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Abstract (oral session)

Intracellular HIV-1 drug resistance mutations may change but do not affect virological success of therapy in multi-failed HIV-1 infected patients

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Objectives: Twenty multi-drug resistance (MDR) patients, who achieved a successful virological suppression with darunavir/ritonavir (DRV/r) containing regimens, were followed for 72 weeks to examine the evolution of intracellular drug resistance associated mutation (RAMs) pattern. The main aim of this analysis was to assess the ability of the archived viral variants to re-emerge during ART and to establish their role in therapy failure. Methods: All patients belonging from a larger cohort of antiretroviral multi-drug experienced HIV-1 subjects, enrolled at the “Sapienza” University Hospital, were included in the study. All subjects have already been failed several therapeutic regimens, with a mean treatment time of 17.6 ± 3.6 years. At the time of the inclusion in the study (80± 16 weeks from the DRV/r start) all subjects had reached a HIV-1 RNA level below the limit of detection (<50 copies/ml). HIV- DNA was extracted from peripheral blood mononuclear cells, amplified and sequenced using the TruGene assay. Intracellular drug resistance mutations were detected at T0 (baseline) and, in most patients, after 18, 36, 54 and, in all patients, 72 weeks from the start of study. Results: During 72 weeks of follow-up all patients had an undetectable viremia. At baseline, all subjects had RAMs in proviral DNA, all of which related to previous ART. Interestingly, 18 patients had intracellular mutations associated to DRV resistance at T0. Specifically, using REGA rules, 6 of 18 subjects showed a genotypic resistance to DRV (score >= 3.5), 8 had an intermediate susceptibility (score >= 2; <3.5) and 4 were fully susceptible to DRV (score < 2). After 72 weeks of follow up, 14 patients had an intracellular DRV genotypic score unchange; whilst in 4 patients the genotypic score changed due to loss and/or acquisition of some DRV RAMs. Considering the patients all together , the number of RAMs increased in 8/20 patients (median value: 4 mutations; range 2-9) and decreased in 6/20 patients (median value: 3 mutations; range 2-10). In the remaining patients the number of mutations detected after 72 weeks was similar to that observed at T0 (± 1 mutation). Conclusions: Although performed in a small group of patients, our study suggest that in patients treated with a salvage therapy, the presence of MDR virus in cellular reservoirs, may change, but does not affect virological response during 150 weeks of follow up.