Maraviroc (Selzentry)

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Maraviroc (*Selzentry*)

**Selzentry**

[sell-ZEN-tree]

300 mg

150 mg
ANTIRETROVIRAL THERAPY

CCR5 Receptor Antagonists
Host Cellular Receptors Involved in HIV Entry

HIV

CD4

Coreceptors

CCR5

CXCR4

Intracellular Space

Host Cell
CCR5 Tropic (R5) HIV-1

Intracellular Space
Host Cell

CD4

Coreceptors

CCR5

CXCR4

R5 HIV
CXCR4 Tropic (X4) HIV-1

X4 HIV

Intracellular Space
Host Cell

CD4

CCR5

CXCR4

CD4
Dual Tropic HIV-1

Intracellular Space

Host Cell

Coreceptors

CD4

Dual-Tropic HIV

CCR5

CXCR4
Mixed Tropic HIV-1

Mixed-Tropic HIV

R5 HIV

X4 HIV

CD4

Coreceptors

CCR5

CXCR4

Intracellular Space

Host Cell
Maraviroc: Mechanism of Action

R5-Tropic HIV

CCR5

Intracellular Space

Host Cell

R5-Tropic HIV

Maraviroc

CCR5 Receptor Conformation Change

Maraviroc: Mechanism of Action
Trofile Coreceptor Tropism Assay

Plasma

HIV RNA

Reverse Transcription

HIV DNA

PCR Amplification

HIV Genes

HIV Envelope Gene

Vector

Envelope Gene (inserted in vector)
HIV Coreceptor Tropism Assays (Trofile) Standard and DNA Tropism Assays

**Trofile Coreceptor Tropism Assay**
- Plasma
  - HIV
  - HIV RNA
  - HIV DNA
  - HIV Envelope Gene

**Trofile DNA Coreceptor Tropism Assay**
- Whole Blood
  - Cells
  - HIV DNA
  - HIV Envelope Gene
<table>
<thead>
<tr>
<th>Coreceptor Tropism</th>
<th>R5</th>
<th>X4</th>
<th>Dual Tropic</th>
<th>Mixed Tropic</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><img src="R5" alt="Image" /></td>
<td><img src="X4" alt="Image" /></td>
<td>![Image](Dual Tropic)</td>
<td>![Image](Mixed Tropic)</td>
</tr>
<tr>
<td>R5</td>
<td>X4</td>
<td>Dual/Mixed Tropic</td>
<td></td>
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<tr>
<td>----------</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Pure R5 Tropic HIV</td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Pure X4 Tropic HIV</td>
<td>Dual-Tropic HIV</td>
<td></td>
<td></td>
</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mixed-Tropic HIV</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
HIV Genotypic Coreceptor Tropism Assay

• Genotypic analysis of gp120 V3 loop sequences
• Commercially available through Quest Diagnostics
• If initial test shows X4 or R5/X4 then no further analysis
• If initial test shows only R5 then reflexes to Ultradeep sequencing
• Detection of 0.5% minority X4 clones with Ultradeep sequencing
• Result available in 7-10 days
• Proviral HIV genotypic tropism assay available (if HIV RNA < 1,000 copies/ml)

Source: Quest Diagnostics: http://education.questdiagnostics.com/faq/FAQ86
HIV Envelope

gp120

V3

Codon 11

Codon 25

# HHS Panel’s Recommendation for Co-receptor Tropism Assays

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>A co-receptor tropism assay should be performed whenever the use of a CCR5 co-receptor antagonist is being considered</td>
<td>AI</td>
</tr>
<tr>
<td>Co-receptor tropism testing is also recommended for patients who exhibit virologic failure on a CCR5 antagonist</td>
<td>BIII</td>
</tr>
<tr>
<td>A phenotypic assay is preferred to determine HIV-1 co-receptor usage</td>
<td>AI</td>
</tr>
<tr>
<td>A genotypic tropism assay should be considered as an alternative test to predict HIV-1 co-receptor usage</td>
<td>BII</td>
</tr>
<tr>
<td>A proviral DNA tropism assay can be utilized for patients with undetectable HIV-1 RNA when a CCR5 antagonist is considered in a new regimen (e.g., as part of a regimen switch or simplification)</td>
<td>BII</td>
</tr>
</tbody>
</table>

