

EUTOS for CML

EUTOS for CML



European Treatment and Outcome Study

Outline

- Overview of EUTOS for CML
- Subproject overviews
 - CML Registry
 - Standardized Molecular Monitoring
 - Pharmacological Monitoring
 - Spread of Excellence
- Summary and close

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- A unique collaboration between industry (Novartis) and academia [European LeukemiaNet (ELN)]
- Collaboration will run for 3 years, from June 2007 until 2010, with a possibility to extend the contract
- Contract is between Novartis and the University of Heidelberg (legal representative of the ELN-CML group)
- For participation, subcontracts are required between individual institutions and the University of Heidelberg



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EUTOS for CML incorporates four subprojects

- **Expanded CML registry**
 - Pan-European baseline, treatment and outcome data
- **Molecular monitoring**
 - RQ-PCR standardization
- **Pharmacological monitoring**
 - Imatinib blood-level testing
- **Spread of excellence**
 - Educational activities and PR

RQ-PCR, real-time quantitative
polymerase chain reaction

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Objectives of EUTOS for CML

- 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 of CML across Europe

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Expanded CML Registry

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Objectives

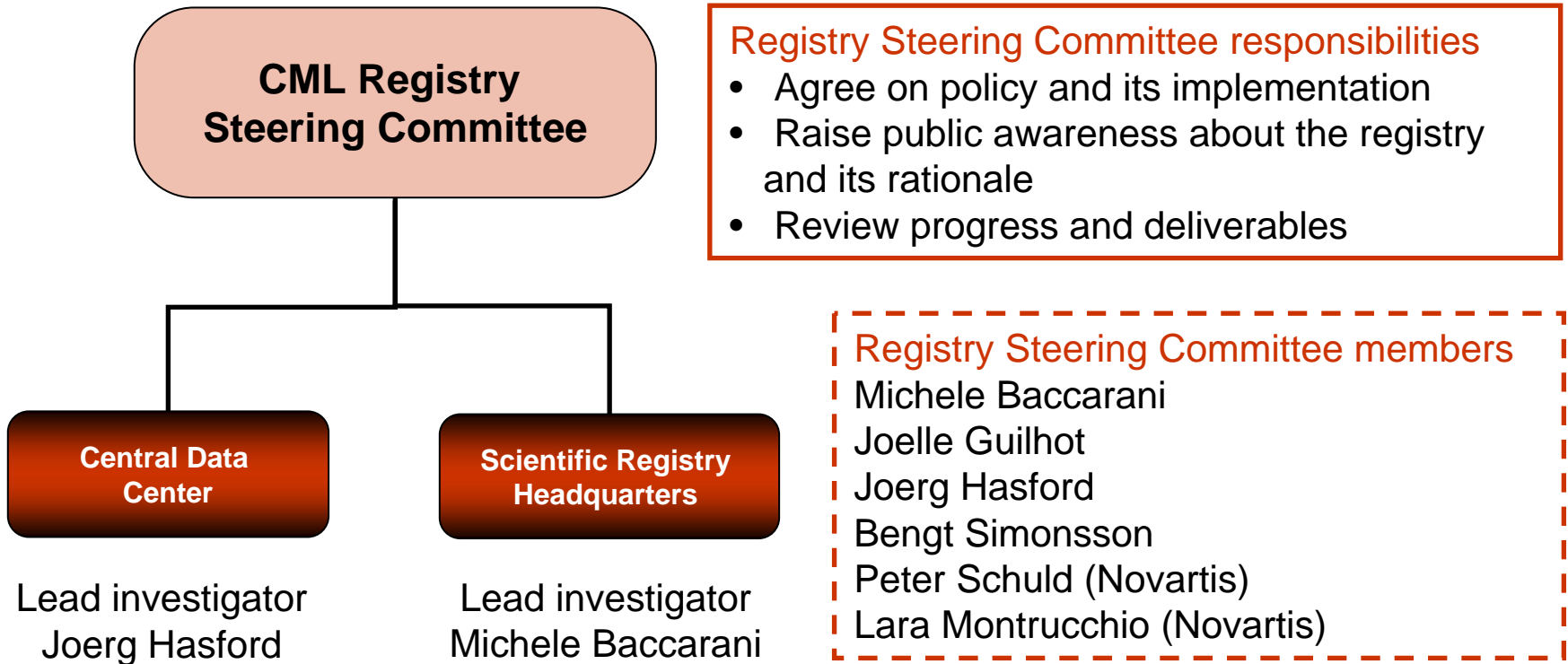
- The CML Registry will collect baseline, treatment and outcome data on patients with CML in Europe, in order to
 - Determine variations considering demographics and geographic region
 - Evaluate quality-controlled outcomes and implementation of ELN recommendations
 - Develop a comprehensive prognostic model to optimize treatment

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Organization



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Composition

- To achieve its objectives, the EUTOS for CML Registry is divided into three patient groups
 - **In-study:** patients from national study groups enrolled in prospective studies, taking imatinib frontline
 - **Out-study:** patients already registered in existing databases, irrespective of frontline treatment
 - **Prospective:** newly diagnosed patients not previously in registries or clinical studies

