



BACKGROUND INFORMATION FOR THE MEDIA

Blood Level Monitoring

The introduction of imatinib mesylate (Glivec[®]), the first selective tyrosine kinase inhibitor, in 2001 revolutionized the management of chronic myeloid leukemia (CML). In clinical practice, imatinib has achieved high response rates, significant reductions in mortality, and is generally well tolerated,¹ and is viewed by many hematologists as the gold standard treatment for CML.²

Achieving a desirable therapeutic effect with Glivec may require dose optimization and management of other factors that may affect imatinib concentration in the blood. Factors which can affect the level of imatinib absorbed through the blood can include:

- Patient compliance: Since imatinib is administered orally, patients may not always take their pills as directed by their physician
- Interactions with other drugs that the patient may be receiving
- The patient's own body: Gastrointestinal abnormalities or other diseases can affect the extent to which imatinib is absorbed and metabolized

While pharmacokinetic monitoring is commonly used in many other branches of medicine such as neurology, cardiology and psychiatry, it has not been widely applied to date in clinical oncology practice. Monitoring of blood levels of imatinib in patients who exhibit a poor dose response to therapy, or who experience an adverse drug reaction, will help physicians understand the cause and use an "evidence based" approach to discussing possible non-compliance with patients.

The minimum effective concentration of imatinib in the blood has not yet been fully defined, and the relationship between imatinib blood levels and outcomes is still under investigation. A large-scale program to measure imatinib blood levels in CML patients, and their corresponding response to therapy, therefore, would help to increase the bank of data available with which to calculate the optimal dosing range of imatinib.

Blood monitoring and the European Treatment and Outcome Study (EUTOS) for CML

The European LeukemiaNet (ELN) and Novartis have established the European Treatment and Outcome Study (EUTOS) for CML, an initiative designed to help European healthcare professionals to optimize treatment and achieve the best possible outcomes for patients with CML. EUTOS for CML will offer healthcare professionals a comprehensive clinical support program, including access to the latest disease management tools and techniques to help further improve treatment outcomes for patients with CML. A key initiative of the study will be

to expand access to imatinib blood level testing. Blood level monitoring in CML patients is designed to help clinicians who believe their patients are not responding as well as expected to treatment, to determine if the patient is maintaining plasma trough level – a target concentration of imatinib in the blood – above the recommended minimum level, whether drug-drug interactions may be a factor, and to eliminate non-adherence as a potential cause of suboptimal response.

Because targeted oral therapies are relatively new in oncology, only recently have healthcare providers recognized that adherence to these regimens may be an issue in cancer patient care. Expanded access to the blood monitoring program will provide a way to further define the incidence and impact of noncompliance as well as enabling physicians to optimize therapy.

The European Treatment and Outcome Study (EUTOS) for CML is funded by Novartis

References

1. O'Brien SG, Guilhot F, Larson RA, et al. Imatinib compared with interferon and low-dose cytarabine for newly diagnosed chronic-phase chronic myeloid leukemia. *N Engl J Med* 2003;348:994–1004
2. Peggs K, Mackinnon S. Imatinib mesylate—the new gold standard for treatment of chronic myeloid leukemia. *N Engl J Med* 2003;348:1048–50