Source: HHS Antiretroviral Guidelines (October 25, 2018)
Maraviroc
Summary of Key Studies

• Trials in Treatment Naïve
  - MERIT: Maraviroc + ZDV-3TC versus Efavirenz + ZDV-3TC
  - A5303: [Maraviroc or Tenofovir DF] + DRV + RTV + FTC
  - A4001078: [Maraviroc or TDF-FTC] + Ritonavir-Boosted Atazanavir

• Trials in Acute HIV
  - OPTIPRIM-ARNS147: 5-Drug versus 3-Drug Regimen for Acute HIV

• Trials in Treatment Experienced
  - MOTIVATE 1 and MOTIVATE 2: Maraviroc [QD or BID] + OBR
  - A4001029: Maraviroc in Treatment-Experienced with non-R5 HIV
<table>
<thead>
<tr>
<th>Maraviroc Summary of Key Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>• <strong>Switch Trials</strong></td>
</tr>
<tr>
<td>- Study 121 (Strategy NNRTI): NNRTI Switch to EVG-COBI-TDF-FTC</td>
</tr>
<tr>
<td>- MARCH: Switch to of Maraviroc from RTV-Boosted PI</td>
</tr>
<tr>
<td>- ROCnROL (ARNS 157): Switch to 2-drug Maraviroc + Raltegravir</td>
</tr>
<tr>
<td>• <strong>Addition of Maraviroc to Increase CD4 Cell Count</strong></td>
</tr>
<tr>
<td>- ACTG 5256: Adding Maraviroc for Suboptimal CD4 Recovery</td>
</tr>
<tr>
<td>• <strong>PreExposure Prophylaxis</strong></td>
</tr>
<tr>
<td>- HPTN 069/ACTG 5305: Maraviroc +/- [TDF or FTC] for PrEP</td>
</tr>
</tbody>
</table>
INITIAL THERAPY

Maraviroc
Maraviroc versus Efavirenz in Treatment-Naïve
MERIT (A4001026) Trial
Maraviroc versus Efavirenz, both with Zidovudine-Lamivudine

**MERIT (A4001026): Study Design**

### Study Design: MERIT Study

- **Background**: Randomized, double-blind, double-dummy, phase 2b/3 study evaluating the efficacy and safety of maraviroc versus efavirenz as part of ART for treatment-naïve persons with HIV infection.

- **Inclusion Criteria (n = 721 treated)**
  - Age ≥16
  - Antiretroviral-naïve patients
  - R5-tropic virus
  - HIV RNA ≥2000 copies/mL
  - No resistance to zidovudine, lamivudine, or efavirenz

- **Treatment Arms**
  - Maraviroc 300 mg BID + ZVD-3TC BID
  - Efavirenz 600 mg QD + ZVD-3TC BID

**MERIT = Maraviroc versus Efavirenz in Treatment-Naive**

Maraviroc versus Efavirenz, both with Zidovudine-Lamivudine
MERIT (A4001026): Result

Week 48: Virologic Response (Primary Analysis)

Maraviroc or Efavirenz, both with Zidovudine-Lamivudine

MERIT (A4001026): Result

Week 48: Virologic Response (Post-hoc Reanalysis*)

![Bar chart showing virologic response at Week 48 for Maraviroc + ZVD-3TC and Efavirenz + ZVD-3TC.]

- **HIV RNA <50 copies/mL (%):**
  - Maraviroc + ZVD-3TC: 68.5% (213/311), 71.8% (127/177), 64.2% (86/134)
  - Efavirenz + ZVD-3TC: 68.3% (207/303), 72.1% (132/183), 62.5% (75/120)

*Excludes patients with non-R5 virus at screening by the enhanced Trofile assay

**Conclusions:** “Twice-daily maraviroc was not noninferior to efavirenz at <50 copies/mL in the primary analysis. However, 15% of patients would have been ineligible for inclusion by a more sensitive screening assay. Their retrospective exclusion resulted in similar response rates in both arms.”

