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In This Issue

Editor's Summaries of the Articles Published in This Issue of Precision Medicine Communications

Editorial Staff

In this issue, Ijaz and colleagues have reported the prevalence of renal and urinary adverse in breast cancer patients receiving cyclophosphamide. They investigated the possible association between the single nucleotide polymorphism in the *CYP450 2B6* and urinary adverse effects in a Pakistani cohort of breast cancer patients receiving cyclophosphamide as a part of therapy. Their results suggest that among the patients with wild type (GG) genotype, about 78 % of the patients did not experience any renal adverse effects, while about 22% did. In patients heterozygous for the polymorphic genotype (GT), more than 81% did not complain of any renal adverse effects, while only 18% showed renal toxicity. The group with TT genotype showed the highest fraction of patients experiencing renal adverse effects (25%). However, Chi-squared analysis did not reveal any association with renal adverse effects and with GT or TT genotype. Therefore, they concluded that the *CYP2B6*6* is not associated with renal adverse effects in Pakistani breast cancer patients who are taking cyclophosphamide.

Qayyum and colleagues have investigated the role of genetic variations on the therapeutic response of angiotensin receptor blockers (ARBs) on blood pressure. They specifically studied the association of Losartan's effect on BP with respect to single nucleotide polymorphisms (SNPs) in the cytochrome P450 (CYP) 2C9 enzyme in hypertensive Pakistani patients. They selected 100 hypertensive patients and genotyped them for *CYP2C9**1, *2, and *3. Their findings suggest that roughly 40% of patients were responsive to antihypertensive treatment per the defined criteria (a reduction of at least 10mm systolic & 5mm diastolic). More than 63% of patients with wild-type *CYP2C9* genotype did not respond to antihypertensive therapy; the rest did respond to the antihypertensive therapy. Similarly, more than 46% of patients having one of the polymorphic genotypes did not respond to therapy, while the rest did. The difference between the two groups, however, was not statistically significantly different. Therefore, their analysis did not show associations between the polymorphism in the *CYP2C9* gene with the antihypertensive therapy with Losartan.

Ullah and colleagues reviewed several genetic polymorphisms associated with the treatment outcome and adverse effects in patients with chronic myelogenous leukemia (also called CML or chronic granulocytic leukemia). CML is a disorder in which the bone marrow generates many white blood cells. It is distinguished by a cytogenetic irregularity comprising a reciprocal translocation between the long arms of chromosomes 22 and 9 [t (9;22)]. CML treatment entails taking a variety of drugs. Administration of these medications can cause unpleasant side effects. Ullah and colleagues sifted through the

literature and compiled studies investigating various gene variants affecting the efficacy and adverse effects of the standard of care treatment in CML. Their undertaking identified some promising candidate genes that may be used as a predictor of certain adverse effects of CML treatment. Finally, they made recommendations to employ these genetic variants in clinical medicine.

Memon and Sheikh reviewed the major genetic variants associated with the efficacy and adverse effects of selective serotonin reuptake inhibitors in treating major depressive disorder (MDD). MDD is a major health condition among the foremost psychological state disorders worldwide. Despite the common mechanism of action, the drugs from within the same class exhibit variations, reportedly 60-70% of patients do not experience remission, and 30-40% of patients lack adequate response to drug therapy, resulting in non-adherence or discontinuation of therapy and prolongation of disease course. The variability of drug response is believed to be due to an individual's variation in drug metabolism at the genetic level. Their review is mainly focused on the *CYP450* enzymes (*CYP2C19*, *CYP2B6*, and *CYP2D6*), their single nucleotide polymorphism (SNPs), and their association with the antidepressants (selective serotonin reuptake inhibitors) efficacy or adverse effects.

Javed and Akmal reviewed significant genetic determinants of hepatic adverse effects of drugs used to treat mycobacterium tuberculosis (TB). Tuberculosis is a significant healthcare burden, especially in the developing world. Current first-line therapies for tuberculosis treatment (isoniazid, pyrazinamide, rifampicin, and ethambutol) have significant efficacy but can all potentially cause hepatotoxicity. Effects produced by these drugs may be asymptomatic with increased levels of aminotransferases in some patients or the development of severe hepatotoxicity in others. In some cases, it can also lead to hepatic failure. In their review, they evaluated the studies on genetic variants showing associations with drug-induced hepatic injury in tuberculosis patients. Several studies on important genes such as *NAT2, AADAC, CYP2E1, HLA, CYP7A1, ALDH1A1, NFkB, PXR, HMOX1, SLCO1B1, UGT1A1, NRF2, and MAFF* were reviewed and discussed for utilizing them as predictors of hepatic injury in tuberculosis patients. The authors recommended the potential of some of these genetic variants as a screening tool for determining patients most likely to experience hepatic adverse effects after receiving standard first-line anti-mycobacterial tuberculosis treatment.

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