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In-study patients

- This group will include ~1900 patients enrolled in on-going studies of imatinib-based regimens frontline
- All patients were diagnosed between 2002 and 2006
- High quality and quantity of data are expected, due to the rigorous study protocols enforced by the respective Study Groups
- Patients in this group will have substantial follow-up data (4–8 years in 2010)

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Out-study patients

- Will include ~1560 patients currently registered in already existing or planned databases of national/regional study groups or reference centers
- All patients were diagnosed between 2002 and 2006
- Out-study patients will serve as a control group for the in-study patients (the selection bias is different)
- Creation of the out-study group also allows countries with no in-study patients to contribute to the Registry
- Patients in this group will have substantial follow-up data (4–8 years in 2010)

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Prospective patients

- The prospective patient group will include ~1700 patients who are newly diagnosed from 2009 onwards
- The prospective patient group should be representative of Europe, including as many countries as possible
- Study groups should include all newly diagnosed CML patients of a whole country or a region of a country but should not exceed 10 million people (details to be negotiated with study groups or with reference centers)

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Scientific committees

Committee

- Prognostic studies
- Population-based registries
- Imatinib failures
- Other/additional chromosomal abnormalities
- Point mutations
- Complete molecular response
- Imatinib discontinuation in complete responders
- Pharmacosurveillance, adverse events

Coordinator

Joerg Hasford

Bengt Simonsson

Joëlle Guilhot

David Marin

Simona Soverini

Francisco Cervantes

Andreas Hochhaus

Juan Luis Steegman

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Current status (Sep 2008)

- A study plan for the **in-study** and **out-study** patient groups has been finalized, including:
 - Patient numbers (per study group) and reimbursement
 - Patient eligibility criteria
 - Minimal core dataset for patient registration
- Data from ~2500 eligible in-study and out-study patients have already been registered at the Central Data Center
- A study plan for the **prospective** patient group will be finalized by the Steering Committee in the coming months

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Summary

- CML Registry will collect baseline, treatment and outcome data on patients with CML in Europe
- Registry is divided into in-study, out-study and prospective groups
- Significant progress has already been made with the in- and out-study registries; data collection for the prospective registry will begin in 2009
- Groups interested in participating in the CML Registry should contact Michele Baccharani (michele.baccharani@unibo.it)

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Standardized Molecular Monitoring

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Rationale for molecular monitoring

- Early recognition of relapse:
 - A rise in BCR-ABL transcript levels may be a warning sign of relapse due to imatinib-resistant BCR-ABL mutations, inappropriate imatinib dosing or lack of patient adherence with therapy
 - The ELN recommendations (2006) note that ‘...there is currently no consensus regarding the degree of increase which should cause concern’
 - The NCCN guidelines (V. 2.2009) suggest that in patients with a 1-log increase in BCR-ABL transcript levels, molecular testing should be repeated in 1–3* months and mutational analysis considered
- Prognostic information:
 - Data from the IRIS trial suggests that patients achieving both MMR and CMR at 12 months of treatment are likely to be free from disease progression to AP/BC at 5 years

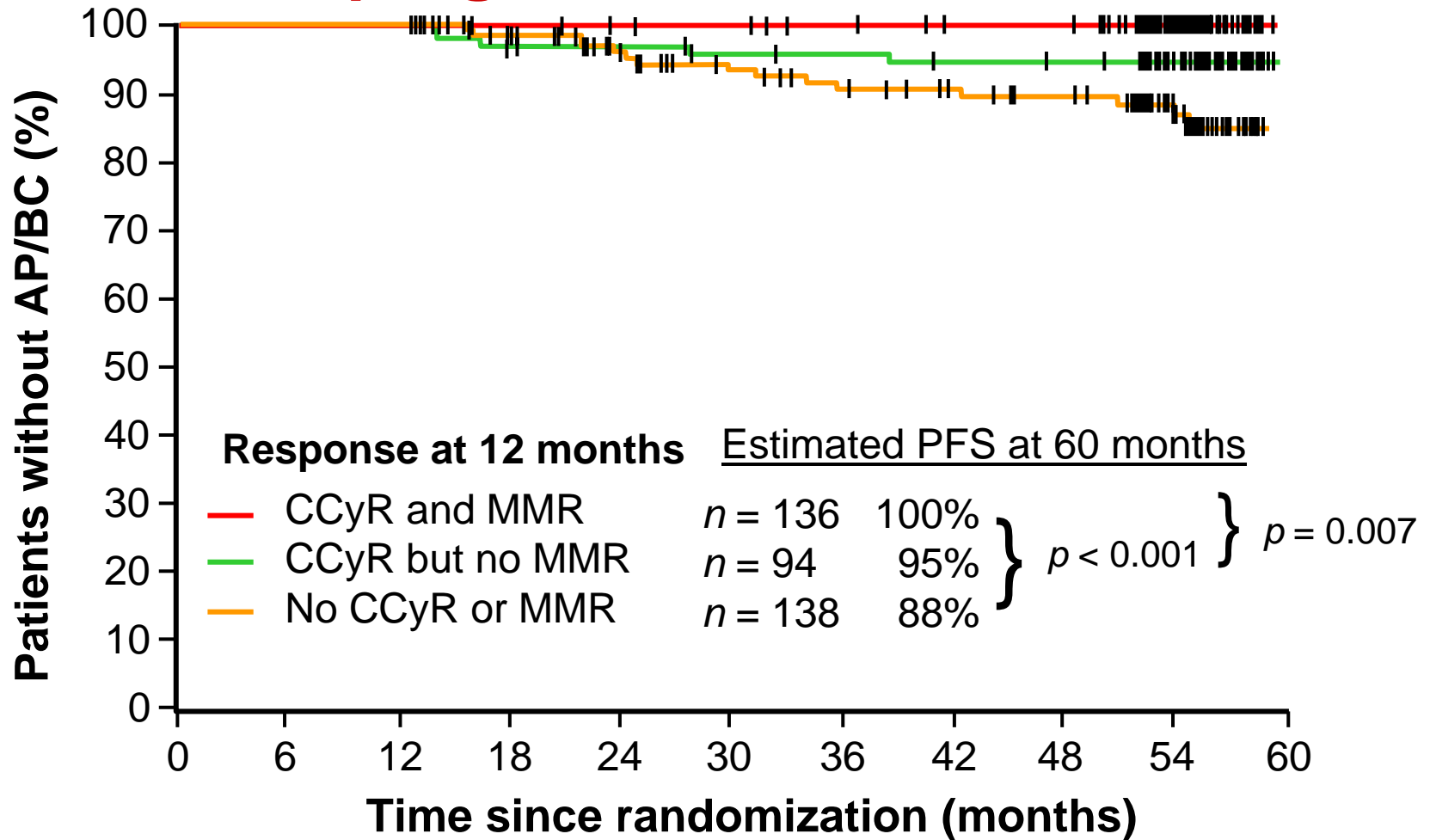
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*In patients without a major molecular response, bone marrow cytogenetics is recommended