Maraviroc versus Efavirenz, plus Zidovudine-Lamivudine MERIT (A4001026): Results

Week 240 (Year 5): Virologic Response

HIV RNA ≤50 copies/mL (%)

<table>
<thead>
<tr>
<th>Baseline HIV RNA</th>
<th>Maraviroc + ZVD-3TC</th>
<th>Efavirenz + ZVD-3TC</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>50.8</td>
<td>45.9</td>
</tr>
<tr>
<td>&lt;100,000 copies/mL</td>
<td>52.5</td>
<td>48.1</td>
</tr>
<tr>
<td>≥100,000 copies/mL</td>
<td>48.5</td>
<td>42.5</td>
</tr>
</tbody>
</table>


*Excludes patients with non-R5 virus at screening by the enhanced Trofile assay.
Conclusions: “Maraviroc maintained similar long-term antiviral efficacy to efavirenz over 5 years in treatment-naive patients with CCR5-tropic HIV-1. Maraviroc was generally well tolerated with no unexpected safety findings or evidence of long-term safety concerns.”

Effects of Maraviroc versus Tenofovir DF on Bone Loss

A5303 Trial
Study Design: A5303 Study

- **Background**: Phase 2b, prospective, double-blind, placebo-controlled study evaluating the effects of maraviroc versus tenofovir DF on bone loss in treatment-naïve persons with HIV

- **Inclusion Criteria (n = 262)**
  - Age ≥18 years
  - Antiretroviral-naïve patients
  - R-5 tropic virus
  - HIV RNA >1000 copies/mL

- **Treatment Arms**
  - MVC + DRV + RTV + FTC
  - TDF + DRV + RTV + FTC

*Dosing: Maraviroc 150 mg QD + Darunavir 800 mg QD + Ritonavir 100 mg QD + Emtricitabine 200 mg QD

*Dosing: Tenofovir 300 mg QD + Emtricitabine 200 mg QD + Darunavir 800 mg QD + Ritonavir 100 mg QD

Bone Effects of Maraviroc vs. Tenofovir DF, with DRV + RTV + FTC

A5303: Results

**Week 48: Changes in Bone Mineral Density from Baseline**

<table>
<thead>
<tr>
<th>Percentage Change (%)</th>
<th>MVC + DRV + RTV + FTC</th>
<th>TDF + DRV + RTV + FTC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Hip</strong></td>
<td>-1.51</td>
<td>-2.40</td>
</tr>
<tr>
<td><strong>Lumbar Spine</strong></td>
<td>-0.88</td>
<td>-2.35</td>
</tr>
</tbody>
</table>

Bone Effects of Maraviroc vs. Tenofovir DF, with DRV + RTV + FTC

A5303: Results

Week 48: Virologic Response

Conclusions: “Maraviroc was associated with less bone loss at the hip and lumbar spine compared with tenofovir DF. Maraviroc may be an option to attenuate ART-associated bone loss.”
Once-Daily Maraviroc in Treatment-Naïve
A4001078 Trial
Once-Daily Maraviroc plus Ritonavir-Boosted Atazanavir A4001078: Study Design

**Study Design: A4001078 Study**

- **Background**: Phase 2b, randomized, open label pilot study evaluating a once-daily, dual-therapy regimen of maraviroc and boosted atazanavir in comparison to standard triple therapy in HIV-infected treatment-naïve patients.

- **Inclusion Criteria (n = 121)**
  - Age ≥16 years
  - Antiretroviral-naïve patients
  - R-5 tropic virus
  - HIV RNA ≥1000 copies/mL
  - CD4 ≥100 cells/mm³

- **Treatment Arms** (all medications once daily)
  - Maraviroc 150 mg +
    Atazanavir 300 mg + Ritonavir 100 mg
  - Tenofovir DF-Emtricitabine +
    Atazanavir 300 mg + Ritonavir 100 mg
  - Maraviroc QD + Atazanavir + Ritonavir (n = 60)
  - Tenofovir DF-Emtricitabine + Atazanavir + Ritonavir (n = 61)

Once-Daily Maraviroc plus Ritonavir-Boosted Atazanavir A4001078: Results

Week 48: Virologic Response (Missing or Discontinued = Failure)

<table>
<thead>
<tr>
<th>Group</th>
<th>HIV RNA &lt;50 copies/ml (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>74.6</td>
</tr>
<tr>
<td>&gt;100K copies/mL</td>
<td>76.7</td>
</tr>
<tr>
<td>≥100K copies/mL</td>
<td>68.8</td>
</tr>
</tbody>
</table>

Conclusions: “The virological activity and immunological benefit of once-daily MVC + ATV/r were confirmed. Indirect hyperbilirubinemia and associated signs were the most commonly reported adverse effects in both study treatment groups and were not associated with significant transaminase increases. No drug resistance occurred.”

