



Blood Level Testing Physician Information

Imatinib Blood Level Testing (BLT) is a method of determining the trough level, or lowest level, of the drug in the blood. While most of the research thus far has focused on CML patients on Gleevec treatment, preliminary data suggests there may be a relationship between the trough levels of imatinib and clinical benefit in GIST. Numerous factors can affect this level, including body metabolism, dosage prescribed, and drug-drug interactions. Research has suggested that a level of 1100 ng/ml may be the therapeutic level, or optimal threshold for drug efficacy. In a recent study conducted in GIST patients, trough imatinib levels below 1100 ng/ml were associated with lower clinical benefit and significantly faster rates of progression¹. Specifically, their data showed that median time to progression in patients with trough levels lower than 1100 ng/ml was 11.3 months, while those with trough levels over 1100 ng/ml had a media time to progression of more than 30 months. A great deal of research is now being devoted to further investigate the relationship between imatinib exposure and efficacy to develop guidelines for the potential of BLT use in clinical practice.^{2,3}

In addition to suggesting clinical benefit, routine blood level testing may also provide the physician with vital information. Drug levels have been shown to change over time, so for new patients starting imatinib treatment, BLT may be useful for determining a baseline level of the drug. Regular monitoring following the initial testing may prove a beneficial tool in tracking the patient's response to the drug over time and managing side effects. Such monitoring can be a helpful tool for providing care as recent studies have shown that disease progression may be due to low imatinib levels while extremely high imatinib levels in the blood may cause severe side effects. A leading GIST specialist has estimated that at least 25% of GIST patients may be under-dosed and that they could have better responses to therapy if their blood concentration were monitored and their dose adjusted based on those results¹. Blood level testing is a crucial tool in developing individualized treatment plans.

Blood Level Testing is now being offered to GIST patients through Avantix Laboratory. It is free for the patient. Novartis is funding the effort at this CLIA-certified laboratory with significant expertise in blood testing. To make this testing easily accessible to our GIST patient community, the Life Raft Group has obtained imatinib BLT test kits from Avantix Laboratory (www.gistalliance.com). With the help of physicians, we hope all patients will be able to utilize this crucial tool to help in their fight against GIST.

[¹] Demetri GD, Wang Y, Wehrle E, Blanke C, Joensuu H, von Mehren M. Correlation of imatinib plasma levels with clinical benefit in patients (Pts) with unresectable/metastatic gastrointestinal stromal tumors (GIST) (abstract, oral presentation). 2008 Gastrointestinal Cancers Symposium. Orlando, January 25–27, 2008

[²] Widmer N, Decosterd LA, Leyvraz S, Duchosal MA, Rosselet A, et al. Relationship of imatinib-free plasma levels and target genotype with efficacy and tolerability. *British Journal of Cancer* 98:1633-1640. 2008

[³] Picard S, Titier K, Etienne G, Teilhet E, Ducint D, et al. Trough imatinib plasma levels are associated with both cytogenetic and molecular responses to standard-dose imatinib in chronic myeloid leukemia. *Blood* 109: 3496-3499

Blood Level Testing is a relatively new procedure offered to GIST patients. If you are unfamiliar with the protocol for this procedure, please read the information below. If you have questions about this procedure, please contact Avantix Lab (1-866-990-0007) or go to: www.gistalliance.com.

- 1. Proper Equipment:** All of the components necessary for blood testing are provided in the kit, including the tubes, needles, and shipping labels. The blood draw procedure also calls for a centrifuge to separate the plasma from the blood. Please be sure you have a centrifuge in your office for the blood centrifugation which should be done within an hour of the blood draw. Also, the procedure calls for direct venipuncture from a forearm vein, but if your patient has a port, blood can be collected from the port. Please make sure the port is properly flushed and prepped before using and discard the first 1 to 2 ml of blood before collecting the blood in the tube provided.
- 2. Registration:** Please register yourself prior to the patient's appointment. The best method for registering is to fax the completed two page Registration Form provided by the LRG to Avantix Lab. Please follow up with a phone call to make sure you are registered and inform them when you are sending out the blood sample.
- 3. Timing your Appointment:** The testing protocol requires the blood be drawn no more than two hours before the next dose. Please be sure the patient's appointment has been made during this time period. For example, if they take their dose at 2:00pm every day, please be sure the blood is drawn between 12:00pm to 2:00pm and they have NOT taken their next dose until the testing has been performed. In circumstances where an appointment cannot be made in that 2-hour window, the blood draw can be taken up to two hours after the scheduled time for dosage, as long as the next dose has NOT been taken, making the range for testing 12:00 – 4:00pm.

Office hours may be an issue if they take their medication during early or late hours of the day. If they cannot get an appointment in your four-hour window, you may want to speak to them about *changing* the time they take their dose to make it possible to perform the test during office hours. Please make certain the patient is on the new dose schedule for one week leading up to the testing.

For patients that split their dose, the test is done when Gleevec drug levels are at their lowest level of the day. This will typically be before their first dose of the day. For example, a patient normally takes Gleevec at 8:00 AM and 5 PM. The test should be scheduled for as close to 8:00 AM as possible, but no later than 10:00 AM and the first dose of Gleevec should not be taken until after the test. If in doubt, determine what time the patient's drug levels will be at their lowest (trough level) and this would be the time to schedule the test.

- 4. Testing Day:** No fasting or other precautions have to be taken. Having all of the prior steps completed, the testing should go smoothly. It is a relatively simple procedure. The blood is drawn, centrifuged, and the plasma that is separated from the blood is collected and sent to the testing site where various procedures determine the trough level of imatinib in patient's blood.
- 5. Shipping Day:** Do not ship samples on either Friday or Saturday.
- 6. Obtaining Results:** Results will be sent back to you in 5-7 days via internet or fax, depending on how you have registered.

Thank you for helping the GIST patients by participating in this Blood Level Testing program. Please feel free to contact the Life Raft Group at (973) 837-9092 if you have any questions about our efforts to help the GIST community. Please contact Avantix Lab (1-866-990-0007) if you have any questions about the BLT program.