

Testing for HIV Viral Tropism & Use of CCR5 coreceptor inhibitor Maraviroc

The expression of the chemokine co-receptors CCR5 or CXCR4 on a cell determines whether it can be infected with R5 or X4 using HIV viral strain respectively. Tropism refers to which co-receptor HIV uses to enter a CD4 cell. Dual-tropic viruses can use either CCR5 or CXCR4 co-receptors. Mixed-tropism refers to a viral population that contains both CCR5 or CXCR4 using viral strains. The current tropism assay cannot differentiate dual-tropic from mixed-tropic, thus the term “dual-mixed” (D/M) virus has emerged.

- R5-only virus usually predominates early in HIV disease (higher CD4 counts, slower disease progression) while X4 virus often marks more advanced disease. Whether this is a causal association or bystander phenomenon remains controversial.
- HIV tropism varies depending on antiretroviral exposure and likely reflects the more advanced disease stage of treatment experienced patients :
 - Antiretroviral-naïve: 80-90% R5-only virus, remainder D/M or X4
 - Antiretroviral treatment-experienced: 50-60% R5-only virus, remainder D/M or X4.
- Currently, only one test commercially available & CLIA-approved to test for HIV viral tropism, a phenotypic assay, **Trofile**, by Monogram Biosciences
 - Requires HIV RNA level of >1000 copies/mL
 - Turnaround time ~2-3 weeks (it is a sendout to Monogram via Mayo)
 - Not completely sensitive for minority variants:
 - Can detect X4 virus with 100% accuracy when X4 makes up $\geq 10\%$ of viral population
 - Detects X4 virus 83% of time when it makes up $\geq 5\%$ of viral population
 - Up to 10% of ARV-treatment experienced patients in clinical trials with initially R5 only virus had D/M on repeat testing 2 weeks later
 - How to order the test at Madison Clinic:
 - Write in “CCR5 assay or Trofile” on routing/order form
 - Assist RNs in completing Monogram form (asks for recent HIV RNA, CD4, provider signature)
 - For your patients with NO insurance, have case manager or Jean Aarvig assist in contacting Monogram to see if patient is eligible for assistance program
 - Test costs nearly \$2000

Maraviroc (MVC, *Selzentry*, Pfizer) is the first chemokine coreceptor antagonist to be FDA approved (August 2007). It is designed to prevent HIV infection of CD4 cells by blocking CCR5.

- MVC indicated for patients with:
 1. Detectable R5 virus only,
 2. Evidence of viral replication (HIV RNA >1000 copies/mL) and
 3. Resistance to multiple antiretroviral agents
- Use of MVC is not recommended in patients with D/M or X4 HIV-1, as efficacy not demonstrated in a phase II study in this patient group

- Safety and efficacy of MVC not established in treatment-naïve adult patients or pediatric patients