Personalized Medicine Corner

HLA-B pharmacogenetics and carbamazepine: Who, when, and how to test

The anti-seizure agent carbamazepine (*Tegretol*, *Equetro*, others) has been strongly associated with potentially fatal adverse skin reactions including toxic epidermal necrolysis (TEN) and Stevens-Johnson Syndrome (SJS). The risk of serious dermatologic reactions with carbamazepine is linked to the presence of a variant of the *HLA-B* gene.

What is the HLA-B gene?

Human leukocyte antigen B (HLA-B) is a gene that encodes a cell surface protein involved in presenting antigens to the immune system.[1] In some cases and with certain medications, this presenting process triggers an inappropriate immune reaction and leads to serious dermatologic adverse events. In individuals who are primarily Caucasian, these reactions occur in about 1 to 6 per 10,000 people. But this risk is increased 10-fold in patients predisposed to carry the at-risk genetic variant, *HLA-B*15:02*, predominantly patients of Han Chinese ancestry and those from India and Southeast Asia.[1-3]

Who should I test?

The FDA recommends *HLA-B*15:02* testing before initiating carbamazepine in patients with ancestry in at-risk populations.[4] Clinical guidelines define at-risk populations as those of Han Chinese descent, followed by those with ancestry in Vietnam, Cambodia, the Réunion Islands, Thailand, India (specifically Hindus), Indonesia, Malaysia, and Hong Kong.[1] While the frequency of *HLA-B*15:02* is low in other populations, patients may be unaware of or fail to disclose a relevant ancestry. Patients are considered *HLA-B*15:02*-positive if they have one or more copies of this allele, while patients who test negative have no copies present.

*How do I order an HLA-B*1502 test?*

Several commercial laboratories offer the *HLA-B*15:02* test, including Pathway Genomics and ApolloGen Inc. Find additional information about commercially available tests through the National Institutes of Health Genetic Testing Registry (https://www.ncbi.nlm.nih.gov/gtr/).

*What should I do if the patient is HLA-B*1502 positive?*

Because SJS and TEN usually manifest in the first three months of therapy, providers can cautiously consider continued use of carbamazepine in patients who have taken it for more than 3 months with no cutaneous adverse reactions.[1] Carbamazepine-naïve patients who test positive for *HLA-B*15:02* should not be started on carbamazepine. Phenytoin and fosphenytoin should also be avoided in phenytoin-naïve *HLA-B*15:02*-positive individuals because this variant has also been linked to adverse events with phenytoin use.[5]

References:

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