Meeting Abstract: 2019 Gastrointestinal Cancers Symposium

Cancers of the Colon, Rectum, and Anus

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Identifying the importance of integrating routine pharmacogenomic testing for *UGT1A1* and *DPYD/tyms* genetic variants in patients receiving irinotecan and/or 5-fluorouracil chemotherapy.

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Background: Adverse toxicities to chemotherapy remain a limiting factor for patients receiving treatment for malignancies. In gastrointestinal cancers, particularly metastatic colorectal cancer, the majority of front line treatment remains chemotherapy containing 5-fluorouracil and/or irinotecan. One particular cause that can predispose a patient to increased toxicity from 5-fluorouracil is genetic variation in the *DPYD* gene, as well as *TYMS* gene. Similarly, genetic variation in the *UGT1A1* gene can increase the risk of irinotecan toxicity. These gene variations may have major implications when deciding on treatment regimens for these types of patients; however, they are not routinely checked. **Methods:** In Mayo Clinic Florida, patients with metastatic colorectal cancer receiving 5-fluorouracil and/or irinotecan chemotherapy during the period of July 2017-July 2018 were tested for genetic variants in *DPYD/TYMS* and *UGT1A1*. This testing was done during routine clinic visit either by buccal swab or blood test. The *DPYD/TYMS* and *UGT1A1* variant results were evaluated together with a pharmacist for recommendations regarding dose reductions on 5-fluorouracil and irinotecan respectively. **Results:** A total of 292 patients were tested. Total number of patients who had a variation in the *DPYD/TYMS* and/or *UGT1A1* gene was 169 (57.9%). The *UGT1A1* variation was the most prevalent with 154 (52.7%) patients having a variant (115 heterozygous variant, 34 homozygous variant and 5 double heterozygous variant). Specifically there were 3 patients with both *UGT1A1* and *DPYD* variants and 3 patients with both *UGT1A1* and *TYMS* variants. One patient had both *DPYD* and *TYMS* variations. **Conclusions:** Routine pharmacogenomic testing for *UGT1A1* and *DPYD/TYMS* genetic variants should be done in all patients receiving irinotecan and 5-fluorouracil chemotherapy respectively. Avoiding or

preemptively dose reducing these agents in patients with gene variations may help prevent toxic adverse events and make treatment more tolerable.

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