Intensive Five-Drug Regimen for Acute HIV Infection

OPTIPRIM-ANRS147
### Five Drug Therapy versus Standard Care for Acute HIV

**OPTIPRIM-ANRS 147 Trial: Study Design**

**Table:**

<table>
<thead>
<tr>
<th>Study Week</th>
<th>0</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Randomize</td>
<td>Analysis</td>
</tr>
</tbody>
</table>

**OPTIPRIM-ANRS: Study Features**
- Open-label
- Detectable HIV-RNA
- Incomplete Western blot (≤4 bands)
- p24 antigenemia
- Symptomatic OR CD4 <500 cells/mm³
- Primary endpoint: HIV-DNA copies per $10^6$ PBMC

**Five Drug Therapy**
- Maraviroc 150 mg BID +
- Raltegravir 400 mg BID +
- Emtricitabine/Tenofovir 300/200 mg +
- Darunavir/Ritonavir 800/100 mg
  (n = 47)

**Standard Therapy**
- Emtricitabine/Tenofovir 300/200 mg +
- Darunavir/Ritonavir 800/100 mg
  (n = 45)

Five Drug Therapy versus Standard Care for Acute HIV OPTIPRIM-ANRS 147 Trial: Results

HIV DNA Load at Month 24

Interpretation: “After 24 months, cART intensified with raltegravir and maraviroc did not have a greater effect on HIV blood reservoirs than did standard cART. These results should help to design future trials of treatments aiming to decrease the HIV reservoir in patients with primary HIV-1 infection.”
TREATMENT EXPERIENCED

Maraviroc
Maraviroc in Patients with Multiclass Drug Resistance

MOTIVATE 1 and 2 Trials
Maraviroc in Patients with Multiclass Drug Resistance

MOTIVATE 1 and 2: Study Design

Study Design: MOTIVATE 1 and 2

- **Background**: Parallel, randomized, double-blind, placebo-controlled, phase 3 trials to evaluate safety and efficacy of maraviroc in treatment-experienced patients

- **Inclusion Criteria** (n = 1049)
  - Age ≥ 16
  - Resistance to ≥ 3 ARV classes
  - R-5 tropic virus
  - On stable ARV regimen or no regimen for ≥ 4 weeks with HIV RNA ≥ 5000 copies/mL

- **Treatment Arms**
  - Maraviroc* once daily + OBT**
  - Maraviroc* twice daily + OBT**
  - Placebo + OBT**

*MOTIVATE = Maraviroc versus Optimized Therapy in Viremic Antiretroviral Treatment-Experienced Patients

- MVC once daily + OBT
  (n = 414)

- MVC twice daily + OBT
  (n = 426)

- Placebo + OBT
  (n = 200)

* MVC dose 300mg daily or BID with PI-containing regimens, 150mg daily or BID with all other regimens
** OBT = Optimized Background Therapy (investigator-selected, 3-6 agents).

Maraviroc in Patients with Multiclass Drug Resistance
MOTIVATE 1 and 2: Results

Week 48: Virologic Response (ITT, missing=nonresponse)

Maraviroc in Patients with Multiclass Drug Resistance
MOTIVATE 1 and 2: Results

Week 48: Change in CD4 Cell Count from Baseline

<table>
<thead>
<tr>
<th>Treatment</th>
<th>MOTIVATE 1</th>
<th>MOTIVATE 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>MVC once daily + OBT</td>
<td>113</td>
<td>122</td>
</tr>
<tr>
<td>MVC twice daily + OBT</td>
<td>122</td>
<td>128</td>
</tr>
<tr>
<td>Placebo + OBT</td>
<td>54</td>
<td>69</td>
</tr>
</tbody>
</table>

# Maraviroc in Patients with Multiclass Drug Resistance

## MOTIVATE 1 and 2: Result

### Grade 2-4 Adverse Events (all causes) Occurring in ≥ 5% of Patients (MOTIVATE 1 and MOTIVATE 2 Study Populations Combined)

