Use of a Commercial HIV Co-Receptor Tropism Assay in Clinical Practice

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Dear Editor:

THE ENTRY OF HIV-1 into target cells involves the sequential binding of the viral gp120 env protein to the CD4 receptor and a chemokine co-receptor, CCR5 (R5), CXCR4 (X4), or both (dual R5X4).¹ CCR5 is the major chemokine co-receptor used by HIV-1, and CCR5 antagonists can be used in the treatment of HIV-1 infection for patients harboring CCR5-tropic HIV strains.

Co-receptor tropism testing is necessary prior to prescribing CCR5 antagonists and plays an important role in the optimal selection of antiretroviral regimens for participants experiencing of virologic failure. A commonly used co-receptor tropism test (Trofile, Monogram Biosciences Inc.) costs \$1960 to perform. In research settings, co-receptor tropism testing has shown that approximately 80% of anti-retroviral-naïve patients and approximately 60% of anti-retroviral-experienced patients harbor the R5 virus, but there are little data documenting use of this assay in clinical practice.²⁻⁴

To examine the utilization of this important assay, a retrospective chart review was conducted among patients with a co-receptor tropism test ordered between March 16, 2009 (first date of enhanced co-receptor tropism availability) and February 14, 2012 at a New York City HIV outpatient clinic. Patients included in the study were at least 18 years old, known to be HIV-1-infected, and had co-receptor tropism testing ordered as an outpatient. We used a standardized data abstraction form to collect demographic information, HIV resistance data, drug allergies, CD4+ T-cell count, and plasma HIV-1 RNA levels within 2 months of tropism testing, and antiretroviral use pre- and post-co-receptor tropism testing. We excluded participants who had co-receptor tropism obtained as part of a clinical trial.

Tropism testing was ordered at the discretion of the provider and the first tropism test was used if multiple were ordered. The assay is a send-out test and is performed at Labcorp Monogram Biosciences (San Francisco, CA) with a turnaround time of approximately 20 days (from the day a sample is collected until the result is registered into our computer system). The study was approved by our Institutional Review Board (IRB).

The demographic details for the 75 unique patients who had co-receptor tropism testing obtained are described in Table 1. Of the 75 patients with co-receptor tropism results available, 49 were R5 (65.3%), 25 were dual-tropic/mixed infections (33.3%), and 1 was X4 (1.3%) (Table 2). Of the 49 patients harboring R5 virus, only 5 (10.2%) were prescribed a CCR5 antagonist within 2 months of the date the co-receptor tropism result became available. For the 44 patients with R5-tropic virus not prescribed maraviroc, patient non-adherence with the initial ARV regimen was the primary reason in 35 of 44 patients (79.5%), as documented by the provider. In other words, the currently prescribed antiretroviral regimen appeared to be active despite ongoing viremia suggesting sub-optimal adherence. A new ARV regimen was prescribed while the tropism assay was pending in 4 of 44 patients (9.1%).

During the study period, 9 patients (12.0%) had more than one tropism test, and 2 patients (2.7%) had three tests (a total of 88 tropism tests were performed during the study period). Repeat tropism testing was performed while the original test was pending or had already been resulted into our computer system and was never acknowledged by the provider. In every case, redundant testing was performed within 18 months of the original tropism test and did not result in addition of maraviroc to the antiretroviral regimen.

We found a higher proportion of antiretroviral-experienced patients with R5-virus than has been previously reported, yet few of these patients were ultimately treated with an CCR5 antagonist. According to the United States Department of Health and Human Services (DHHS) guidelines, maraviroc is an important component of HIV management in the setting of virologic failure.⁵ HIV-1 co-receptor tropism is a necessary tool for determining eligibility for CCR5 antagonist therapy and is predictive of HIV-1 disease progression.⁶ Tropism testing was frequently ordered at the same time as genotype testing for suspected or confirmed virologic failure. Follow-up visits indicated poor adherence rather than emergent antiretroviral resistance as the cause of virologic failure. The cost of tropism testing was significant in this study (\$172,480) as 88 tests were performed on 75 unique patients, resulting in maraviroc initiation in 5 patients within 2 months of testing.

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TABLE 1. PATIENT DEMOGRAPHICS OF 75 PATIENTS AT A MANHATTAN HIV CLINIC AT TIME OF FIRST TROPISM TESTING FROM YEAR TO YEAR

	N = 75
Age, years (median, range)	48 (19–70)
Male gender, <i>n</i> (%)	44 (58.7%)
Absolute CD4 count, cells/mm ³ (median, IQR) ^a	229 (121–409)
Plasma HIV-1 RNA, copies/ml (median, IQR) ^a	34,623 (1548–58,890)
Duration of HIV, years (median, range) ^a	16 (2–30)
Resistance at time of Trofile testing, <i>n</i> (%) ^a	
NRTI	41 (54.7%)
M184V	34 (45.3%)
Other	28 (37.3%)
NNRTI	36 (48.0%)
PI	15 (20.0%)
Darunavir	7 (9.3%)
Major	15 (20.0%)
INI	3 (4.0%)
ARV allergy/side effect, <i>n</i> (%) ^b	11 (14.7%)
ARV regimen, <i>n</i> (%) ^a	
Not on ARVs	23 (30.7%)
PI-based	41 (54.7%)
NNRTI-based	8 (10.7%)
INI-based	3 (4.0%)
Number of HIV genotype tests sent at the same times as the tropism testing, <i>n</i> (%) ^a	70 (93.3%)

^aThese labs were drawn within 2 weeks before or after the tropism testing.

^bAbacavir, atazanavir, stavudine, indinavir, efavirenz.

TABLE 2. TROPISM ASSAY RESULTS AMONG 75 PATIENTS AT A MANHATTAN HIV CLINIC EVALUATED FOR VIROLOGIC FAILURE FROM 2009 TO 2012

Tropism result, <i>n</i> (%)	
R5 virus	49 (65.3%)
D/M virus	25 (33.3%)
X4 virus	1 (1.3%)
Impact of R5 tropism on HAART SNM regimen, <i>n</i> (%)	49
Yes, changed with addition of MRV	5 (10.2%)
Yes, changed without addition of MRV	21 (42.9%)
No change	23 (46.9%)
Chart review of why MRV not used among 44 patients with R5 virus, <i>n</i> (%)	
Poor adherence with current regimen	35 (79.5%)
New regimen started while tropism result pending	4 (9.1%)
Tropism result not acknowledged	1 (2.3%)
No reason given but setting in which tropism sent:	
acute HIV	1 (2.3%)
transfer of care	2 (4.5%)
renal failure	1 (2.3%)

This study has several limitations. In some cases, the prescribing physician never acknowledged the co-receptor tropism test result, making an interpretation of ordering practices difficult. In other cases, the physician may have obtained the tropism testing as a baseline test result in the event that the patient went on to experience virologic failure, although this is not recommended as a standard practice.

In summary, our data suggest suboptimal adherence without the emergence of resistance as the primary reason for virologic failure in patients for whom co-receptor tropism testing was obtained. We suggest that, for patients failing their antiretroviral regimen, an HIV genotype should first be obtained by the provider with reflex to co-receptor tropism if need for new ART regimen has been documented. This alternative approach could save both the patient and provider the time and resources associated with unnecessary testing.

Author Disclosure Statement

Dr. Genzen serves as Medical Director of the Automated Core Laboratory at ARUP Laboratories. Dr. Wilkin has received travel support from GSK/ViiV to attend a study investigator's meeting. Drs. McCarthy and Singh report no disclosures.

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