

Procedure	Result	Units	Ref Interval	Accession	Collected	Received	Reported/Verified
HLA-B*58:01 Genotyping, Allopurinol Hyp	<b>Positive *f@</b>			18-347-900070	13-Dec-18	13-Dec-18	24-Dec-18
					10:49:00	10:49:00	13:40:53

13-Dec-18 10:49:00 HLA-B\*58:01 Genotyping, Allopurinol Hyp:  
 Result: Positive for the HLA-B\*58:01 allele

Interpretation: The HLA-B\*58:01 allele was detected in this patient. The presence of this allele increases risk for allopurinol-induced severe cutaneous adverse reactions (SCAR), including Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN). Allopurinol treatment is contraindicated. Therapy should be discontinued immediately if symptoms of SJS or TEN develop. Alternative medication should be used as first line therapy. Other genetic or non-genetic factors that may affect hypersensitivity to allopurinol are not identified. Rare and undocumented alleles may occur which could lead to false positive or false negative results.

13-Dec-18 10:49:00 HLA-B\*58:01 Genotyping, Allopurinol Hyp:  
 Performed at: UUHC: Histocompatibility and Immunogenetics, 417 Wakara Way, Ste. 3220, SLC, UT 84108

13-Dec-18 10:49:00 HLA-B\*58:01 Genotyping, Allopurinol Hyp:

BACKGROUND INFORMATION: HLA- B\*58:01 Genotyping, Allopurinol Hyp

CHARACTERISTICS: Allopurinol is the most commonly used drug for the treatment of hyperuricemia and gout. It inhibits xanthine oxidase, a key enzyme involved in uric acid formation. However, allopurinol is one of the most common causes of life-threatening severe cutaneous adverse reactions (SCAR), which include drug hypersensitivity syndrome, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). The presence of HLA-B\*58:01 allele shows strong association with allopurinol-induced SCAR, including TEN and SJS. Although allopurinol-induced SCAR is rare with an estimated risk of 0.1-0.4 percent in allopurinol users, the severity can be high, with a mortality rate of up to 25 percent. Symptoms include rash, combined with eosinophilia, leukocytosis, fever, hepatitis and progressive kidney failure. Due to the severity of adverse reactions, it is recommended to test for the HLA-B\*58:01 allele prior to initiation of the drug.

INCIDENCE: HLA-B\*58:01 allele frequency varies by ethnicity. In the US population, the highest incidence at 5.3 percent is found in Asians, 3.8 percent in African Americans, 1.45 percent in Native Hawaiians or Pacific Islanders, 1.35 percent in Hispanics, 1.19 percent in American Indians or Alaska Natives and 0.8 percent in Caucasians. Frequencies may be higher in other countries, up to 20 percent in Singapore, Taiwan and among Han Chinese, 15.4 percent in India, 14.2 percent in Hong Kong, 12 percent in China and Korea, 11 percent in Indonesia.

CAUSE: Allopurinol-induced SCAR, including SJS and TEN, is strongly associated with the presence of one or two copies of HLA-B\*58:01 allele. The mechanism is immune mediated and involves direct interactions between the allopurine metabolite oxypurinol, and HLA-B\*58:01, which may result in drug-induced changes in peptide presentation, allowing activation of self-reactive T lymphocytes.

ALLELES TESTED: HLA-B\*58:01 allele.

CLINICAL SENSITIVITY AND SPECIFICITY: 71 percent sensitivity and 92 percent specificity, overall mean values from pooled populations (Yu KH at al, Int J Rheum Dis 2017). Higher in populations with increased HLA-B\*58:01 allele frequency.

METHODOLOGY: PCR followed by Sequence Specific Oligonucleotide Probe Hybridization of HLA-B locus.

\* Abnormal, # = Corrected, C = Critical, f = Footnote, H = High, L = Low, t = Interpretive Text, @ = Reference Lab

ANALYTICAL SENSITIVITY AND SPECIFICITY: Greater than 99 percent.

LIMITATIONS: Copy number of HLA-B\*58:01 will not be reported. Other genetic and non-genetic factors that influence allopurinol hypersensitivity are not evaluated. Other rare, or novel alleles may occur which may lead to false positive or false negative results.