<table>
<thead>
<tr>
<th>Event</th>
<th>Maraviroc once daily + OBT (n = 414)</th>
<th>Maraviroc twice daily + OBT (n = 426)</th>
<th>Placebo (n = 219)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>43 (10%)</td>
<td>32 (8%)</td>
<td>20 (10%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>13 (3%)</td>
<td>21 (4%)</td>
<td>13 (6%)</td>
</tr>
<tr>
<td>Fever</td>
<td>9 (2%)</td>
<td>24 (6%)</td>
<td>9 (4%)</td>
</tr>
<tr>
<td>Headache</td>
<td>22 (5%)</td>
<td>9 (2%)</td>
<td>12 (6%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>25 (6%)</td>
<td>25 (6%)</td>
<td>15 (7%)</td>
</tr>
<tr>
<td>Upper respiratory infection</td>
<td>16 (4%)</td>
<td>20 (5%)</td>
<td>3 (1%)</td>
</tr>
<tr>
<td>Death</td>
<td>6 (1%)</td>
<td>9 (2%)</td>
<td>2 (1%)</td>
</tr>
</tbody>
</table>

Conclusions: “Maraviroc, as compared with placebo, resulted in significantly greater suppression of HIV-1 and greater increases in CD4 cell counts at 48 weeks in previously treated patients with R5 HIV-1 who were receiving OBT.”
Maraviroc in Treatment-Experienced Patients with non-R5 HIV

A4001029 Trial
Maraviroc in Treatment-Experienced Patients with non-R5 HIV
A4001029: Study Design

Study Design: A4001029

- **Background**: Randomized, double-blind, placebo-controlled, phase 2b trials to evaluate safety and efficacy of maraviroc in treatment-experienced patients infected with non-R5 tropic HIV

- **Inclusion Criteria (n = 190)**
  - Resistance to ≥2 ARV classes, or ≥3 months of treatment ≥3 ARV classes
  - X4, dual, or mixed-tropic HIV

- **Treatment Arms**
  - Maraviroc 300 mg once daily + OBT*
  - Maraviroc 300 mg twice daily + OBT*
  - Placebo + OBT*

*OBT = Optimized Background Therapy (investigator selected, 3-6 agents). MVC dose reduced to 150 mg (daily or BID) in patients taking protease inhibitors (except tipranavir) or delavirdine.

Maraviroc in Treatment-Experienced Patients with non-R5 HIV A4001029: Results

Week 24: Virologic Response*

*Values for patients with missing data or who discontinued treatment imputed as 0

Maraviroc in Treatment-Experienced Patients with non-R5 HIV A4001029: Results

Week 24: Change in CD4 Cell Count from Baseline*

*Using last observation carried forward method

**Conclusions:** “In this exploratory study involving extensively treatment-experienced patients with advanced, non-R5 HIV-1 infection, neither superiority nor noninferiority was statistically demonstrated for either maraviroc dosage compared with placebo at 24 weeks of treatment.”

Adding Maraviroc to Suppressive ART for Suboptimal CD4 Recovery

ACTG 5256
Adding Maraviroc to Suppressive ART for Suboptimal CD4 Recovery
ACTG 5256: Study Design

Study Design: ACTG 5256

- **Background**: Single-arm, pilot trial of adding maraviroc to suppressive ART in setting of suboptimal CD4 recovery to evaluate whether maraviroc intensification is associated with an increase of at least 20 cells/mm³ in the CD4 count

- **Inclusion Criteria (n = 34)**
  - HIV-1 infected adults
  - Receiving stable ART with HIV RNA below limit of detection for at least 48 weeks
  - Stable but suboptimal CD4 recovery over previous year (<250 cells/mm³ and slope of annual change between -20 and 20 cells/mm³)
  - No prior exposure to a CCR5 antagonist

- **Single Treatment Arm**
  - Maraviroc added to ART for 24 weeks, then stopped and patient followed another 24 weeks

Adding Maraviroc to Suppressive ART for Suboptimal CD4 Recovery
ACTG 5256: Results

Change in CD4 Count with Maraviroc Intensification

*The median increase in CD4(+) T-cell count from baseline to week 24 was 12 cells/mm³.

Conclusions: “Adding maraviroc to suppressive ART for 24 weeks was not associated with an increase in CD4$^+$ T-cell counts of at least 20 cells/mm$^3$. Further studies of CCR5 antagonists in the dampening of immune activation associated with HIV infection are warranted.”

