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
**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

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Phenotype details</th>
<th>Genotype</th>
<th>Examples of diplotype</th>
<th>Therapeutic recommendations for azathioprine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homozygous wild type</td>
<td>High enzyme activity. Found in ~80-97% of patients.</td>
<td>Two or more functional alleles</td>
<td>*1/*1</td>
<td>• Start with normal starting dose. Adjust doses of azathioprine based on disease-specific guidelines. Allow 2 weeks to reach steady state after each dose adjustment.</td>
</tr>
<tr>
<td>Heterozygous</td>
<td>Intermediate enzyme activity. Found in ~3-14% of patients.</td>
<td>One functional allele plus one non-functional allele</td>
<td>*1/*2, *1/*3A, *1/*3B, *1/*3C, *1/*4</td>
<td>• 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.</td>
</tr>
</tbody>
</table>

**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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Sometimes, we get deviated from reaching our destination

Dr Lal PathLabs

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