



Poster H-1247

# Impact of Adding Maraviroc to HIV Patients with Undetectable Plasma RNA but are Non-CD4 Progressors (CD4~200 Cell/mm<sup>3</sup>)

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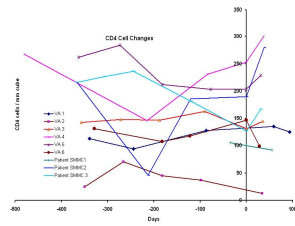
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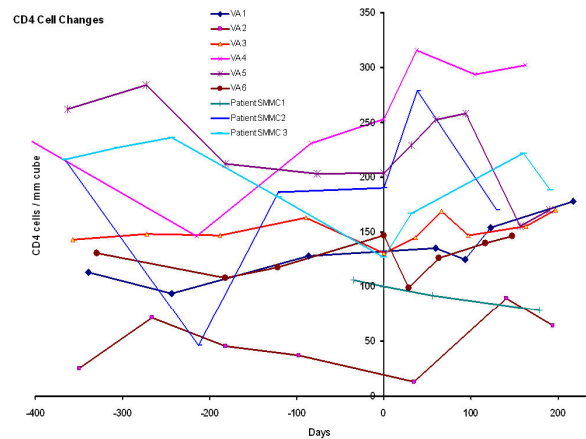
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## Abstract

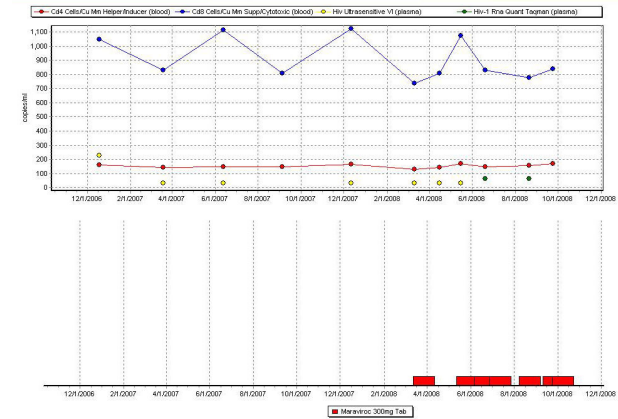
**Background:** There is a subpopulation of HIV-1 infected with apparent good viral suppression (<50 plasma RNA/ml over months to yrs) and yet, their CD4 counts do not increase with HAART. Recent MERIT studies showed that regardless of tropism of R5, X4 or dual/mixed, CD4 increased. Plasma endotoxin has been postulated to affect CD4 locally. There may be benefit of improving CD4 recovery in this subpopulation by adding Maraviroc to the current ART regimen. **Methods:** Pts with chronically low CD4 cells, with undetectable plasma HIV RNA, and requiring OI prophylaxis were offered Maraviroc to be added to their current HAART. Profile cannot be done due to plasma RNA of <50 copies/mL. In the VA pts plasma endotoxin levels were also obtained. **Results:** At 30-60 days of Maraviroc, the pts' plasma RNA remained <50 copies/mL. The CD4 cell changes were: +16, -29, -5, +112, -11, -20, -14, +130, -48. The average change from the avg CD4 of the last 365 days was 14 cells. When the 2 high +variants were excluded (+112,+130), average change was -16. **Conclusions:** In this limited subpopulation of 9 CD4 non-progressors, Maraviroc did not enhance CD4 recovery to the expected normal rate of +10 to +15 cells/month. Two pts with high variance in CD4 counts had higher recovery rates of +121,+130/month. Longer follow-up and endotoxemia data will be available at ICAAC



## Results CD4 Recovery



## A Typical Patient Profile



## Results/Discussion

A total of 6 patients from the VA and 3 from St Michaels Medical Center had Maraviroc added to their ART regimen and followed for a minimum of 150 days or 5 months. The CD4/mm<sup>3</sup> is shown in the left top panel (chart is an extension of results shown in original graph of Abstract). A comparison of CD4 levels before and on treatment has p>0.39 using t-test analysis.