Switch from Boosted PI to Maraviroc with Suppressed HIV MARCH
Switch from Boosted PI to Maraviroc with Suppressed HIV

MARCH: Study Design

**Study Design: MARCH**

- **Background**: Randomized, multicenter, open-label switch study

- **Inclusion Criteria (n = 395)**
  - Adults with HIV-1
  - R5-tropic HIV
  - HIV RNA <200 copies/mL on stable (>24 weeks) 2 NRTI + boosted PI regimen
  - Non-pregnant, not breastfeeding, no hepatitis B coinfection, no past virologic failure or resistance mutations

- **Treatment Arms**
  - Maraviroc + 2 NRTIs
  - Maraviroc + Boosted PI + dual therapy
  - Continue current ART

Switch from Boosted PI to Maraviroc with Suppressed HIV MARCH: Results

Week 48 Results (Intention to Treat Analysis, ITT)

![Graph showing HIV RNA suppression results after 48 weeks for Maraviroc + 2 NRTIs, Maraviroc + RTV-Boosted PI, and Control groups.]

- Maraviroc + 2 NRTIs: 91.7%
- Maraviroc + RTV-Boosted PI: 77.7%
- Control: 95.1%

Conclusions: “These data support MVC as a switch option for ritonavir-boosted PIs when partnered with a 2-N(t)RTI backbone, but not as part of N(t)RTI-sparing regimens comprising MVC with PI/r.”
Maraviroc plus Raltegravir
ROCnROL (ANRS 157) Trial
### Study Design: ROCnRAL (ANRS 157)

**Background:** Pilot, phase II, single-arm trial to evaluate capacity of a dual regimen of raltegravir plus maraviroc to maintain viral suppression in virally suppressed HIV-infected patients with hyperlipidemia.

**Inclusion Criteria (n = 44)**
- Adults
- On ART for ≥5 years
- Naïve to integrase inhibitors and maraviroc
- HIV RNA <200 copies/mL ≥24 months
- HIV RNA <50 copies/mL for ≥12 months
- R5 tropism

**Treatment Arm**
- Raltegravir 400 mg BID + Maraviroc 300 mg BID

Maraviroc + Raltegravir
ROCnRal (ANRS 157): Result

Week 24 Virologic Response

Maraviroc + Raltegravir
ROCnRal (ANRS 157): Result

Analysis of Lipids on Dual Therapy (Median time = 19.4 weeks)

Maraviroc + Raltegravir
ROCNRal (ANRS 157): Result

Change in Bone Mineral Density from Baseline (Median interval: 26 wks)

Dual Therapy with Raltegravir plus Maraviroc in Patients Receiving Suppressive ART who have Lipohypertrophy ROCnRAL (ANRS 157): Result

<table>
<thead>
<tr>
<th>Patient</th>
<th>HIV RNA at Failure (copies/mL)</th>
<th>Integrate Resistance Mutations</th>
<th>Tropism at Failure</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2,973</td>
<td>None</td>
<td>CCR5</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1,453</td>
<td>Y143H</td>
<td>CXCR4</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>8,070</td>
<td>N155H</td>
<td>CXCR4</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>259</td>
<td>None</td>
<td>CCR5</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>2,820</td>
<td>F121Y</td>
<td>CCR5</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>2,820</td>
<td>F121Y</td>
<td>CCR5</td>
<td>HBV reactivation, AST/ALT &gt;20x ULN</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td>Cutaneous rash and diarrhea, possibly related to study drugs</td>
</tr>
</tbody>
</table>
Conclusions: “In long-term-experienced patients, maraviroc/raltegravir therapy lacks virological robustness despite a benefit in lipid profile and bone density.”