Rationale for molecular monitoring: prognostic information



CCyR, complete cytogenetic response;
MMR, major molecular response

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Druker *et al.* *N Engl J Med* 2006;355:2408.

ELN recommendations 2006*: monitoring treatment response

	Hematologic response	Cytogenetic response	Molecular response
Frequency	<ul style="list-style-type: none"> ▪ Every 2 weeks until a complete response has been achieved and confirmed ▪ Every 3 months unless otherwise required 	<ul style="list-style-type: none"> ▪ Every 6 months until a complete response has been achieved and confirmed ▪ Then every 12 months 	<ul style="list-style-type: none"> ▪ Every 3 months
Methods	<ul style="list-style-type: none"> ▪ Complete blood count with differential 	<ul style="list-style-type: none"> ▪ Conventional cytogenetic examination ▪ FISH (only before treatment) 	<ul style="list-style-type: none"> ▪ RQ-PCR

*ELN recommendations due for update in 2009

FISH, fluorescence *in situ* hybridization

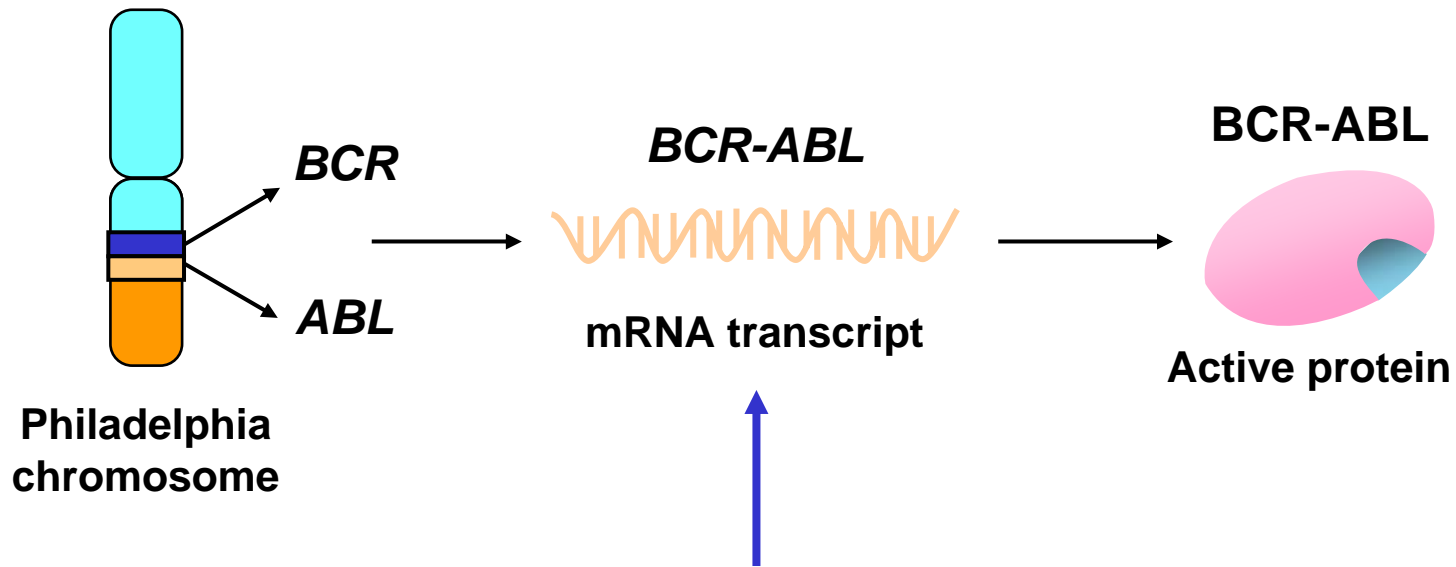
Baccarani *et al. Blood* 2006;108:1809.

