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[PL6.2] INFLUENCE OF THE STAGE OF LIVER FIBROSIS ON PLASMA LEVELS OF ANTIRETROVIRAL DRUGS IN HIV-INFECTED PATIENTS WITH CHRONIC HEPATITIS

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PURPOSE OF THE STUDY: Most antiretrovirals are metabolised in the liver, and lower doses could be advisable in patients with chronic hepatitis C, particularly in those with severe hepatic insufficiency.

METHODS: Plasma drug levels were measured in HCV/HIV-coinfected patients receiving nevirapine (NVP), efavirenz (EFV), lopinavir/ritonavir (LPV/r) or atazanavir (ATZ) r at standard doses for longer than 12 weeks. Liver fibrosis (LF) staging was measured using transient elastometry (FibroScan).

SUMMARY OF RESULTS: A total of 268 HCV/HIV-coinfected patients were analysed. Mean plasma drug concentrations were: 6.1 mg/ml for NVP ($n=35$); 2.8 mg/ml for EFV ($n=46$); 5.8 mg/ml for LPV ($n=56$); 0.4 mg/ml for ATZ ($n=58$) and 0.7 mg/ml for ATZ/r ($n=73$). The distribution of patients with Metavir score was: 39% F0-F1, 16% F2, 11% F3 and 34% F4. Drug concentrations were higher in cirrhotics as compared to non-cirrhotics for EFV (median, 3.4 vs 1.9 mg/ml [$p<0.01$]) and NVP (median, 6.6 vs 5.8 mg/ml [$p=0.33$]). The prevalence of EFV plasma levels above the toxic threshold (>4 mg/ml) was higher in cirrhotics than in non-cirrhotics (31% vs 3%; $p<0.001$). The same trend was recognised for NVP plasma levels >8 mg/ml (50% vs 27%; $p=0.27$). Plasma levels of protease inhibitors (PI) did not differ significantly.

CONCLUSIONS: Liver clearance of NNRTI, particularly of EFV, seems to be impaired in cirrhotics, what translates into higher plasma drug levels. These patients might benefit from therapeutic drug monitoring to avoid drug overexposure. No similar effect was seen for PI. LF assessment by non-

invasive tools may identify HCV/HIV patients that warrant antiretroviral dose adjustments in order to minimize toxicities.

Plenary Session: HIV-related Infections, Co-infections and Malignancies I

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