



A Continuing Medical Education Activity
The 18th Conference on
Retroviruses and Opportunistic Infections (CROI):
Online Expert Poster Review and Discussion

Jointly sponsored by the Postgraduate Institute for Medicine and ViralEd, LLC

The Immunomodulatory Effects of Maraviroc Intensification among ART-suppressed Patients with Incomplete CD4 Recovery

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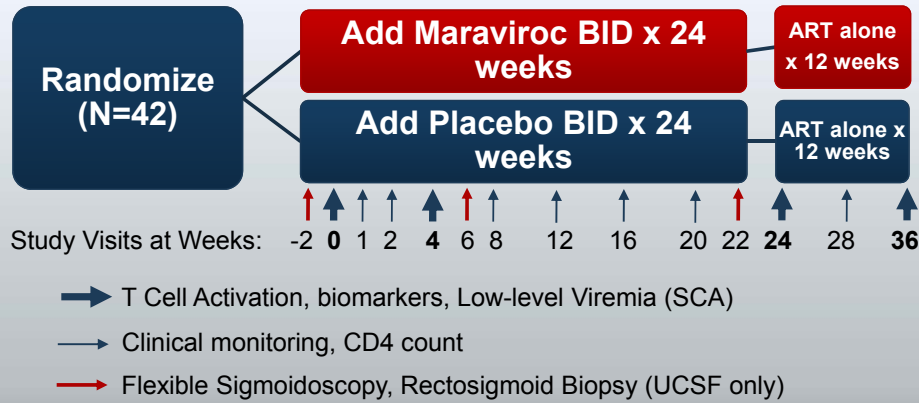
Hunt P, et al. 18th CROI; Boston, MA; February 27-March 2, 2011. Abst. 153LB.

Inclusion/Exclusion Criteria

- **Incomplete CD4 Recovery During Suppressive ART:**
 - Stable ART regimen > 1 year
 - All plasma HIV RNA levels <48 c/ml in last year
 - Detectable VL “blips” <500 c/ml in last yr OK if flanked by VLs <48 c/ml
 - All CD4 counts <350 cells/mm³ in last year
 - CD4 count gain <100 cells/mm³ in last year
 - >90% self-reported ARV adherence
- **Excluded for:**
 - Anticipating Δ in ARV of HBV/HCV Rx in next 6 months
 - Immunomodulatory/suppressive Rx in last 4 months
 - Serious illness past 3 months
 - ANC<1.0, plts <50, HgB<8, CrCl<40, AST/ALT>2.5x ULN
 - Pregnancy/Breastfeeding
 - Concurrent ddl+TDF use in ART regimen

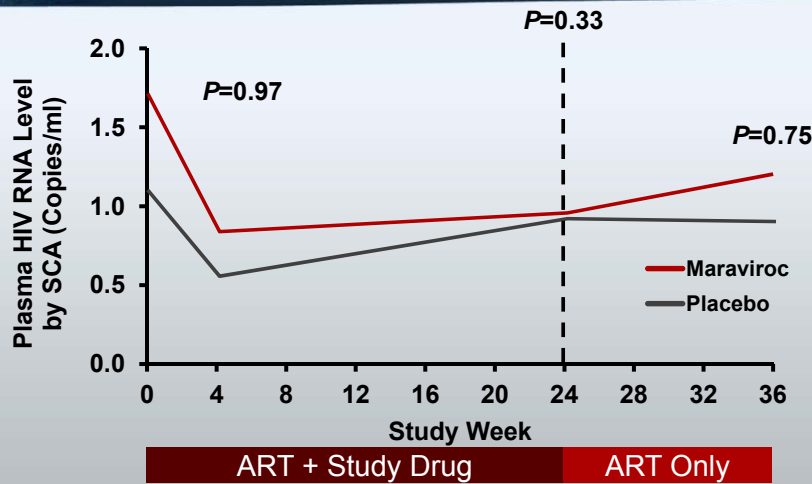
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Maraviroc Intensification Trial Schematic



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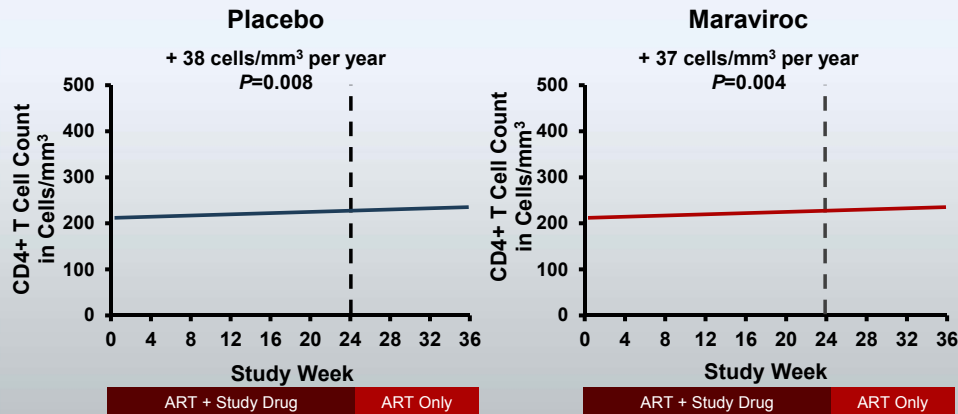
VL by Single Copy Assay Declines in Both Arms But no Difference between Groups



