ARUP LABORATORIES
800-522-2787 | aruplab.com
500 Chipeta Way, Salt Lake City, UT 84108-1221
Jonathan R. Genzen, MD, PhD, Chief Medical Officer

Client: Example Client ABC123
123 Test Drive
Salt Lake City, UT 84108
UNITED STATES

Physician: Doctor, Example

Patient: Patient, Example

DOB	11/14/1953
Gender:	Male
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

HLA-B*58:01 Genotyping, Allopurinol Hypersensitivity

ARUP test code 3001393

HLA-B*58:01 Genotyping, Allopurinol Hype	Negative Result: Negative for the HLA-B*58:01 allele Interpretation: The HLA-B*58:01 allele was not detected. This patient is not at risk for allopurinol-induced severe cutaneous adverse reactions (SCAR), including Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN). Allopurinol can be used per standard dosing guidelines. This negative result does not replace the need for therapeutic drug or other clinical monitoring. Other genetic or non-genetic factors that may affect hypersensitivity to allopurinol are not identified. Allopurinol therapy should be discontinued in all individuals if symptoms of SJS or TEN develop, regardless of HLA-B*58:01 status.

H=High, L=Low, *=Abnormal, C=Critical

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

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 et 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.

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.

Test systems were developed and their performance characteristics determined by the H&I laboratory at the University of Utah Health, under the accreditation guidelines from the American Society for Histocompatibility and Immunogenetics (ASHI).

Performed at: Histocompatibility & Immunogenetics Laboratory, University of Utah Health, 417 Wakara Way, Suite 3220, Salt Lake City, UT 84108.
CLIA Number: 46D0679773

H=High, L=Low, *=Abnormal, C=Critical

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
HLA-B*58:01 Genotyping, Allopurinol Hype	24-058-105490	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

H=High, L=Low, *=Abnormal, C=Critical