

## Publication

### Is Pharmacogenetic Panel Testing Applicable to Low-Dose Methotrexate in Rheumatoid Arthritis? - A Case Report.

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Pharmacogenetic (PGx) panel testing could help to determine the heritable component of a rheumatoid arthritis (RA) patient's susceptibility for therapy failure and/or adverse drug reactions (ADRs) from methotrexate (MTX). Considering the literature mentioning the potential applicability of PGx panel testing within MTX regimens, we discuss the case of a patient who was treated with MTX, suffered from ADRs, and obtained a reactive PGx panel testing.; We used a commercial PGx panel test involving the ABC-transporters P-glycoprotein (P-gp; gene:: ABCB1; ), and breast cancer resistance protein (BCRP; gene:: ABCG2; ), the solute carriers reduced folate carrier 1 (RFC1; gene:: SLC19A1; ), and organic anion transporting polypeptide 1B1 (OATP1B1; gene:: SLCO1B1; ), and the enzymes inosine triphosphatase (ITPA), and glutathione transferase P1 (GSTP1). In addition, we genotyped the patient for the enzymes 5-aminoimidazole-4-carboxamide ribonucleotide formyltransferase (AICAR)/inosine monophosphate (IMP) cyclohydrolase (gene name::ATIC; ), gamma-glutamyl hydrolase (gene name::GGH; ) and methylenetetrahydrofolate reductase (gene name::MTHFR; ).; The PGx profile of the patient revealed genetic variants in SLC19A1, ABCB1, and MTHFR, which may explain the ADRs experienced during the treatment with MTX and a potentially lower efficacy of MTX. Based on our interpretation of the PGx profile, we recommended the patient to avoid MTX in the future.; The MTX pathway is complex, which makes the interpretation of genetic variants affecting metabolism challenging. A reactive PGx panel test was applicable to explain ADRs experienced during MTX treatment for a patient with RA. However, the clinical utility of PGx-guided MTX treatment in a primary care setting is still limited. In order to base a recommendation for MTX on PGx data, we need genome-wide association studies, large prospective multicenter studies and PGx studies, which analyze different multi-gene haplotypes and gene-drug-drug interactions for MTX.

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