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UGT1A1-28 Genotyping for Irinotecan Toxicity

Detection of the most common polymorphisms are detected in this assay: (TA)5 *UGT1A1**36, The (TA)6 *UGT1A1**1, (TA)7 *UGT1A1**28 and (TA)8 *UGT1A1**37. Additional rare polymorphisms exist but are not assessed with this assay.

Indications for Molecular Testing

- Patient with cancer that may be treated with Irinotecan Therapy

Testing Methodology

Polymerase Chain Reaction (PCR) amplification of the promoter of UGT1A1 is performed with fluorescently-tagged analyte specific reagent primers as described (Shulman K, 2011). PCR Products are separated by capillary electrophoresis. (PCR is utilized pursuant to a license agreement with Roche Molecular Systems, Inc).

Interpretation of DNA analysis

The active form of Irinotecan, an antineoplastic agent, is deactivated by glucuronidation action of the *UGT1A1* enzyme. Studies of patients treated with irinotecan have reported that major dose-limiting toxicities are associated with polymorphisms in the TATA box of the *UGT1A1* gene. Individuals who are homozygous for *UGT1A1*-28 allele with 7 TA repeats may have a benign, congenital condition, Gilbert's syndrome, in the absence of cancer. Many studies report that patients who possess the *UGT1A1**28 genotype have a greater risk for irinotecan-induced toxicities, including severe diarrhea or grades 4 neutropenia. Patients who have 2 allels each with 6 TA repeats (6/6 homozygous) demonstrate full glucuronidation activity of SN-38, the active metabolite of irinotecan, with standard risk of toxicity. Patients with one 6 TA allele and one 7 TA allele (6/7 heterozygous) demonstrate reduced glucuronidation activity of SN-38, with about 12.5% risk of neutopenia toxicity. Patients with 2 alleles each with 7 TA repeat (7/7 homozygous) demonstrate severely reduced glucuronidation activity of SN-38, with about 50 % risk of severe toxicity. The homozygous 7/7 copy patient is at significant risk for grade 4 neutropenia or severe diarrhea following irinotecan treatment.

Specimen Requirements

Peripheral Blood--1 lavender-top (EDTA) tube. Invert several times to mix blood. Do not freeze, forward promptly at ambient temperature to the following address:

Molecular Diagnostic Laboratory
Barnes-Jewish Hospital, Institute of Health
Mail Stop 90-28-344
425 South Euclid Avenue, Room 5970
St. Louis, MO 63110

Clinical information must be provided with specimen referral in order to correctly interpret test results.

Current Pricing

Contact Lab Customer Service for current pricing 314 362-1470.
CPT code: 81350

Ando Y, Saka H, Ando M, et al. Polymorphisms of UDP-glucuronosyltransferase gene and irinotecan toxicity: a pharmacogenetic analysis. Cancer Res 2000;60:6921-6.
Marcuello E, Altres A, Menoyo A, et al. UGT1A1 gene variations and irinotecan treatment in patients with metastatic colorectal cancer. Br J Cancer 2004;91:678-82.
Palomaki GE, Bradley LA, Douglas MP, et al. Can UGT1A1 genotyping reduce morbidity and mortality in patients with metastatic colorectal cancer treated with irinotecan? An evidence-based review. Genet Med. 2009;11:21-34.
Shulman K, Cohen I, Barnett-Griness O, et al. Clinical implications of UGT1A1*28 genotype testing in colorectal cancer patients. Cancer 2011;117:3156-62.
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