TPMT TESTING IN THE TREATMENT OF INFLAMMATORY BOWEL DISEASE
HOW ARE THIOPURINES METABOLIZED?

US FDA recommends TPMT testing prior to initiation of therapy

Cytotoxicity and immunosuppression
Plan to Initiate Thiopurine Therapy for IBD

TPMT Activity Assay

TPMT Genotyping Assay

Dose selected based on results; patient begins therapy

TPMT Metabolite Monitoring Assay
Plan to Initiate Thiopurine Therapy for IBD

TPMT Activity Assay

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TPMT Metabolite Monitoring Assay
ENZYME ACTIVITY ASSAY (MAYO TEST ID: TPMT3)

WHAT SUBSTRATES DOES THE NEW MAYO CLINIC TPMT ASSAY MEASURE?
- 6-MP to 6-MMP (previously included)
- 6-MPR to 6-MMPR (new)
- 6-TGR to 6-MTGR (new)

Performed by LC-MS/MS

BENEFITS OF THIS ASSAY
- The new reactions do not interfere with one another and both compete for TPMT.
- The testing process is newly automated, which minimizes pre-analytical variability.

POST-ANALYTICAL INTERPRETATION
Post-analytical interpretation is aided by Mayo Clinic-developed, multivariate pattern recognition software (CLIR).
- CLIR automatically generates a detailed “biochemical fingerprint”, allowing detection of pattern differences unique to the TPMT phenotype (deficient, heterozygote, normal, hyperactive).
- This type of phenotyping is capable of driving precision medicine.
- TPMT3 reduces clinical uncertainty.
Plan to Initiate Thiopurine Therapy for IBD

TPMT Activity Assay

TPMT Genotyping Assay

Dose selected based on results; patient begins therapy

TPMT Metabolite Monitoring Assay
GENOTYPING ASSAY (MAYO TEST ID: GTPMT OR OTPMT)

PATIENTS ARE CLASSIFIED BASED ON PREDICTED PHENOTYPE:
- Normal (extensive) metabolizer
- Intermediate metabolizer
- Poor metabolizer

<table>
<thead>
<tr>
<th>TPMT Allele</th>
<th>cDNA Nucleotide Change</th>
<th>Effect on Enzyme Metabolism</th>
</tr>
</thead>
<tbody>
<tr>
<td>*1</td>
<td>None (wild type)</td>
<td>Extensive (normal) metabolizer</td>
</tr>
<tr>
<td>*2</td>
<td>c.238G&gt;C</td>
<td>Nonfunctional, no activity</td>
</tr>
<tr>
<td>*3A</td>
<td>c.460G&gt;A and c.719A&gt;G</td>
<td>Nonfunctional, no activity</td>
</tr>
<tr>
<td>*3B</td>
<td>c.460&gt;G</td>
<td>Nonfunctional, no activity</td>
</tr>
<tr>
<td>*3C</td>
<td>c.719&gt;G</td>
<td>Nonfunctional, no activity</td>
</tr>
<tr>
<td>*4</td>
<td>c.626-1G&gt;A</td>
<td>Nonfunctional, no activity</td>
</tr>
<tr>
<td>*5</td>
<td>c.146T&gt;C</td>
<td>Nonfunctional, no activity</td>
</tr>
<tr>
<td>*8</td>
<td>c.644G&gt;A</td>
<td>Reduced-function/decreased activity</td>
</tr>
<tr>
<td>*12</td>
<td>c.374&gt;T</td>
<td>Reduced-function/decreased activity</td>
</tr>
</tbody>
</table>
Plan to Initiate Thiopurine Therapy for IBD

- TPMT Activity Assay
- TPMT Genotyping Assay

Dose selected based on results; patient begins therapy

TPMT Metabolite Monitoring Assay
METABOLITE MONITORING ASSAY (MAYO TEST ID: FPMET)

MML TEST WILL INCLUDE*:

- 6-mercaptopurine (6-MP)
- 6-methylmercaptopurine (6-MMP or MeMP)
- 6-thioguanine nucleotides (6-TGN)
  * New test, Mayo ID: TPMTS, available Q2 2017

Performed by LC-MS/MS

RECOMMENDED¹:

- 4 weeks after starting treatment to ensure patient compliance and to look for early risk of toxicity
- 12-16 weeks (after TGN metabolites have reached steady-state)
- Annually

CONTACT US

FOR CLINICAL QUESTIONS ABOUT TPMT TESTING OR MORE INFORMATION ABOUT TEST ORDERING:

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