P values are for comparison of change from baseline between groups

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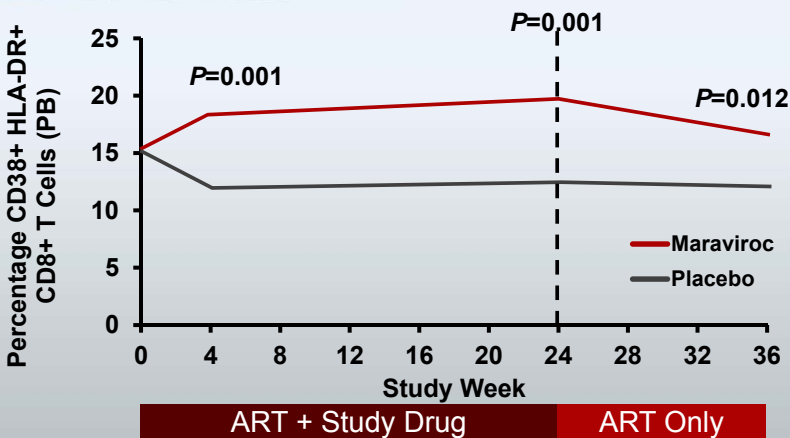
Similar CD4 Count Increase in Both Arms



No evidence for difference in the rate of CD4+ T cell recovery between arms, P=0.97

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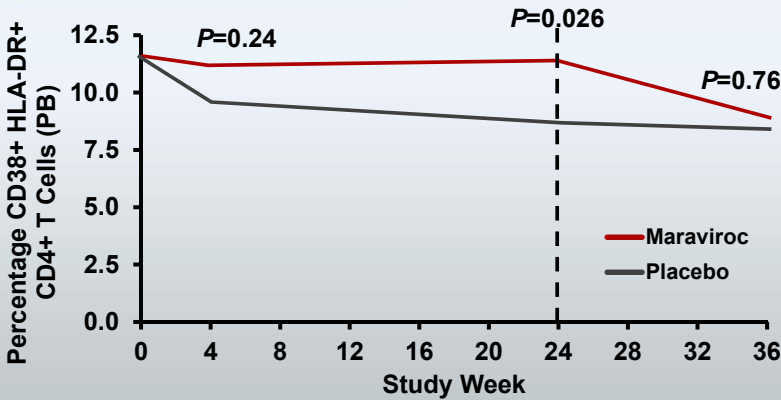
Maraviroc Increases CD8 Activation Compared to Placebo



P values represent difference between groups in the change from baseline at each time point.

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Maraviroc Prevents the Decline in CD4 Activation Compared to Placebo

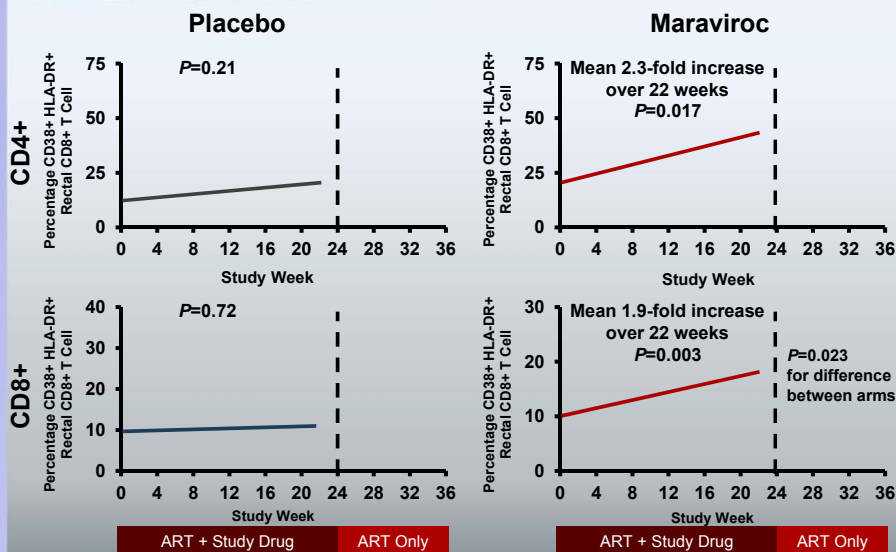


ART + Study Drug ART Only

P values represent difference between groups in the change from baseline at each time point.

