viral load and VL>50 cps/ml at baseline showed a trend with higher risk of VF (Table 3).

Figure 2: Estimated probabilities of virological failure

Conclusions:
Elvitegravir-containing ARV regimens resulted in a good rate of virological suppression, regardless the presence of pre-existing resistance mutations. In naïve patients it seems particularly prudent to the presence of transmitted NRTI resistance.