Personalized Prescribing Inc.

Dear Dr,

Marry has sought out a consultation with a clinical pharmacist at Personalized Prescribing Inc in regard to the use of Capecitabine as well as Oxaliplatin. This consultation included a pharmacogenomic test.

According to a high level of evidence and as per the Clinical Pharmacogenetic Implementation Consortium (CPIC), Patients with the CC genotype for gene **DPYD rs3918290** (**DPYD *1/*1**) and cancer who are treated with fluoropyrimidine-based chemotherapy (i.e.. Capecitabine) may have:

1) increased clearance of fluoropyrimidine drugs
2) decreased, but not non-existent, risk for drug toxicity as compared to patients with the **CT** or **TT** genotype (**DPYD *1/*2A or *2A/*2A**).

DPYD (Dihydropyridine Dehydrogenase) is a gene responsible for the creation of an enzyme called Dihydropyridine Dehydrogenase which is responsible for the breakdown of pyrimidines into uracil and thymine. When this break down fails to occur, these molecules remain in the blood, causing toxicity.

Fluoropyrimidines are often used in combination chemotherapy such as **FOLFOX** (fluorouracil, leucovorin and oxaliplatin), **FOLFIRI** (fluorouracil, leucovorin and irinotecan) or FEC (fluorouracil, epirubicin and cyclophosphamide) or with other drugs such as bevacizumab, cetuximab, raltitrexed. The combination and delivery of the drug may influence risk for toxicity. Other genetic and clinical factors may also influence response to fluoropyrimidine based chemotherapy.

Though according to a lower level evidence as per CPIC, tested genes indicate only a moderate likelihood of response on Capecitabine and Oxaliplatin in combination, Marry showed good response to Capecitabine as per tested gene, moderate response to Oxaliplatin and is at low risk of Folinic acid deficiency on Capecitabine, as per **MTHFR** gene **rs1801133 GA** and **rs1801131 TT**. The standard dose of Leucovorin can be used. A moderate level of evidence also states (level 2A and level 2B) that Marry may be at risk of hematological toxicity as per detoxification gene (**GSTP1 rs1695 AA**) as well as nephrotoxicity as per DNA repair protein **(ERCC1 rs3212986 CA** and **rs11615 GA).** Blood work should be monitored carefully, watch out for neutropenia.

References:

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1) Database, Gene. “ERCC1 Gene (Protein Coding).” *GeneCards*, www.genecards.org/cgi-bin/carddisp.pl?gene=ERCC1.
2) Database, Gene. “GSTP1 Gene (Protein Coding).” *GeneCards*, www.genecards.org/cgi-bin/carddisp.pl?gene=GSTP1.
3) “Dihydropyrimidine Dehydrogenase Deficiency - Genetics Home Reference - NIH.” *U.S. National Library of Medicine*, National Institutes of Health, ghr.nlm.nih.gov/condition/dihydropyrimidine-dehydrogenase-deficiency#genes.
4) “Home Page.” *CPIC*, cpicpgx.org/.

Other untested clinical and genetic factors can also affect response. Patients have been informed to follow-up with their physician prior to making any changes to their medications.

Please feel free to contact me should you have any questions.

Regards,

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