



Genetic testing to avoid allopurinol hypersensitivity

Bulletin for Prescribers | September 2019

HLA testing can identify individuals at high genetic risk of developing a severe cutaneous adverse reaction to allopurinol.

Allopurinol has a long-established role in the management of hyperuricaemia and gout. However, allopurinol can also cause a hypersensitivity reaction that varies in severity from a mild rash to a severe cutaneous adverse reaction (SCAR), which includes Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) and systemic eosinophilia.¹ SCAR typically occurs with two months of commencing treatment with allopurinol. The incidence of SCAR is between 1:250 and 1:1,000 in patients commencing therapy with allopurinol.² The mortality rate is up to 25%. Clinical Pharmacogenetics Implementation Consortium (CPIC) has summarised the evidence from the published literature and developed peer-reviewed guidelines for allopurinol use based on HLA-B genotype.²

Association of allopurinol SCAR and an HLA variant

The risk of allopurinol-induced SCAR is associated with the presence of a specific HLA variant, HLA-B*58:01.² The frequency of this variant varies in different populations, being highest (10–20%) in people of Chinese (Han), Korean or Thai ancestry. Allopurinol-induced SCAR is more common in these populations. The variant, and the frequency of allopurinol-induced SCAR, is less common in other populations.

The HLA-B*58:01 variant is strongly associated with allopurinol-induced SCAR, but it is not the only factor. In at-risk Asian populations, most of the patients with allopurinol-induced SCAR have the HLA-B*58:01 variant. However, in European populations, only half of those with allopurinol-induced SCAR have that HLA variant. Screening patients for the presence of the HLA-B*58:01 variant prior to prescribing can reduce the incidence of allopurinol-induced SCAR in patients with Chinese (Han), Korean, or Thai ancestry, but may be of less benefit in other patients.

Screening for susceptibility to allopurinol-induced SCAR

Testing for the HLA-B*58:01 variant is readily available.

The American College of Rheumatology recommends that all Chinese (Han) and Thai patients, and Korean patients with impaired renal function, be screened for presence of the HLA-B*58:01 variant prior to treatment with allopurinol.³ Note that a person need only have such ancestry on one side of the family to have an increased chance of having this HLA variant.

Patients who have either one or two copies of the HLA-B*58:01 variant should avoid allopurinol.^{2,4}

References

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Evidence of the utility of screening before prescribing

The clinical utility of screening for the HLA-B*58:01 variant prior to prescribing allopurinol has been studied in Taiwan (which has a predominantly Chinese (Han) population). Because of the recognised association of the HLA variant with allopurinol-induced SCAR, this was a non-randomised cohort study rather than a randomised blinded study.

The investigators used information over four years from a national health insurance database to document that, in the absence of HLA screening, 0.3% of patients taking allopurinol developed SCAR each year. This amounted to 300–450 cases annually. The risk of this severe reaction was such that the prescribing of allopurinol was falling by 9% per year.

When screening for the HLA-B*58:01 variant was introduced, 354 patients (20%) had the variant and were prescribed a variety of medications other than allopurinol. The remaining 2,173 patients (80%) lacked the variant and were prescribed allopurinol.

Once screening was introduced, there were no instances of allopurinol-induced SCAR. The reduction in incidence of SCAR among those with the HLA-B*58:01 variant treated with other medications was highly significant ($p < 0.005$).

*Screening for the HLA-B*58:01 variant is available nationally through Sonic Genetics.*

The cost is \$75 and a Medicare rebate is not available. The turnaround time is up to seven business days, and results can be accessed electronically via Sonic Dx, by fax or by phone.*

*Correct at time of print. Please refer to www.sonicgenetics.com.au/pricing for current price