Know Your Biomarker

RAF | CEA | ctDNA | DPYD | FAP | HER2 | KRAS | Lyn

# UGT1A1

MSI | MSS | NRAS | NTRK

K3CA | TMB | Tumor Location/Sidedness | UGT1A1 | P

**Who should have UGT1A1 biomarker testing?**

Patients who experience severe toxic effects of irinotecan chemotherapy should be tested for UGT1A1. Recommendations for pre-treatment UGT1A1 testing are different around the world. Talk to your medical team about whether pre- treatment testing would benefit you.

**What is UGT1A1?**

UGT1A1 is the gene that encodes a UDP-glucuronosyltransferase enzyme called UGT1A1. That means that the UGT1A1 gene gives your cells the recipe or instructions to make the UGT1A1 enzyme. The UGT1A1 enzyme is needed to break down and clear irinotecan chemotherapy in your body. If you have a mutation leading to decreased UGT1A1 enzyme level or function, your body does not break down irinotecan properly. This leads to increased levels of irinotecan metabolites (breakdown products) which may cause severe toxic effects, like severe neutropenia.

5-10% of people have a decreased level or function of UGT1A1 due to a mutation. UGT1A1 mutations are not the cause or result of your colorectal cancer, but they are relevant to your cancer treatment and treatment side effects. Mutations in the UGT1A1 gene are hereditary.

**How is UGT1A1 tested? How are the results reported?**

When testing for UGT1A1, your medical team is looking specifically at your genes, not your tumor's genes. UGT1A1 is tested in a blood sample or in cells collected from your mouth or saliva.

Sometimes, UGT1A1 is first tested by phenotyping, in this case measuring unconjugated bilirubin in blood. People with decreased UGT1A1 enzyme level or function have low unconjugated bilirubin. If phenotyping results are normal, no genotype testing is needed, you are not at higher risk of severe irinotecan toxicity. If phenotyping results indicate decreased UGT1A1 enzyme, you are at higher risk of severe irinotecan toxicity, and genotyping will be done to determine your UGT1A1 mutation and more specific level of risk. Both phenotyping and genotyping are good ways to determine whether your UGT1A1 status puts you at high risk for severe irinotecan related toxicity.

| If your UGT1A1 gene has: | Then the results are reported as: |
|---|---|
| no mutation (wild-type) | UGT1A1*1/*1 |
| one mutated copy | UGT1A1*1/*28 or<br>UGT1A1*1/*6 or<br>UGT1A1*1/*93 |
| two mutated copies | UGT1A1*28/*28 or<br>UGT1A1*28/*6 or<br>UGT1A1*28/*93 or<br>UGT1A1*6/*6 or<br>UGT1A1*6/*93 or<br>UGT1A1*93/*93 |

There are several different mutations that may be present in the UGT1A1 gene. The most common mutations that are relevant to your risk of severe irinotecan toxic effects are called *28, *93, and *6. The wild-type (WT) non-mutated UGT1A1 is called *1. Everyone has two copies of each gene in their cells, so you can have no mutation, one mutated copy, or two mutated copies.

The *28 mutation is commonly found in people of African (43%) or European (39%) ancestry, and is less common in those of East Asian ancestry (16%). The *93 mutation is also common in those of African (34%) and European (27%) ancestry, and less common in people of East Asian ancestry (13%). The *6 mutation is most common in those of East Asian ancestry (15%), and uncommon in people of African (0.1%) and European (1%) ancestry.

**What do my UGT1A1 results mean for me? How do they impact my treatment?**

If you have no mutation in UGT1A1 (wild-type)

→ You are at average risk of severe irinotecan toxicity.

→ Your treatment can include irinotecan at the usual doses.

If you have one mutated copy of UGT1A1 and one normal wild-type copy

→ You are at higher risk of severe irinotecan toxicity.

→ The risk of severe effects increases with increasing irinotecan dose.

→ If your planned irinotecan dose is more than 240 mg/m2, then your medical team may adjust your dose.

If you have two mutated copies of UGT1A1

→ You are at the highest risk of severe irinotecan toxic effects.

→ The risk of severe effects increases with increasing irinotecan dose.

→ If your planned irinotecan dose is more than 180 mg/m2, then your medical team will adjust your dose or use an alternative chemotherapy drug.

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Biomarker testing can give you and your medical team valuable knowledge about your cancer and help guide your treatment choices. For more information about colorectal cancer biomarkers, please visit knowyourbiomarker.org and talk to your medical team.