Chairs: Mariadelfina Molinaro, Italy / Mitsuru Sugawara, Japan  
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[O25-7-4] Effects of cobicistat on tenofovir durability: is it time to rethink at tenofovir alafenamide trials?  
Dario Cattaneo¹, Sara Baldelli², Davide Giacomelli³, Davide Minisci⁴, Cristina Mazzali⁵, Paola Meraviglia⁶, Cristina Gervasoni⁷ (¹Luigi Sacco University Hospital, ²Luigi Sacco University Hospital, ³Luigi Sacco University Hospital, ⁴Luigi Sacco University Hospital, ⁵Politecnico di Milano, ⁶Luigi Sacco University Hospital, ⁷Luigi Sacco University Hospital)  
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Background  
The dose of tenofovir alafenamide (TAF) is reduced from 25 to 10 mg daily when given with boosting agents. However, such dose reduction has never adopted for tenofovir disoproxil fumarate (TDF). Here we investigated the effects of cobicistat on TDF durability in real life setting.

Methods  
HIV-positive patients receiving TDF-containing antiretroviral therapies with at least one assessment of tenofovir plasma trough concentrations were included in the study (n=510). Survival and Cox analyses were carried out considering as the primary outcome TDF discontinuation.

Results  
Overall, a total of 149 cases of TDF discontinuation were recorded during a mean period of 1149± 3537 days of follow-up, of whom 75/207, 41/178, 13/49 and 20/76 cases were detected in patients treated concomitantly with protease inhibitors, non-nucleoside reverse transcriptase inhibitors, integrase inhibitors (dolutegravir or raltegravir) or elvitegravir/cobicistat coformulation, respectively. The Kaplan Meier survival analysis revealed a highly significant difference between elvitegravir/cobicistat and other antiretroviral regimens (Log-Rank p=0.0002). Results of a multivariable Cox regression analysis assessing the time fixed factors at baseline associated with the risk to experience TDF discontinuation confirmed that elvitegravir/cobicistat concomitant therapy was associated with a significantly higher risk to develop TDF toxicity (hazard ratio: 2.2).

Conclusions  
Despite the lower follow-up due to the more recent introduction on the market of the elvitegravir/cobicistat coformulation, patients treated concomitantly with cobicistat experienced a 3-fold higher rate to of TDF discontinuation in the first 1-2 years of therapy compared with other antiretroviral regimens. These findings add further evidence that the dose of TDF should be reduced when combined with boosting agents. This concept is important not only when considering the tolerability of TDF per se, but also when comparing it with that from TAF. Indeed, according to our findings, it cannot be excluded that the lack of proper dose adjustment for TDF when given with cobicistat (or ritonavir) might have biased the safety results between TAF and TDF during registrative trials.