

LBPEB021 - Poster Exhibition

TITLE

Administration of CC-11050, a phosphodiesterase 4 inhibitor, is well tolerated but does not significantly decrease immune activation in treated HIV+ persons

PRESENTER

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AUTHORS

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Background: Phosphodiesterase 4 inhibitors (PDE4i) are novel anti-inflammatory medications that block degradation of cAMP and decrease productions of inflammatory cytokines. Apremilast and roflumilast are PDE4i approved for treatment of psoriasis and COPD respectively. PDE4i are also being tested as host-directed therapy (HDT) in TB. In the current study, we examined the safety of CC-11050 in HIV+ people with suppressed viral load on ART and hypothesized that CC-11050 would also decrease inflammation.

Methods: Phase

1, placebo-controlled, double-blinded study to examine safety of CC-11050 administered over 12 weeks in HIV+ persons on ART for at least 1 year with plasma HIV viremia (VL) < 50 c/mL. Eligible patients were randomized 2:1 to CC-11050 200 mg BID or placebo. Plasma cytokines were measured at weeks 0, 2, 4, 8 and 12. Monocyte and T-cell activation profile was assessed by flow cytometry. For comparisons between time points T-test or Wilcoxon rank sum tests were used for comparison of continuous variables. To compare biomarker levels over all treatment time points, linear generalized estimating equations (GEE) were used. All analyses were performed in R.

Results: 45 persons were screened and 30 were randomized (19 active drug and 11 placebo) as planned, 20% of whom were women and 43% African American. The median age was 49.5 years (44-55), median BMI 26.8 and median Hemoglobin 13.5. 53% were on NNRTI and 47% on ISTI regimens. The median CD4 at baseline was 459 cells/ μ L and CD8 712 cells/ μ L. Most frequent AEs (grade 1 and 2 only) in active drug recipients were headache (8/19), diarrhea (5/19), cough (2/19), nasal congestion (2/19) and restlessness (2/19). There were no statistically significant changes in CD4 or CD8 T cell counts and no changes in VL. Efavirenz levels were not affected significantly. There were no significant differences between the two randomization groups in the average level over the treatment weeks, in the unadjusted or adjusted GEES models, for TNF-a, IL-6, IL-8, IL-10, IFN-g, sCD14, CRP, D-dimer.

Conclusions: Administration of CC-11050 in suppressed HIV-infected patients is well tolerated and can be co-administered with efavirenz, but at the studied dose has minimal effect on systemic inflammatory markers or immune activation.

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