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Molecular monitoring: measuring *BCR-ABL* transcript levels



Quantitative detection of *BCR-ABL* transcripts
by real-time quantitative PCR (RQ-PCR)

Adapted from Mensink *et al.*
Br J Haematol 1998;102:768.

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Objectives of the EUTOS for CML Molecular Monitoring project

- International standardization of RQ-PCR analysis for BCR-ABL quantification and for detection of BCR-ABL mutations
- Determine prognostic significance of BCR-ABL mutations
- Establish at least one ELN-certified lab per country that can serve as a national reference lab.
- An exchange program for scientists and technicians to allow spread of quality controlled, standardized RQ-PCR methodologies all over Europe
 - Regular control rounds using patient material (lysates of CML cells in normal cells) will ensure high-quality reliable results in the monitoring of CML patients in all countries

Final aim – European standardization

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Molecular Monitoring Working Group

- Nick Cross (UK)
- Andreas Hochhaus (Germany)
- Giuseppe Saglio (Italy)
- Alfredo Covelli – Novartis

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Rationale for standardized molecular monitoring

- Differences in testing methods and control genes have caused variability between laboratories, making it difficult to
 - Compare results for the same patient measured in different laboratories
 - Compare the results seen in a patient with those observed in the IRIS trial
- Standardization of RQ-PCR methodology and reporting allows the results from different laboratories to be compared with one another, and also with the IRIS data
- The EUTOS for CML Molecular Monitoring project is facilitating the standardization of RQ-PCR monitoring across Europe

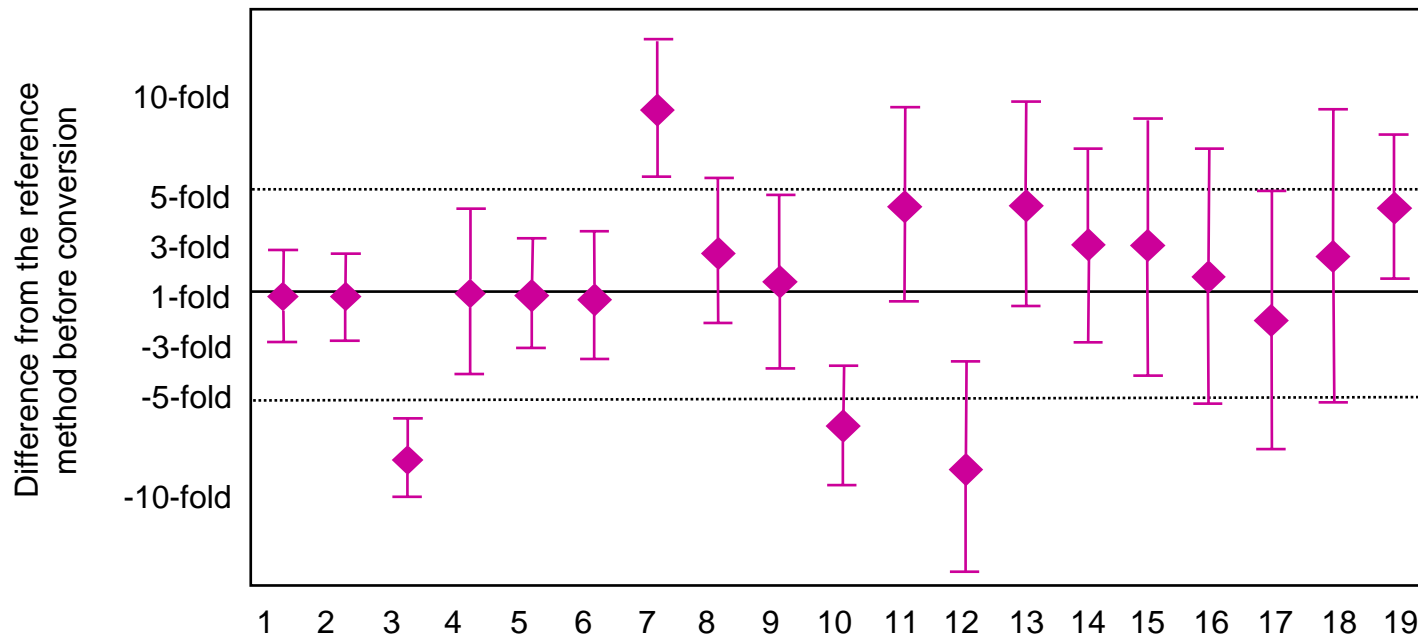
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19 BCR-ABL transcript quantification methods: results before conversion to IS

- Branford et al completed validation procedures for 19 BCR-ABL transcript quantification field-methods
- Before conversion the average difference between each field method ranged from 7.7-fold lower to 8.1-fold higher



