



BACKGROUND INFORMATION

The European Treatment and Outcome Study (EUTOS) for CML

The European Treatment and Outcome Study (EUTOS) for chronic myeloid leukemia (CML) was initiated in October 2007. EUTOS for CML is a collaboration between the European LeukemiaNet (ELN) and Novartis and is the first of its kind to unite a pharmaceutical company and an academic network in a program to improve treatment and outcomes for patients.

The objectives of the EUTOS for CML program are to:

- enhance understanding of the nature and management of CML
- improve standardized evaluation and monitoring and provide quality controlled outcomes for CML
- optimize diagnosis and treatment for CML across Europe

Over the past three years, EUTOS for CML has aimed to improve the management of this disease across Europe through four key projects

1. A patient registry to track the incidence and treatment of CML
2. Molecular monitoring to assess disease status
3. An educational program to share clinical expertise
4. Blood level testing to support management of treatment with imatinib

1. Gaining an understanding of the incidence and treatment of CML across Europe: Patient registry

The aim of the EUTOS for CML registry is to provide an understanding of the epidemiology of CML, the outcomes associated with treatment regimens and the management of the disease. Target enrollment of 4,000 patients has been achieved.

2. Standardized molecular monitoring program: Assessing disease status

Disease surveillance is important in tracking response to therapy to enable clinicians to make informed treatment decisions.

Molecular monitoring is conducted through a process called RQ-PCR (real-time quantitative polymerase chain reaction) or 'PCR' blood test, the most sensitive and accurate test to monitor CML. Philadelphia chromosome-positive, chronic myeloid leukemia, or Ph+ CML, is characterized by an abnormality known as the Philadelphia chromosome which produces a protein called Bcr-Abl. This protein has been identified to play a causal role in CML development. The level of Bcr-Abl in the blood correlates with disease severity.

Easily interpretable molecular monitoring results are needed to assess whether a patient with Ph+ CML has achieved or is making progress toward a desired response to CML therapy, and to ensure that a patient's treatment is optimized over time. There is evidence that reductions in the level of Bcr-Abl transcripts correlate with cytogenetic response and progression-free survival in patients with CML¹

The use of different testing methods can produce variation in measured responses between laboratories² and, until recently, it was essential for patients to be tested in the same laboratory over time to ensure comparable results. The EUTOS for CML program has expanded access to standardized PCR testing, with 51 standardised molecular monitoring laboratories validated across 28 countries to ensure that reliable, comparable results are secured to monitor disease status and inform treatment decisions.

European LeukemiaNet experts recommend continued molecular monitoring during targeted therapy and that patients with Ph+ CML should have molecular response assessment performed at regular three month intervals.^{3,4} A steady decline in Bcr-Abl transcripts indicate an ideal response to therapy. Scientists and technicians are becoming well versed in quality-controlled, standardized methodologies across Europe which will be important moving forwards in ensuring limited inter-lab variation.

3. Sharing clinical expertise: Spread of Excellence program

An educational program has been developed to inform clinicians about the optimal management of CML, the initiatives available as part of the EUTOS for CML program, and, ultimately, the learnings and data gathered as a result of the program.

To date, the Spread of Excellence program has produced:

- A EUTOS for CML website (<http://www.eutos.org>)
- ELN frontiers meetings: pan-European educational events involving hundreds of physicians and a select group of the next generation of hematologists
- Meetings for blood level testing training
- Physician newsletters, slide kit and resource packs
- ELN recommendations pocket cards
- ELN exhibition booth, posters and flyers
- Scientific publications
- Speaker training programs

4. Optimizing CML treatment: Validated pharmacological monitoring

Regular monitoring of response and other biological parameters is essential to ensure that every patient has the best chance of an optimal treatment response. Monitoring tyrosine kinase inhibitor blood levels in patients who experience a poor response to therapy or adverse drug reaction may help physicians understand the cause and provide an 'evidence based' approach to discussing possible non-compliance with the patient, take steps to ensure that the patient's imatinib dosing is appropriate or to discuss possible consequences of non-compliance with patients.

EUTOS for CML has offered free access to imatinib blood level testing, to supply clinicians with the data needed to optimize treatment. Approximately 10,000 imatinib blood levels tests have been conducted and 47 laboratories were set up across Europe, quality controlled through the Bordeaux central laboratory. Through the EUTOS for CML program, blood level testing has become an established part of the treatment protocol and as laboratory standards are now in place, this will not be a focus of the program going forward.

The future of EUTOS for CML

Following the success of EUTOS for CML, it is intended to extend the program beyond its original scope and to run it for a further two years.

ENDS

The European Treatment and Outcome Study (EUTOS) for CML is a collaboration between the European LeukemiaNet and Novartis

Please see Glivec (imatinib) and Tasigna (nilotinib) safety information on a separate page in this packet.

References

1. Kantarjian HM, O'Brien S, Cortes JE, *et al.* Complete Cytogenetic and Molecular Responses to Interferon- α -Based Therapy for Chronic Myelogenous Leukemia Are Associated with Excellent Long-Term Prognosis. *Cancer*. 2003;97:1033-1041.
2. Mueller MC, Erben P, Saglio G, *et al.* Harmonization of BCR-ABL mRNA quantification using a uniform multifunctional control plasmid in 37 international laboratories. *Leukemia*. 2008;22:96–102.
3. Hehlmann R, Hochhaus A, Baccarani M on behalf of the European LeukaemiaNet: Chronic myeloid leukaemia. *Lancet*. 2007;370:342-50.
4. Baccarani M, Saglio G, Goldman J, *et al.* Evolving concepts in the management of chronic myeloid leukemia: recommendations from an expert panel on behalf of the European LeukemiaNet. *Blood*. 2006;108:1809-20.