Test Highlight

- Individuals who inherit two non-functional TPMT alleles (~1 in 178 to 1 in 3,736) experience life-threatening myelosuppression, due to high levels of TGNs (6-Thioguanine) , if they receive conventional doses of Azathioprine
- Individuals who are heterozygous for non-functional TPMT alleles (~3–14%) are at a significantly higher risk for toxicity than individuals with two functioning alleles

Methodology

Real Time PCR

Test Code

N071

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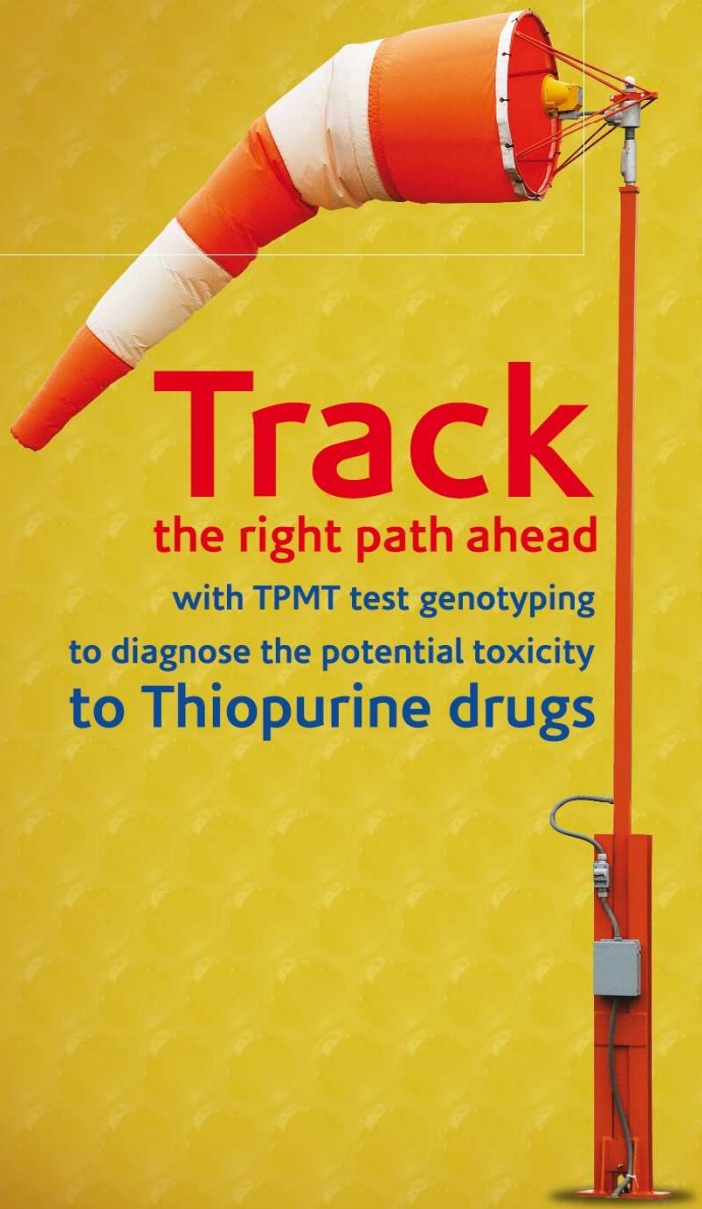

Track

the right path ahead

with TPMT test genotyping
to diagnose the potential toxicity
to Thiopurine drugs

Dr Lal PathLabs presents
TPMT (Thiopurine Methyl Transferase) genotyping

Clinical Use

- Identify patients at risk for toxicity from Thiopurine drugs
- Determine need to adjust drug dosage or select alternative therapy

Phenotype	Phenotype details	Genotype	Examples of diplotypes	Therapeutic recommendations for azathioprine
•Homozygous wild-type ("normal")	•High enzyme activity. Found in ~86-97% of patients.	•Two or more functional alleles	•*1/*1	•Start with normal starting dose. Adjust diseases of azathioprine based on disease-specific guidelines. Allow 2 weeks to reach steady state after each dose adjustment.
•Heterozygous	•Intermediate enzyme activity. Found in ~3-14% of patients.	•One functional allele plus one non-functional allele	•*1/*2 •*1/*3A •*1/*3B •*1/*3C •*1/*4	•Consider starting at 30-70 % of the full dose, if treatment of the disease normally starts with a full dose. Titrate dose based on tolerance. Allow 2-4 weeks to reach steady state after each dose adjustment.
•Homozygous variant	•Low or deficient enzyme activity. Found in ~1 in 178 to 1~3736 patients.	•Two non-functional alleles	•*3A/*3A •*2/*3A •*3C/*3A •*3C/*4 •*3C/*2 •*3A/*4	•Consider alternative agents. If using azathioprine, start with drastically reduced doses (reduce daily dose by 10-fold and dose thrice weekly instead of daily). Adjust doses of azathioprine based on degree of myelosuppression and disease-specific guidelines. Allow 4-6 weeks to reach steady state after each dose adjustment.

Reference : Table is adapted from Relling M.V. et al. Clinical Pharmacogenetics Implementation Consortium guidelines for thiopurine methyltransferase genotype and thiopurine dosing. Clinical pharmacology and therapeutics.

Recommendations

- The FDA recommends TPMT genotyping or phenotyping before starting treatment with Azathioprine
- The Clinical Pharmacokinetics Implementation Consortium (CPIC) has made recommendations on the dosing of Azathioprine based on an individual's TMPT phenotype

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