Field method number
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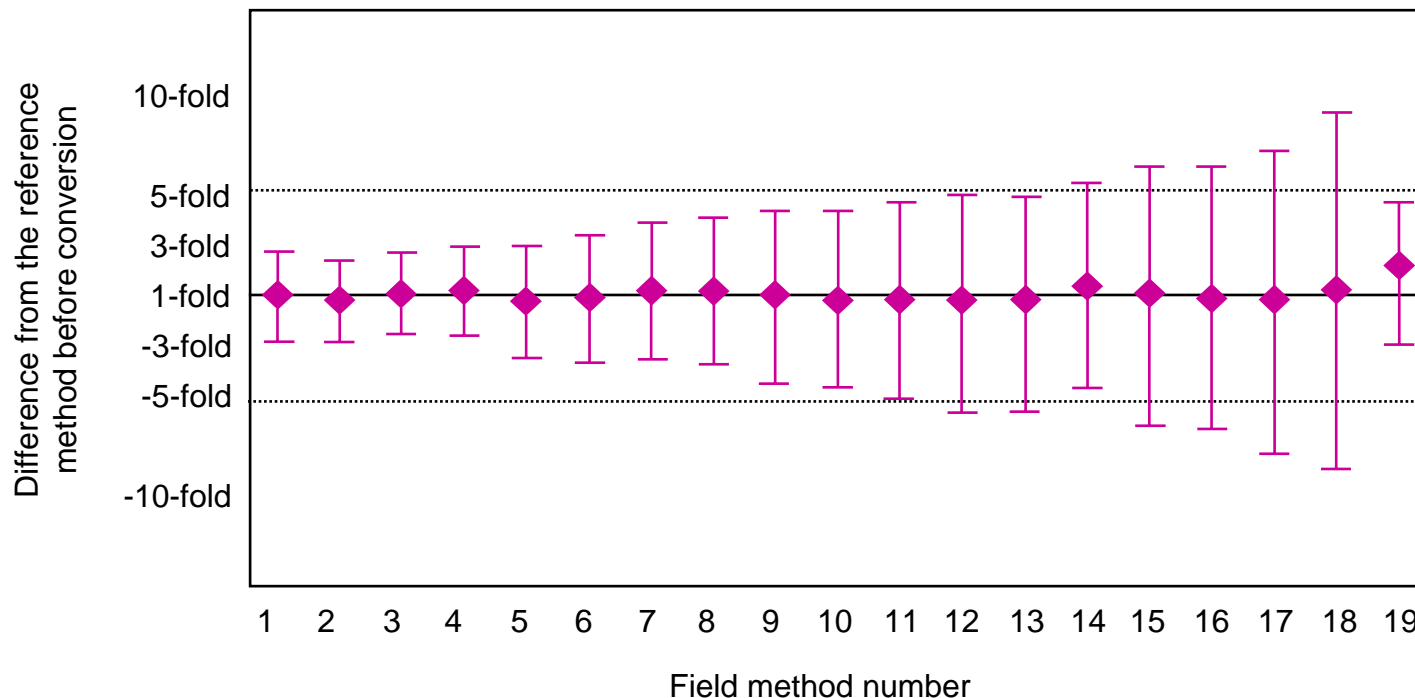
Branford *et al. Blood* 2008;112:3330–3338.



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19 BCR-ABL transcript quantification methods: results following conversion to IS

- Following conversion the average differences between each field method were within +/- 1.2-fold*



*95% limits of agreement varied

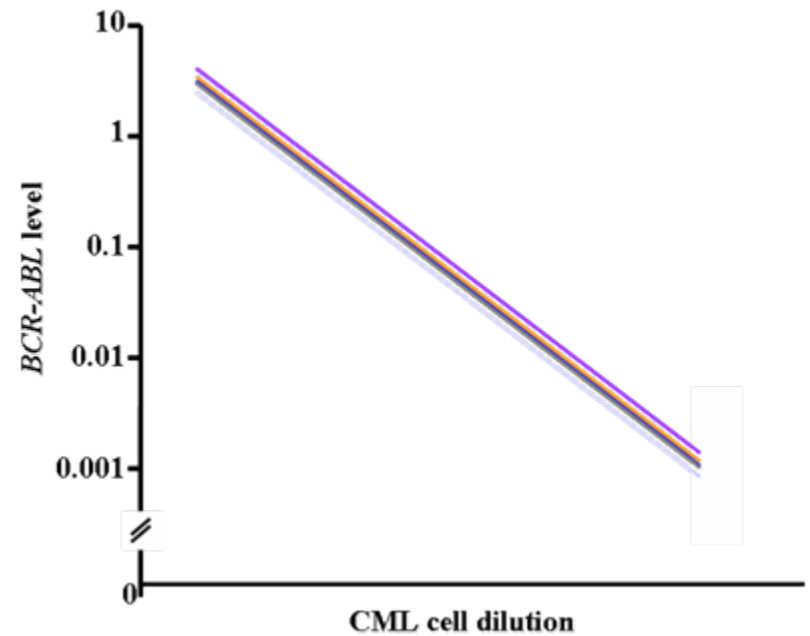
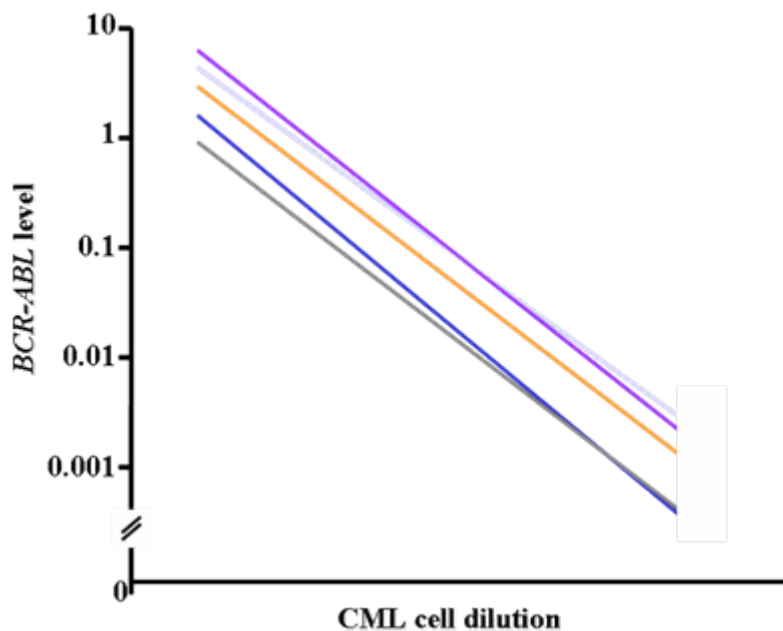
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Branford *et al. Blood* 2008;112:3330–3338.

