

HIV-1 Phenoscript™

Phenotyping for resistance

Overview

Phenotyping is a procedure which measures the susceptibility of a patient's virus to antiretroviral drugs *in vitro* compared to a control virus. Phenotyping can be used to test for resistance in a patient undergoing therapy or on treatment-naïve patients to select the optimal therapeutic regime and avoid prescribing drugs to which the patient's virus may be resistant.

Specialty's Phenoscript™ gives a rapid (~8-15 day turnaround time) assessment of an individual's likelihood to respond to any of fifteen FDA-approved drugs, based on a comparison between the ability of a drug to inhibit the replication of that individual's virus compared to a control virus. The difference in viral replication between the patient's virus and the reference virus in the presence of drugs is expressed as a ratio called the **Patient Resistance Index (PRI)**. The results of the testing are reported out as an **Estimated Contribution to Response (ECR)** in an easy-to-read, color-coded report, and describes the likelihood of the patient responding to the drug as either "Likely", "Possible" or "Unlikely", based on an assessment of the RI, compared to a cut-off value.

Phenoscript™ utilizes recombinant virus technology reporting the degree of drug susceptibility of the patient's

virus compared to a wild-type reference virus. In two independent studies presented at the 5th International Workshop on HIV Drug Resistance and Treatment Strategies 2001, Phenoscript™ showed good overall correlation with both Virco's Antivirogram[?] and ViroLogic's PhenoSense™^{1,2}. Since the Phenoscript™ assay is based on a single cycle of viral replication, there is no risk that the virus population will change during the assay, which can occur during the longer term viral replication used by some other phenotypic assays. The Phenoscript™ assay yields a virus population that is not affected by the potential bias implicit in ligation and amplification of pooled clones used by some other tests.

Specialty's Phenoscript™ assay has nine drugs with ECRs based on clinical cut-offs, the most of any company performing this test. The clinical cut-off represents the correlation between actual patient virologic response and phenotypic susceptibility to various drugs or the drug susceptibility level at which a patient's probability of treatment failure with a particular drug significantly increases. The use of clinical cut-offs provides a more accurate estimation of the potential contribution of any one drug to the response of a multiple-drug therapy.

Clinical Utility & Reimbursement

- ?? Assesses likelihood of response to drugs in treatment-naïve or treatment-experienced patients
- ?? Helps optimize treatment regimes in patients with complex mutation patterns as determined by genotyping
- ?? Electronic interfacing capability for rapid resulting and decreased turnaround time
- ?? Favorable reimbursement in most States (for details visit <http://www.idsociety.org/HIV/CEN/resistance11700.htm>)

Ordering Information & Specimen Requirements

Test Code	Test Name	Specimen Requirements	Turnaround Time
7420	HIV-1 Phenoscript™	Primary: 4 (2) mL Plasma EDTA; FROZEN. Alternates: 4 (2) mL Plasma ACD; FROZEN. OR 4 (2) mL Plasma EDTA in PPT Tube; Ship FROZEN on dry ice.	8-15 days

Methodology

RT-PCR, Recombinant Culture

Related Tests

9874 HIV-1 RNA UltraQuant[®]

9878 HIV-1 RNA UltraQuant[®] Reflex to HIV-1 Phenoscript[™]

7480 HIV-1 GenotypR[™] PLUS

9885 HIV-1 DNA DetectR[™]


5732 HIV-1 Proviral DNA AccuQuant[®]

HIV Drug MonitR[™]s (Therapeutic drug monitoring of most FDA-approved drugs; see directory for test codes)

References

1. Dam E, et al. Comparison of HIV-1 resistance phenotypes obtained by two different assay systems. Presented at 5th International Workshop on HIV Drug Resistance and Treatment Strategies, June 4-8, 2001; Scottsdale, Arizona.
2. Miller V, et al (EuroGuidelines Group). Comparison of HIV-1 drug susceptibility (phenotype) results reported by three major laboratories. Presented at 5th International Workshop on HIV Drug Resistance and Treatment Strategies, June 4-8, 2001; Scottsdale, Arizona.

Sample Report



SPECIALTY LABORATORIES
2211 Michigan Avenue Fax 310-828-6634
Santa Monica, CA 90404-3900 800-421-7110

Patient:

Sex: _____ Age: _____

Birth Date: _____

Patient ID: _____

Physician: _____

Collection Date: _____

Account Number	Accession Number
Date Received	Date Printed

7420 · HIV-1 Phenoscript[™]

Generic Name	Trade Name	Technical Cut-Off	Clinical Cut-Off	Patient Resistance Index	Estimated Contribution to Response
Nucleoside RT Inhibitors					
AZT Zidovudine	Retrovir [®]	3.5	4.5 *	2.0	Likely
3TC Lamivudine	Epivir [®]	3.0	5.5 *	4.1	Possible
ddI Didanosine	Videx [®]	2.0	2.5	12.3	Unlikely
ddC Zalcitabine	Hivid [®]	3.5	3.5 *	4.0	Unlikely
dHT Stavudine	Zerit [®]	3.0	3.0	> 15.0	Unlikely
Abacavir	Ziagen [®]	2.5	8.0	14.0	Unlikely
Tenofovir	Viread [™]	2.5	4.0	3.3	Possible
Non-nucleoside RT Inhibitors					
Nevirapine	Viramune [®]	2.0	6.5 *	1.1	Likely
Delavirdine	Rescriptor [®]	2.5	10.0 *	3.0	Possible
Efavirenz	Sustiva [®]	2.0	5.0	2.4	Possible
Protease Inhibitors					
Indinavir	Crixivan [®]	2.5	20.0	1.1	Likely
Ritonavir	Norvir [®]		**		**
Saquinavir	Fortovase [®]	2.5	11.0	11.0	Unlikely
Nelfinavir	Viracept [®]	2.5	3.0 *	3.2	Unlikely
Lopinavir+Ritonavir	Kaletra [™]	2.5	10.0	8.4	Possible
Amprenavir	Agenerase [®]	2.5	7	4.8	Possible

Remarks

Comments

Technical Cut-Off: Based on the reproducibility of the assay at a 50% CI.

Clinical Cut-Off: Based on the correlation between phenotype and serological responses.

***Treatment-Naive Range (TNR):** Upper limit of the range of drug susceptibilities seen for the virus from a panel of treatment-naive subjects, used if clinical cut-off unavailable.

****:** Ritonavir is no longer prescribed for its own antiviral activity, but as a pharmacological enhancer for the other PIs.

Patient Resistance Index: The fold-difference in drug susceptibility between the tested virus and the drug-sensitive control virus tested in parallel.

Est. Contribution to Response: Likelihood that this drug will be effective as based on the patient resistance index value.

Likely: Values below the technical cut-off indicate that the tested virus is not different from the drug-sensitive control virus.

Possible: Values at or above the technical cut-off and below the clinical cut-off (or within TNR) indicate the drug may retain clinical activity despite depressed susceptibility.

Unlikely: Values at or above the clinical cut-off (or outside the TNR) indicate that no contribution to clinical response is expected from the tested drug.

This test or one or more of its components was developed and its performance characteristics determined by Specialty Laboratories. It has not been determined or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes. It should not be regarded as investigational or for research. This laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high complexity clinical laboratory testing.

3L-RT-7420-08-7420Phenoscript v. 1.04/10/2008

For complete information on this or other related HIV tests, please visit our Web site at www.specialtylabs.com and sign-up for our e-mail notification program or call Client Services at 800-421-4449.