

Ordered Items

UGT1A1 Irinotecan Toxicity

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
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UGT1A1 Irinotecan Toxicity

01

Result: ^A

Single copy of the UGT1A1*28 allele

Interpretation:

One copy of the *28 allele was detected in this individual (heterozygous pattern).

SN-38 is the active metabolite of irinotecan (CPT-11, CamptosarTM) and is glucuronidated by uridine diphosphate-glucuronyl transferase enzyme 1A1 (UGT1A1). People with a variant allele (UGT1A1*28) containing seven TA repeats (TA)7 compared to the normal six (TA)6 have reduced irinotecan glucuronidation and are at increased risk for irinotecan toxicity, which can include significant neutropenia, diarrhea, and less commonly, death. About 10% of the North American population has two copies of (is homozygous for) the *28 allele. An individual with two copies of *28 may benefit from a lower starting dose of irinotecan. Individuals with one copy of *28 may be at increased risk for neutropenia, but clinical results are variable and a typical starting dose can be considered. Refer to the irinotecan monograph for more information on dosing in the presence of *28.

Additional Information: ^B

01

This test detects the (TA)5, (TA)6, (TA)7, and (TA)8 alleles in the promoter of the UGT1A1 gene.

UGT1A1 variants have also been reported in patients with disorders of bilirubin metabolism, such as Crigler-Najjar Types I and II, as well as Gilbert syndrome. Between 80 - 100% of Caucasian patients with Gilbert syndrome are reported to have either one or two copies of UGT1A1*28. G71R(*6), a UGT1A1 variant reported in Asian patients with Gilbert syndrome, is not detected by this assay.

Methodology:

Polymerase chain reaction (PCR) analysis is used to amplify the promoter region of the UGT1A1 gene. The fluorescent amplification products are analyzed by capillary electrophoresis for the presence of the four variants above.

References:

1. Innocenti F, Undevia SD, Iyer L, et al. Genetic variants in the UDP-glucuronosyltransferase 1A1 gene predict the risk of severe neutropenia of irinotecan. J Clin Oncol. 2004; 22:1382-1388.
2. Beutler E, Gelbart T, and Demina A. Racial variability in the