Why do we need a conversion factor? Inter-laboratory results before and after conversion



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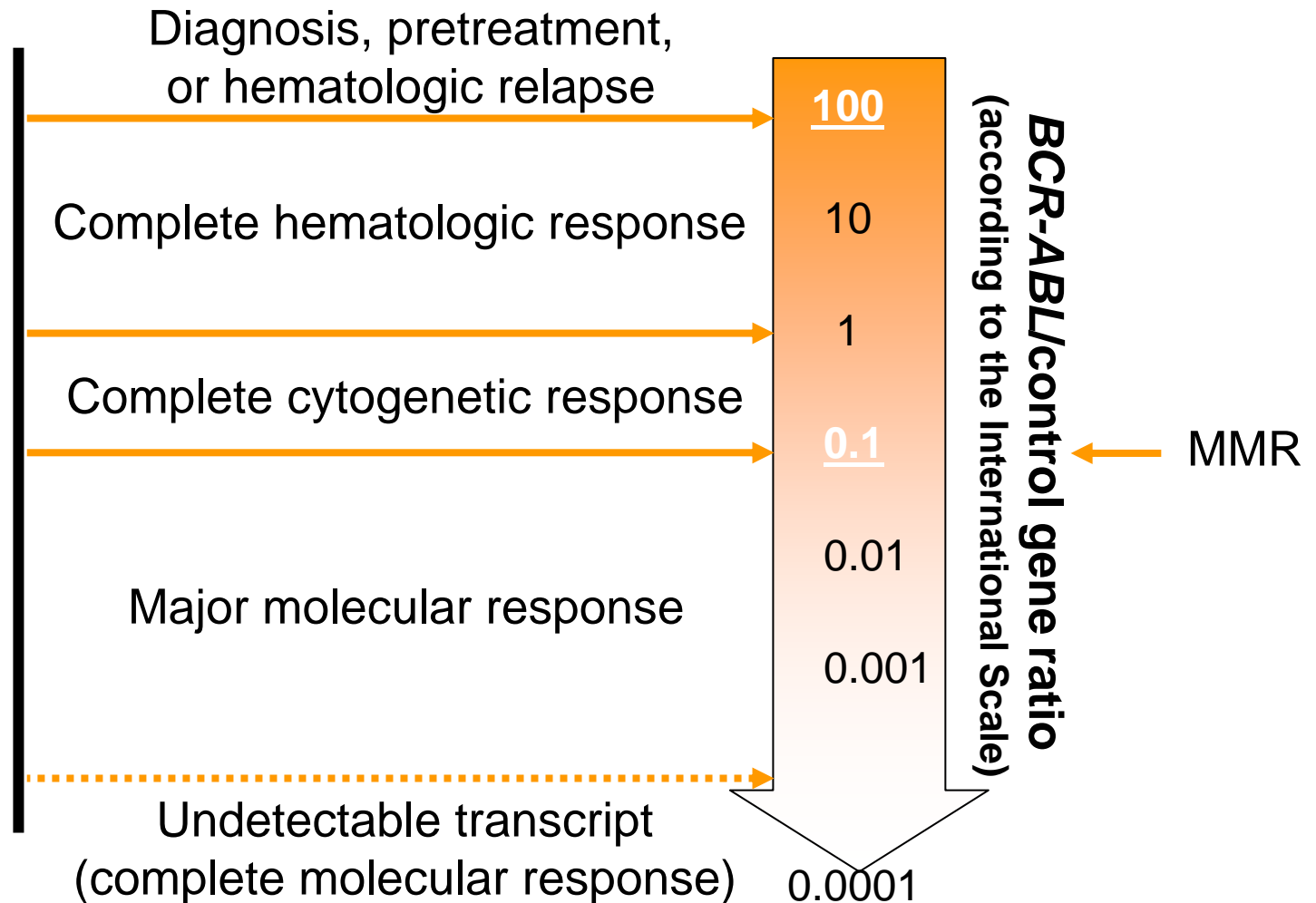
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International Scale

- The International Scale (IS) is based on the ratio of *BCR-ABL* copy numbers to control gene copy numbers
- It is dependent on two anchor values
 - A standardized baseline for the ratio of *BCR-ABL* to control gene (taken as 100% on the IS)
 - A 3-log reduction from this baseline (taken as 0.1% on the IS). This value is equivalent to MMR



Anchor values in the International Scale



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Hughes *et al.* *Blood*
2006;108:28–37.