Six of the VA patients had plasma samples measured for endotoxin levels. Only 4 patients had baseline plasma samples available. While 3 of the 6 patients have endotoxin levels trending down on treatment, a comparison of endotoxin levels before and on Maraviroc treatment showed a p value of >0.12. Maraviroc had little impact on endotoxin levels in our small population.

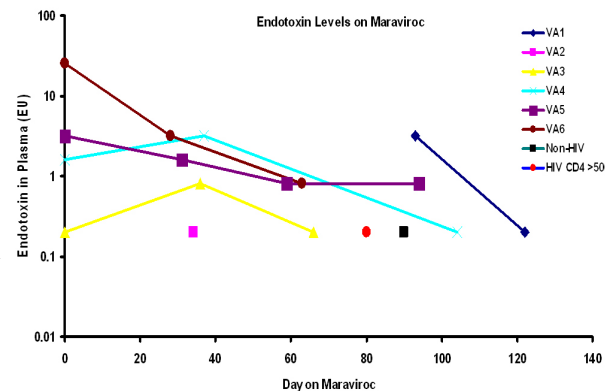
## Background

Maraviroc in naive patient trials was able to increase CD4 count in patients regardless of R5 virus or X4/mixed<sup>1,2,3</sup>. It may be able to protect the depletion of CD4 cells in HIV infected. CD4's are destroyed by gut derived endotoxin activation of these cells<sup>4</sup>. It is possible that HIV patients who have HIV controlled (viral load <50 c/mL) but non-recovering CD4s (<250 mm<sup>3</sup>) can benefit from Maraviroc. The presumed benefit being protection of CD4 cells from destruction by binding to the CCR5 receptors. We added Maraviroc to the treatment regimen of patients with these characteristics. The hope is that their CD4 counts would increase, representing immune recovery and eliminate the risk for opportunistic infections.

## Methods

HIV patients with viral suppression for at least a year to the level of <50 c/ml and little to no CD4 recovery (still <250/mm<sup>3</sup> and not increasing) had Maraviroc added to their treatment regimen. Profiles were not possible because of undetectable viremia. CD4 and viral loads were followed and extra plasma collected from the lab was frozen at -70°C for batched endotoxin assays. Plasma endotoxin determinations were done using the Sigma Chemical E-Toxate Kits. Plasma were diluted 1:10 and put in 75°C Water bath for 5 minutes. Endotoxin standards and heated samples were diluted 1:10 and then 1:2 serially before Limulus E-Toxate were added. The reaction tubes were incubated at 37°C before reading the last tube that was coagulated. Sample endotoxin levels were calculated from knowing the last dilution of the standard that coagulated vs. that of the unknown samples.

## Results Endotoxin



## Conclusions

1. Maraviroc does not appear to increase CD4 cell counts when added to patients with full viral suppression on ART but previous CD4 recovery. The observations were made in a small population of 9 patients followed for >5 months. (p>0.39)
2. In these patients with added Maraviroc, plasma endotoxemia levels had no significant reduction. (p>0.12) Trends in 3 patients appear promising. Perhaps a larger patient sample may be able to show a significant endotoxemia reduction.

## References

1. Gulick RM, Lalezari J, Goodrich J et al. Maraviroc for Previously treated patients with R5 HIV-1 Infection. N Engl J Med 2008; 359:1429-41.
2. Fätkenheuer G, Nelson M, Lazzarin A et al. Subgroup Analyses of Maraviroc in Previously Treated R5 HIV-1 Infection. N Engl J Med 2008; 1442-55.
3. Waters L, Mandalia S, Wildfire A, Randell P, Gazzard B, Moyle G. HIV co-receptor tropism in treatment-naïve patients: impact on CD4 decline and subsequent response to HAART. Presented at: 46th Interscience Conference on Antimicrobial Agents and Chemotherapy; September 27-30, 2006; San Francisco, Calif. Abstract H-1667.
4. Emmanouil Papisavvas, Maxwell Pistill, Aidan Hancock, Griffin Reynolds, Agnieszka Mackiewicz, Cecile Gallo, Jay, R Kostman, Karam Mounzer, Jane Shull, and Luis J Montaner. Lack of Effect of Short Viremic Episodes in LPS Plasma Levels in Chronically HIV-1-infected Subjects. CROI, 2008