Imatinib Therapeutic Drug Monitoring

Imatinib (Gleevec, Glivac) is a tyrosine kinase inhibitor (TKI) used in the treatment of different types of cancers, including chronic myelogenous leukemia (CML), some gastrointestinal stromal tumors (GIST), and myelodysplastic/myeloproliferative diseases. Imatinib may also be used in the treatment of other diseases. Testing patients using imatinib evaluates individual pharmacokinetics for dosing decisions, monitors treatment effectiveness, and identifies resistance to therapy.

Drug Overview

Drug-gene and drug-drug 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 steady state achieved, no change in dose or dosing should be made 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

Additional Resources

National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: gastrointestinal stromal tumors (GIST), Version 1.2021. [Last update: Oct 2020; Accessed: April 2021]

Tests to Consider

Imatinib 3000539

Method: Immunoturbidimetry

Optimize dose, detect variable pharmacokinetics, and monitor therapy effectiveness

For more information, see https://www.aruplab.com/topics/imatinib

Related Tests

BCR-ABL1, Major (p210), Quantitative 2005017

Method: Quantitative Reverse Transcription Polymerase Chain Reaction

Aid in diagnosis and therapeutic monitoring for CML or acute lymphoblastic leukemia (ALL)

BCR-ABL1 Mutation Analysis for Tyrosine Kinase Inhibitor Resistance by Next Generation Sequencing 2008420

Method: Massively Parallel Sequencing

Order only for patients with an established diagnosis of a *BCR-ABL1*-positive leukemia

Cytochrome P450 Genotyping Panel 3001524

Method: Polymerase Chain Reaction/Fluorescence Monitoring

Assess risk of abnormal drug metabolism affected by genetic variants in *CYP2C19, CYP2C8, CYP2C9, CYP2D6, CYP3A4*, and *CYP3A5*

Verheijen RB, Yu H, Schellens JHM, et al. Practical recommendations for therapeutic drug monitoring of kinase inhibitors in oncology. Clin Pharmacol Ther. 2017;102(5):765-776. PubMed

Yu H, Steeghs N, Nijenhuis CM, et al. Practical guidelines for therapeutic drug monitoring of anticancer tyrosine kinase inhibitors: focus on the pharmacokinetic targets. Clin Pharmacokinet. 2014;53(4):305-325. PubMed

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