Gene test information

THIOPURIN TOXICITY (TPMT GENE TEST)

- **Background**

  The thiopurine drugs 6-mercaptopurine (6-MP), azathioprine (AZA) and thioguanine are widely used for the treatment of a variety of diseases, including childhood acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), inflammatory bowel disease, autoimmune hepatitis, rheumatic diseases, dermatologic conditions and in transplantation medicine. However, thiopurine drugs have a relatively narrow therapeutic index and are capable of causing life-threatening toxicity, most often myelosuppression.

  Thiopurine S-methyltransferase (TPMT), an enzyme metabolizing these drugs, exhibits a genetic polymorphism. This polymorphism causes leads to reduced TPMT activity in 10% of Caucasians and complete TPMT deficiency in about 1/300 individuals.

  In Caucasians, three common TPMT gene variants (*2, *3A, *3C) are associated with diminished TPMT activity. Analysis of TPMT genotypes can help to predict the individual risk for thiopurine toxic side effects.

- **TPMT genotypes**

Class	Frequency	Genotypes (examples)	Commentary
No TPMT Deficiency	89%	*1*1	No sign for reduced TPMT activity (wild-type genotype)
Heterozygous deficiency	11%	*1*2, *1*3A, *1*3C	Reduced TPMT activity
Homozygous deficiency	0.3%	*3A*3A, *3A*3C, *3A*2A	Deficient TPMT activity.

- **Indications for testing**

  Estimation of individual risk for thiopurine toxicity

References:

Sahasranaman S et al. Clinical pharmacology and pharmacogenetics of thiopurines. Eur J Clin Pharmacol. 2008;64:753-67.

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