Current status (Sep 2008)

- Fifty national reference centers to be included in the project
 - Phase I, 23 labs
 - Phase II, 27 additional labs
- Standardized lysates have been sent out to labs
- Educational documents describing project and providing lab guidelines have been circulated

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Summary

- Variability between testing laboratories has made it difficult to compare molecular monitoring data between labs
- The International Scale reduces variability and allows for standardized testing and reporting
- Through EUTOS for CML, 50 labs will be standardized around Europe

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Pharmacological Monitoring

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Blood level testing (BLT)

- A physician may want to consider imatinib BLT if a patient is
 - **Not responding to imatinib as well as expected**
 - Thought not to be adhering to their imatinib regimen
 - Thought to be experiencing drug–drug interactions
 - Experiencing side effects that are unusually severe for the prescribed dosage

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Patient not responding as well as expected

French BLT study

- Trough plasma levels of imatinib were measured in patients with Ph+ CML
- Results from this study indicated
 - Trough plasma levels of imatinib were associated with the likelihood of achieving CCyR and MMR
 - Mean imatinib plasma levels were significantly higher in patients with CCyR (n=56) than in those without (n=12)
 - Mean imatinib trough plasma levels were significantly higher in patients with MMR (n=34) than in those without (n=34)

CCyR, complete cytogenetic response;
MMR, major molecular response

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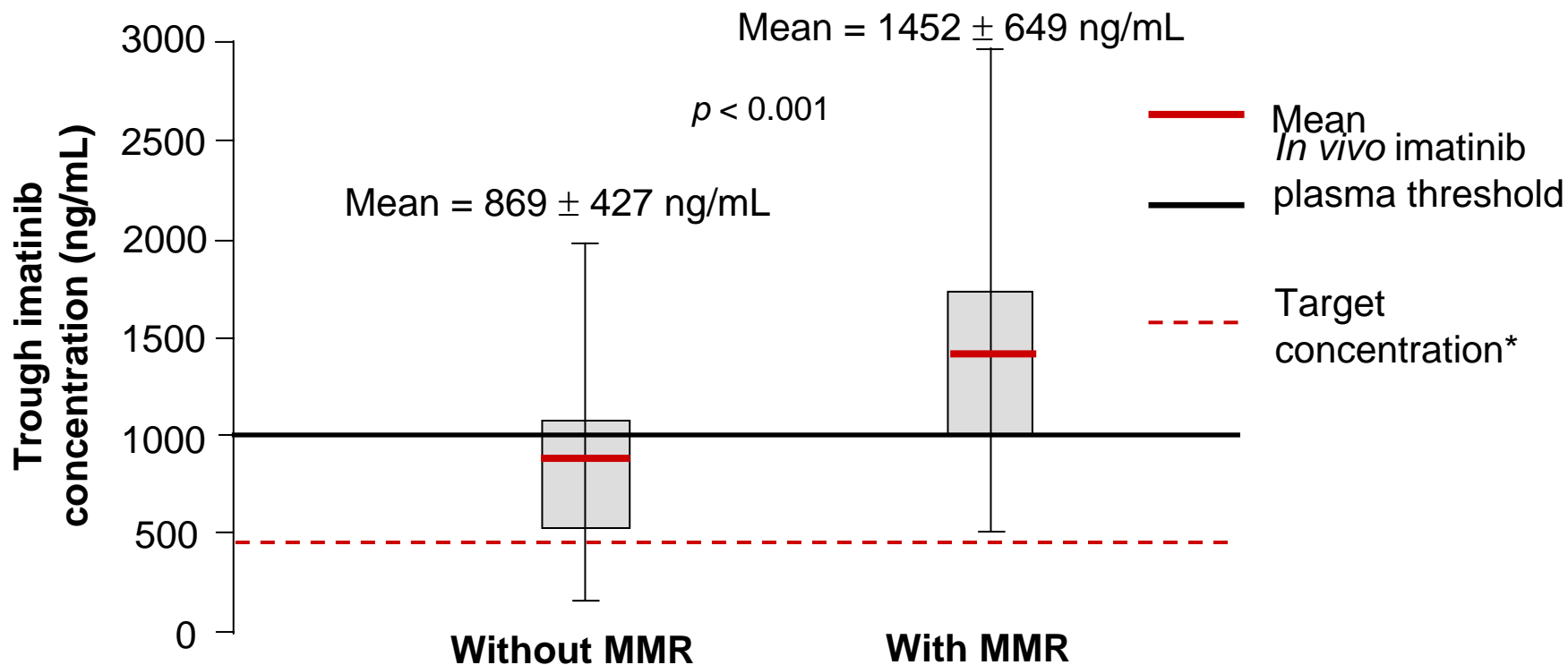


European Treatment and Outcome Study

Picard *et al.* *Blood* 2007;109:3496–3499.