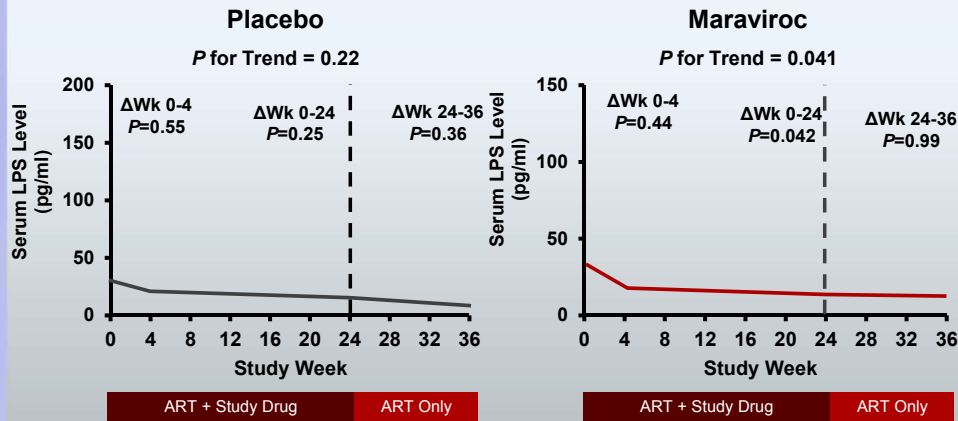
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But Maraviroc Intensification Results in a Nearly 2-fold Increase in Rectal T Cell Activation



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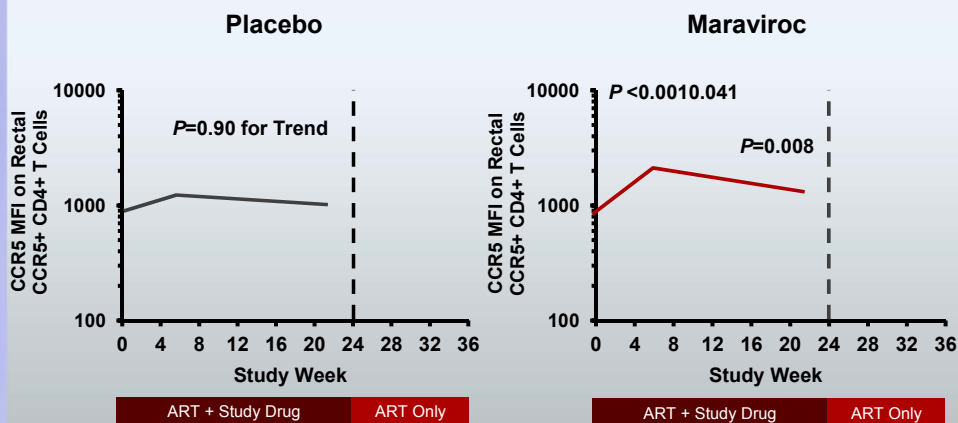
Plasma LPS Declines Significantly During Maraviroc Intensification



Difference between arms is not statistically significant, however

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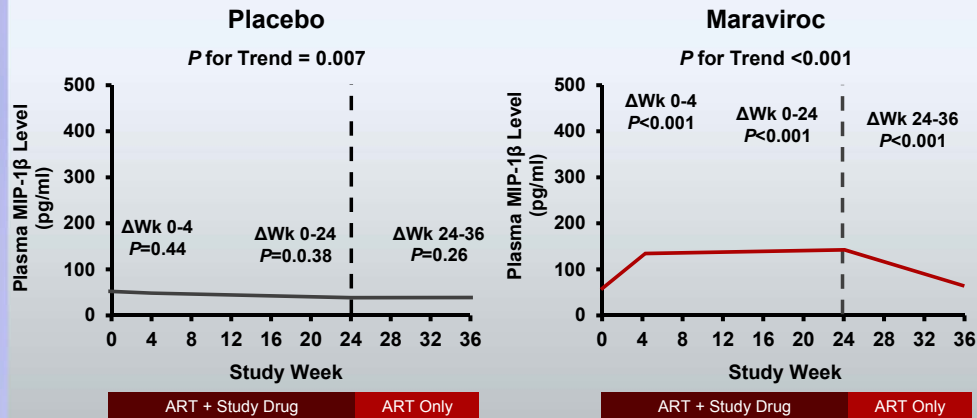
>2-fold Increase in CCR5 Expression (MFI) on Rectal CD4+ T cells During MVC Intensification



Similar trends observed on Rectal CD8+ T cells and B cells

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>2-fold Increase in Plasma MIP-1 β (CCR5 Ligand) Levels During Maraviroc Intensification



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Conclusions

Maraviroc intensification in HIV+ subjects with incomplete ART-mediated CD4 recovery:

- Causes a nearly 2-fold increase in T cell activation in GALT, and more modest increases in peripheral blood
- Appears to redistribute CD8+ T cells from lymphoid tissues into blood while having little effect on CD4 counts
- May decrease plasma LPS levels while increasing sCD14, compatible with enhanced macrophage-mediated clearance
- CCR5 ligand signaling through other chemokine receptors should be explored as a possible causal mechanism
- The clinical implications of these findings are unclear
 - CADIRIS, ANRS studies with clinical endpoints ongoing

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