

How are you tomorrow?™

HIV Pharmacogenetics Report: HLA-B*5701

PATIENT AND SAMPLE DETAILS

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|------------------|------------|---------------|------------|
| Patient ID | 00000 | Date of Birth | 01/01/1960 |
| Patient Initials | | Lab21 ID | 00000 |
| Sample ID | 00000 | Sample Date | 03/01/2011 |
| Sample received | 04/01/2011 | Report Date | 08/01/2011 |

CLINIC DETAILS

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|----------|--------------|-----------|--------------|
| Clinic | DD00000 | Town | Imaginary |
| Hospital | HIV Hospital | Physician | Dr Physician |

HLA-B*5701 status **Negative**

Authorised: Lab Director

Date: 08/01/2011

NOTES

Guidelines for the treatment of HIV-infected adults with antiretroviral therapy recommend HLA-B*5701 testing to identify patients with a lower risk of developing abacavir hypersensitivity^{1, 2}. A high negative predictive value of HLA-B*5701 has been shown³, but has not been fully evaluated in different patient populations, including patients in the UK.

Absence of B*5701 in a patient does not exclude hypersensitivity or other adverse reactions to abacavir. The decision to provide abacavir is made on clinical judgement based on risk versus benefit. Clinicians are advised to follow the manufacturer's recommendations regarding patient monitoring and the identification and management of suspected hypersensitivity when prescribing abacavir.

Molecular genetic test results are often extremely complex since they impart a probabilistic risk of disease rather than an objective positive/negative or quantitative answer. Physicians and counsellors may require guidance to convey such subtle and emotionally charged information to patients in an understandable manner. In order to derive the most meaningful benefit from this testing, it is recommended that the results and subsequent options from these complex genetic tests be discussed with patients by a trained genetics professional.

The HLA-B*5701 gene is a member of the Human Leukocyte Antigen family of genes otherwise known as the Major Histocompatibility Complex (MHC). The HLA-B*5701 family consists of at least 20 closely related genes, and the product of the *5701 gene has been associated with abacavir hypersensitivity (1, 3). Approximately 5-8% of the Caucasian population express the *5701 antigens but the incidence is rarer in other ethnic groups, for example it is found in less than 2% of people of African origin (3).

DNA is extracted from blood and is tested for the presence or absence of HLA-B*57 gene family. The overall test is a proprietary method using Analyte Specific Reagents (ASP) performed using the Polymerase Chain Reaction (PCR). At least two different PCR tests specific for B*5701 are used. As an internal control, DNA is tested at the same time for gene sequences present in everybody, so that a negative result for *57 like sequences is always accompanied by a positive result for the other genes. PCR fragments are detected using Agarose Gel Electrophoresis and a fluorescent dye that shows the presence of DNA under UV light. No HLA-B specific fragment, or DNA band, is seen if there is no *57 gene member present in the sample. At this stage negative results will be reported. Any suspect positive for the *57 family is then re-tested using DNA sequence based typing techniques (This service is performed by **Qiagen Genomic Services, Sequencing Services, Max Vomer Str-4, Hilden, Germany, D-40724**). The sequence is compared at 12 different points to either confirm the presence of B*5701 or to exclude genes that are not associated with hypersensitivity (e.g. HLA-B*5702 or *5703). Sequence data from our experiments and from external laboratories clearly show that this produces only the PCR fragments we expect from the known sequence of the gene. Our test predicts the presence of B*5701, B*5708 and B*5710 (The last two family members are rare and there is not yet significant data as to whether these antigens are not included in hypersensitivity reactions).

References

1. British HIV Association guidelines for the treatment of HIV-1-infected adults with antiretroviral therapy 2008. HIV Med. 2008, 9: 563-608
2. Guidelines for the Clinical Management and Treatment of HIV Infected Adults in Europe. European AIDS Clinical Society (EACS), Madrid, 2007.
3. S Mallal et al. HLA-B*5701 Screening for Hypersensitivity to Abacavir. The New England Journal of Medicine, 2008; 358: 568-579.

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