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Efficient immune reconstitution in HIV+ naïve patients (pts) starting a first lopinavir/ritonavir-containing regimen with low CD4 counts

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Purpose of the study

Investigate immune restoration profile, T-cell activation and microbial translocation in HIV+ naïve pts starting a first LPV/r-containing regimen with low CD4.

Methods

40 HIV+ antiretroviral-naive pts starting a first tenofovir/emtricitabine + LPV/r-containing ART with CD4 <350 (20 Late Presenters —LPs, CD4 <100/μL and 20 Non-Late Presenters —NLPs, CD4, 200—350/μL) were followed for 12 months (T12). Microbial translocation (MT) by plasma lipopolysaccharide (LPS) and sCD14 (LAL assay and ELISA), CD38+CD8, CD45R0+38+CD8, CD127+CD4/CD8 (flow cytometry), and plasma IL-7 (ELISA) were tested at T0 and T12. T0 and T12 differences were analyzed by Mann Whitney U test.

Summary of results

At T12, all 40 HIV+ pts displayed a significant CD4 rise, HIV viremia reduction (p=0.0006; p<0.0001, respectively) and a decrease in activated CD38+CD8 (p<0.0001), with a trend to an increase in CD127+CD8 (p=0.07). By T12, both LPs and NLPs displayed a significant CD4 increase (LPs: p=0.0001; NLPs: p=0.001), with LPs maintaining significantly lower CD4 at T12 (p=0.0001). At T12, NLPs and LPs displayed a significant reduction in CD38+CD8+ (p=0.009; p=0.018, respectively); only NLPs displayed a decreasing trend in terminally-differentiated CD45R0+CD38+CD8 (p=0.077). Compared to LPs, NLPs featured higher CD127+CD4 proportions at all timepoints (T0, p=0.0001; T12, p=0.001), with a significant increase in CD127+CD8 by T12 (p=0.012), whereas no changes were seen in LPs. NLPs also displayed a significant rise in circulating IL-7 (p=0.049), whereas LPs showed a decreasing trend (p=0.074). At T0, NLPs showed higher levels of MT markers (LPS: p=0.01; sCD14: p=0.007). By T12, only NLPs displayed a significant reduction in LPS (p=0.022) and in sCD14 (p=0.005), whereas no changes were shown in LPs.

Conclusions

In HIV+ antiretroviral-naive pts with low CD4, LPV/r-containing regimens resulted in adequate immune reconstitution and restoration of the IL-7/IL-7R system. Interestingly, microbial translocation was efficiently controlled only in patients with less advanced HIV infection. However, LPV/r-based treatment resulted in a significant reduction of peripheral T-cell activation also in patients with late presentation. Given that T-cell activation is predictive of disease progression, our data advocate the efficacy of LPV/r regimens in broad immune reconstitution in HIV-infected pts with advanced infection.

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