LABORATORY TESTING FOR

IMMUNOSUPPRESSANT THERAPIES

New laboratory assays to support treatment decisions of patients receiving **immunosuppressant therapies**

Thiopurine Drug

Thiopurine-related testing may be used to assess dosing before and during treatment, as well as to identify patients who may be at risk for drug toxicity.[1] Variants in the TPMT gene that lead to low enzyme activity can lead to an increased risk of thiopurine toxicity.[1-3] Because of the potentially severe bone marrow toxicity that can occur even with standard thiopurine dosages in patients with TPMT enzyme deficiency, the FDA-approved label recommends consideration for testing for the most common TPMT gene mutations (genotype) or TPMT activity (phenotype) before beginning treatment. The information can be used to adjust the drug dosage or can suggest the use of an alternative treatment.[4]

TPMT Genetic Test

- Utilize prior to treatment to identify common mutations that cause low TPMT activity
- Clinical sensitivity approximately 95% for TPMT mutations *2, *3A, *3B, and *3C[5]
- Not sensitive to red blood cell transfusion or environmental factors that can cause inaccurate results for TPMT phenotypic assay
- Interpretive reports support initial dosing decisions

TPMT Activity Test

- Utilize prior to treatment as a screen for low TPMT activity
- Directly measures red blood cell thiopurine S-methyltransferase phenotypic activity
- May detect rare clinically relevant mutations that are not detected in the TPMT Genetic Test
- Interpretive reports support initial dosing decisions

Thiopurine Metabolites Test

- Utilize during treatment to help reach and maintain therapeutic goal[1]
- Assists with evaluating unresponsive patients[1]
- Monitors responsive patients to avoid potential toxicity[1]
- Drug concentrations reported for 6-TG (6-thioguanine) and 6-MMP (6-methylmercaptopurine)

Anti-TNF Therapy

Serum measurement of anti-TNF drugs and antibodies to the drug can help characterize patients who maintain versus lose responsiveness to therapy.[6,7]

Adalimumab Concentration and Anti-Adalimumab Antibody (ATA) Test
Infliximab Concentration and Anti-Infliximab Antibody (ATI) Test

- Monitors drug concentration levels to help physicians to optimize dosing and frequency of treatment.
- Identifies those patients who fail therapy or have diminished response as a result of an antibody development to the drug.
- Routine pre-testing sample treatment reduces drug interference and provides clinically valid antibody results at drug levels well above treatment targets (>100 µg/mL for Infliximab and >30 µg/mL for Adalimumab).[8,9]
- Allows for testing to be ordered at anytime during therapy.

Immunosuppressant Therapies

Drug Name	Drug Class	Brand Names	Laboratory Tests
Azathioprine	Thiopurine	Azasan® and Imuran®	TMPT Genetic Test TMPT Activity Thiopurine Metabolites
6-mercaptopurine	Thiopurine	Purinethol®	
6-thioguanine	Thiopurine	Tabloid®	
Adalimumab	Anti-TNF	Humira®	Adalimumab Concentration and Anti-Adalimumab Antibody (ATA)
Infliximab	Anti-TNF	Remicade®	Infliximab Concentration and Anti-Infliximab Antibody (ATI)

Test Name	Test N°	Reference Intervals	Methodology
TPMT Genetic Test	504142	• Normal: Two TPMT*1 alleles • Heterozygous for low TPMT variant: One TPMT*1 allele and one mutant allele (TPMT*2, *3A, *3B, or *3C) • Homozygous for low TPMT variant: Two mutations (TPMT*2, *3A, *3B, or *3C)	PCR and multiplex minisequencing
TPMT Activity	510750	Normal: 15.1-26.4 units/mL RBC Heterozygous for low TPMT variant: 6.3-15.0 units/mL RBC Homozygous for low TPMT variant: <6.3 units/mL RBC	Enzymatic endpoint/liquid chromatography/tandem mass spectrometry LC/MS-MS
Thiopurine Metabolites	503800	**6-TGN** Suboptimal dosing: <235 pmol 6-TG/8x10^8 RBC Optimal dosing: 235-450 pmol 6-TG/8x10^8 RBC Increasing risk for myelotoxicity and leukopenia: >450 pmol 6-TGN/8x10^8 RBC **6-MMPN** Hepatotoxicity risk: >5700 pmol 6-MMP/8x10^8 RBC	LC/MS-MS after acidic hydrolysis
Adalimumab Concentration and Anti-Adalimumab Antibody (Serial Monitor)	503890	Concentration: <0.6 µg/mL Results of 0.6 or higher indicates detection of adalimumab. **Note:** measures free drug concentration Antibodies: <25 ng/mL Results of 25 or higher indicate detection of anti-adalimumab antibodies. ≤100 ng/mL Low antibody titer, no apparent impact on free drug level 101-300 ng/mL intermediate antibody titer, variable impact on free drug level ≥301 ng/mL High antibody titer, significant impact on free drug level	Electrochemiluminescence Immunoassay (ECLIA)
Infliximab Concentration and Anti-Infliximab Antibody (Serial Monitor)	503770 503870	Concentration: <0.4 µg/mL Results of 0.4 or higher indicate detection of infliximab. Antibodies: <22ng/mL Results of 22 or higher indicate detection of anti-infliximab antibodies. ≤200 ng/mL Low antibody titer, no apparent impact on free drug level 201-1000 ng/mL intermediate antibody titer, variable impact on free drug level ≥1001 ng/mL High antibody titer, significant impact on free drug level	Electrochemiluminescence Immunoassay (ECLIA)

For complete test information, including specimen requirements, methodology, CPT coding, and RUO/IUO status, please visit **www.labcorp.com/testmenu.**

References

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7. Karmiris K, Paintaud G, Noman M, et al. Influence of trough serum levels and immunogenicity on long-term outcome of adalimumab therapy in Crohn's disease. Gastroenterology. 2009 Nov; 137(5):1628-1640.
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