Imatinib Quantification in Plasma

Indications for Ordering

For patients who have been prescribed imatinib
- Evaluate patient pharmacokinetics and dosing
- Routine monitoring of adherence
- Evaluate resistance to therapy

Test Methodology

Immunoturbidimetry

Tests to Consider

Primary test

Imatinib 3000539
- Optimize dose, detect variable pharmocokinetics, and monitor patient adherence
- For more information, see https://www.aruplab.com/topics/imatinib

Related test(s)

BCR-ABL1, Major (p210), Quantitative 2005017
- Aid in diagnosis and therapeutic monitoring for chronic myelogenous (CML) or acute lymphoblastic leukemia (ALL)

BCR-ABL1 Mutation Analysis for Tyrosine Kinase Inhibitor Resistance by Next Generation Sequencing 2008420
- Order only for patients with an established diagnosis of a *BCR-ABL1*-positive leukemia

Cytochrome P450 Genotype Panel 2013098
- Assess genetic risk of abnormal drug metabolism for drugs metabolized by *CYP2D6, CYP2C9, CYP2C19*, and *CYP3A5*

Drug Overview

Imatinib mesylate (Gleevec, Glivac) is a tyrosine kinase inhibitor (TKI)
- Treatment
  - Philadelphia chromosome-positive CML
  - Some gastrointestinal stromal tumors (GIST)
- Drug-gene and drug-drug interactions
  - Such interactions can be identified and managed with therapeutic drug monitoring of imatinib
  - May exhibit variability in blood concentrations due to drug metabolism
  - Metabolism mediated by several isozymes of the cytochrome P450 system, including CYP3A4 and, to a lesser extent, CYP1A2, CYP2D6, CYP2C9, and CYP2C19

Resistance to imatinib therapy may be explained by
- Subtherapeutic dosing
- Poor adherence to therapy
- Pharmacokinetic variability leading to subtherapeutic blood concentrations
- Change in pathophysiology of the disease

In CML patients
- Optimization of imatinib dose with timed blood concentrations has been shown to yield a similar response as second-generation TKIs

Test Interpretation

Results

Concentrations above 1000 ng/mL in CML patients and above 1100 ng/mL in GIST patients are statistically associated with an improved response

Limitations

Therapeutic range based on plasma predose (trough) blood collection at steady-state concentration
- May require at least 29 days of imatinib therapy to achieve steady state
- Once at steady state there should be no change in dose or dosing for at least 8 days prior to blood collection
  - Blood should be collected at least 21 hours after last dose for once-daily dosing and at least 9 hours after last dose for twice-daily dosing

References

- Verheijen RB, et al. Practical recommendations for therapeutic drug monitoring of kinase inhibitors in oncology. *Clin Pharmacol Ther* 2017;102(5):765–76
- Yu H, et al. Practical guidelines for therapeutic drug monitoring of anticancer tyrosine kinase inhibitors: focus on the pharmacokinetic targets. Clin Pharmacokinet 2014;53(4):305–25