

How predictive of abacavir hypersensitivity (HSR) is the HLA-B*5701 test?

The largest study of the HLA-B*5701 test to date, the PREDICT-1 study (funded by abacavir manufacturer GlaxoSmithKline) recruited 1956 abacavir-naive subjects from 314 centres in Europe and Australia. Patients were randomised to start an abacavir regimen under the standard of care (clinically diagnosed hypersensitivity) or to start abacavir with the standard of care plus HLA-B*5701 screening. In the second group, anyone with a positive HLA-B*5701 test got excluded, whilst those with a negative test continued.

The results of this randomised, double-blind trial showed that only 27 of 803 people (3.4%) in the HLA-B*5701-screened group had a clinically suspected reaction and 66 of 847 (7.8%) in the control group had clinically suspected hypersensitivity, meaning that screening cut the risk of a clinically suspected reaction 60% ($P < 0.0001$). For immunologically confirmed hypersensitivity, HLA-B*5701 had a negative predictive value of 100%, and for clinically suspected hypersensitivity, the gene test had a negative predictive value of 96%. To date, several studies have reported an association between HLA-B*5701 positivity and abacavir hypersensitivity. The HLA-B*5701 test is practically more useful for its negative predictive value; i.e. used to rule out patients (who are HLA-B*5701 positive) from receiving abacavir. Note, however, that HLA-B*5701 negativity does not rule out the possibility of abacavir hypersensitivity.

Can the HLA-B*5701 test be used to screen to prevent abacavir HSR?

The authors of PREDICT-1 suggest that their study "provides the high level of evidence required to support the implementation of HLA-B*5701 screening into routine clinical practice."

The researchers concluded that "The results from this landmark study demonstrate that prospective HLA-B*5701 screening results in a dramatic, clinically relevant and statistically significant reduction in abacavir hypersensitivity reactions."

HLA-B*5701 screening may augment clinical management of hypersensitivity but must never substitute for clinical vigilance. It is crucial that patients starting abacavir are warned of hypersensitivity and other side effects, and vigilance is maintained in accordance with the manufacturer's recommendations in the Summary of Product Characteristics. This includes advice that patients are monitored closely, particularly during the first eight weeks, with consultation every two weeks during this period.

Can the HLA-B*5701 test be used to predict other abacavir toxicities, or hypersensitivity reactions to other drugs?

No. HLA-B*5701 has not been found to have any predictive value for other adverse reactions to abacavir, or for other anti-retroviral toxicities.

Can HLA-B*5701 be used to confirm abacavir hypersensitivity reactions?

No. Abacavir hypersensitivity may overlap with other clinical syndromes and it is possible that HLA-B*5701 testing may be used by some clinicians to confirm whether patients, who have in the past developed a clinical syndrome of uncertain aetiology, did indeed have symptoms attributable to abacavir hypersensitivity. Whilst an HLA-B*5701 positive test result in this context might be taken to indicate a greater likelihood of abacavir hypersensitivity, a negative HLA-B*5701 test does not exclude abacavir hypersensitivity, **and the patient should not be re-challenged with abacavir.**

Please note: retrospective use of HLA-B*5701 to diagnose abacavir hypersensitivity in this manner has not been validated in clinical trials.

I have a large African patient cohort. How applicable is the PREDICT-1 data to this group of patients?

It had been suggested that the association between HLA-B*5701 genotype and abacavir HSR was weaker in individuals of African origin. The SHAPE trial was a GSK-sponsored retrospective case-control study designed to evaluate the sensitivity and specificity of HLA-B*5701 in White and African Americans.

The authors of the study concluded that: "Similar results seen in Blacks imply that screening for HLA-B*5701 is a broadly generalisable approach for reducing abacavir HSR rates."

When should I use the HLA-B*5701 test?

The authors of the study conclude: "The PREDICT-1 study provides the high level of evidence required to support the implementation of HLA-B*5701 screening into routine clinical practice and is the first randomised, blinded and powered study to validate pharmacogenetic screening as a clinical tool to personalise therapy."

Where can I obtain information on the science and technology of HLA testing?

Please download our scientific FAQs at:

www.delphicdiagnostics.com/pdf/EU_PGx_5701_EU_SCI_FAQ.pdf

How can I obtain this test?

Delphic has operated a routine clinical service for HLA-B*5701 testing since 2005. Our laboratory is certified to ISO 9001:2000. Our turnaround time is 7 days from receipt of sample as our UK laboratory. The cost is €90 per sample. Whole blood samples can be stored and shipped at ambient temperature enabling weekly shipments. For details on how to set up an account and for full Sample-handling Instructions go to www.delphicdiagnostics.com/products/pharmacogenetics/5701eu/index.php. Alternatively, please contact us (below) and we will be able to set-up an account and receive samples immediately.

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References

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