PREEXPOSURE PROPHYLAXIS

Maraviroc
Maraviroc +/- FTC or TDF for Preexposure Prophylaxis

HPTN 069/ACTG 5305
**Maraviroc +/- FTC or TDF for Preexposure Prophylaxis**

**HPTN 069/ACTG 5305: Study Design**

<table>
<thead>
<tr>
<th><strong>Study Design: HPTN 069/ACTG 5305</strong></th>
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<tbody>
<tr>
<td><strong>Background:</strong> Phase 2b, randomized, double-blind study of the safety and tolerability of maraviroc (alone or combined with FTC or TDF) for preexposure prophylaxis (PrEP), as compared to TDF-FTC, for at-risk men and transgender women</td>
</tr>
<tr>
<td><strong>Inclusion Criteria (n = 406)</strong></td>
</tr>
<tr>
<td>- Men and transgender women who have sex with men who self-reported condomless anal sex with at least one man within last 90 days</td>
</tr>
<tr>
<td>- Creatinine clearance $\geq$ 70 mL/min</td>
</tr>
<tr>
<td>- Negative HIV Ag/Ab and RNA</td>
</tr>
<tr>
<td>- Negative hepatitis B surface Ag</td>
</tr>
<tr>
<td>- No reported injection-drug use</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Maraviroc</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 101)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Maraviroc + Emtricitabine</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 106)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Maraviroc + Tenofovir DF</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 99)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Tenofovir DF-Emtricitabine</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 100)</td>
</tr>
</tbody>
</table>

### HPTN 069/ACTG 5305: Adverse Events (AE’s) at Week 48 ITT Analysis

<table>
<thead>
<tr>
<th></th>
<th>MVC (n = 101)</th>
<th>MVC + FTC (n = 106)</th>
<th>MVC + TDF (n = 99)</th>
<th>TDF-FTC (n = 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Permanent study drug</td>
<td>7 (7%)</td>
<td>9 (9%)</td>
<td>12 (12%)</td>
<td>8 (8%)</td>
</tr>
<tr>
<td>discontinuation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time to permanent</td>
<td>120 (74-263)</td>
<td>66 (42-222)</td>
<td>113 (42-260)</td>
<td>67 (34-141)</td>
</tr>
<tr>
<td>discontinuation, median days</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(IQR)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3-4 AE’s, # of</td>
<td>13, 15</td>
<td>11, 15</td>
<td>11, 14</td>
<td>20, 23</td>
</tr>
<tr>
<td>participants, # of events</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3-4 AE’s, adverse</td>
<td>0.17</td>
<td>0.16</td>
<td>0.17</td>
<td>0.19</td>
</tr>
<tr>
<td>event rate per person-year</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Number discontinuing and time to discontinuation did not differ among study regimens (P = .60). Rates of grade 3–4 adverse events did not differ among regimens (P = .37).

Maraviroc +/- FTC or TDF for Preexposure Prophylaxis
HPTN 069/ACTG 5305: Results

Week 48 Results (Intention to Treat Analysis, ITT)

### HIV Infections that Occurred During the HPTN 069/ACTG 5305 study

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>HIV Risk Group</th>
<th>Study Arm</th>
<th>1st Reactive HIV Test, Study Week</th>
<th>HIV RNA, copies/mL</th>
<th>HIV Tropism</th>
<th>Genotypic Drug Resistance</th>
<th>Study drug concentration at seroconversion visit, ng/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20</td>
<td>MSM</td>
<td>MVC + TDF</td>
<td>9</td>
<td>122,150</td>
<td>R5</td>
<td>None</td>
<td>MVC: 0, TFV: 0</td>
</tr>
<tr>
<td>2</td>
<td>61</td>
<td>MSM</td>
<td>MVC</td>
<td>16</td>
<td>981</td>
<td>R5</td>
<td>None</td>
<td>MVC: 145</td>
</tr>
<tr>
<td>3</td>
<td>21</td>
<td>MSM</td>
<td>MVC</td>
<td>28</td>
<td>106,240</td>
<td>R5</td>
<td>None</td>
<td>MVC: 0</td>
</tr>
<tr>
<td>4</td>
<td>35</td>
<td>MSM</td>
<td>MVC</td>
<td>38</td>
<td>13,626</td>
<td>R5</td>
<td>None</td>
<td>MVC: 6.7</td>
</tr>
<tr>
<td>5</td>
<td>36</td>
<td>MSM</td>
<td>MVC</td>
<td>48</td>
<td>52,191</td>
<td>R5</td>
<td>None</td>
<td>MVC: 0.7</td>
</tr>
</tbody>
</table>

Conclusions: “MVC-containing regimens were safe and well tolerated compared with TDF + FTC; this study was not powered for efficacy. Among those acquiring HIV infection, drug concentrations were absent, low, or variable. MVC-containing regimens may warrant further study for pre-exposure prophylaxis.”
Acknowledgment

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