Patient not responding as well as expected

Mean trough imatinib level was significantly higher in patients who achieved MMR than in those who did not



*Required to result in *BCR-ABL*-positive cell death *in vitro*.

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Picard *et al.* *Blood* 2007;109:3496–3499.

Patient not responding as well as expected

- The study identified a plasma 'threshold' of 1002 ng/mL
- The majority (76%) of patients with MMR had trough plasma levels exceeding the 1002 ng/mL threshold
- The majority (71%) of patients without MMR had trough plasma levels below the threshold

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European Treatment and Outcome Study

Picard *et al.* *Blood* 2007;109:3496–3499.

Patient not responding as well as expected

Imatinib trough blood levels – correlation with clinical response (Larson *et al.* 2008; IRIS data)

- Study assessed
 - Clinical significance of imatinib plasma concentration, as measured at steady state (day 29 of treatment)
 - How variability in imatinib exposure correlates with responses
- Included 351 (of 553) patients randomized to initial imatinib 400 mg/day in the IRIS trial, with imatinib plasma levels available on day 29 of treatment
- Imatinib plasma trough levels were grouped into three plasma concentration categories based on distribution among four quartiles (Q1, Q2–Q3, and Q4)
- These categories were used for retrospective subgroup analysis

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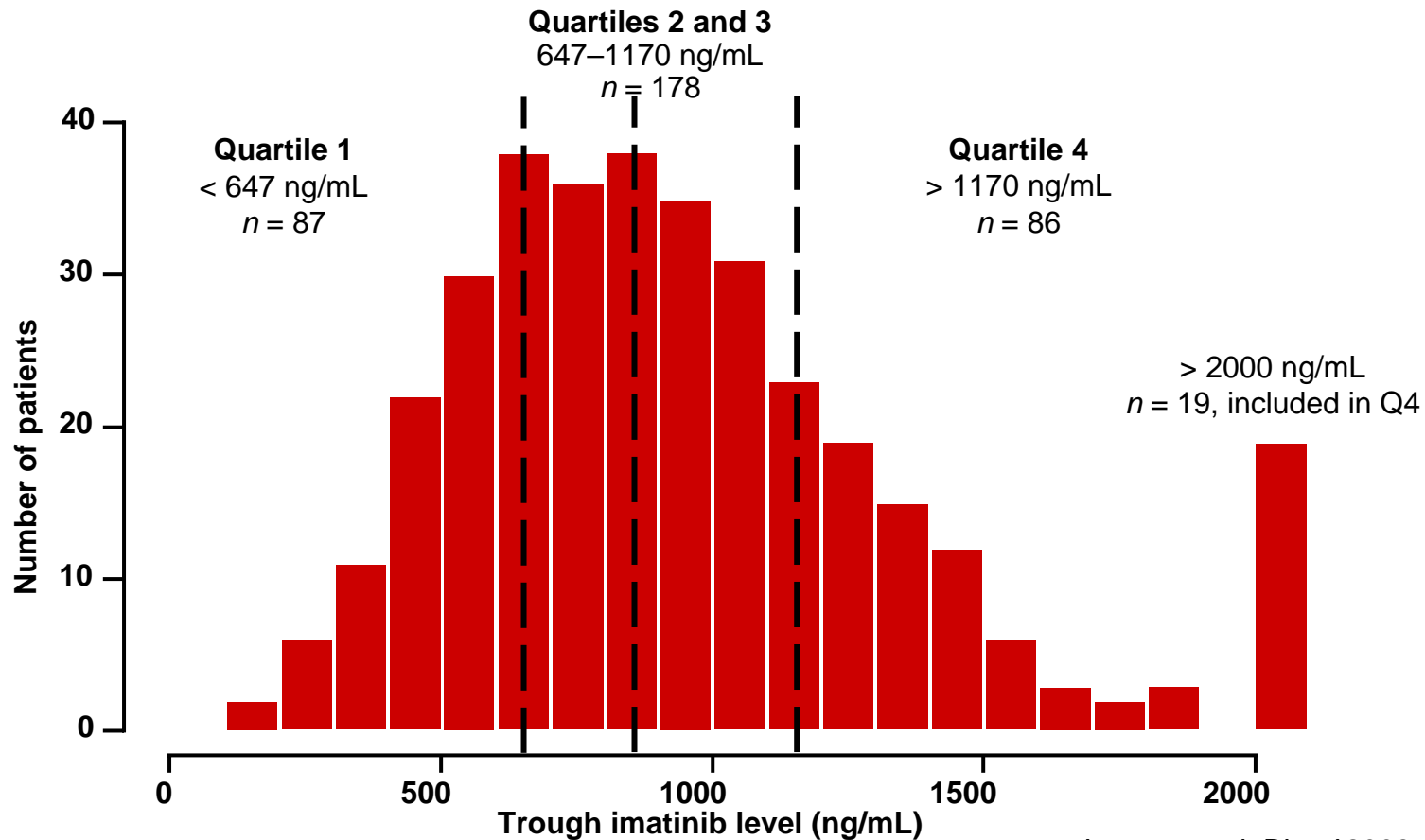


European Treatment and Outcome Study

Larson *et al.* *Blood* 2008;111:4022–8.

Patient not responding as well as expected

Patients were divided into four quartiles according to imatinib blood level

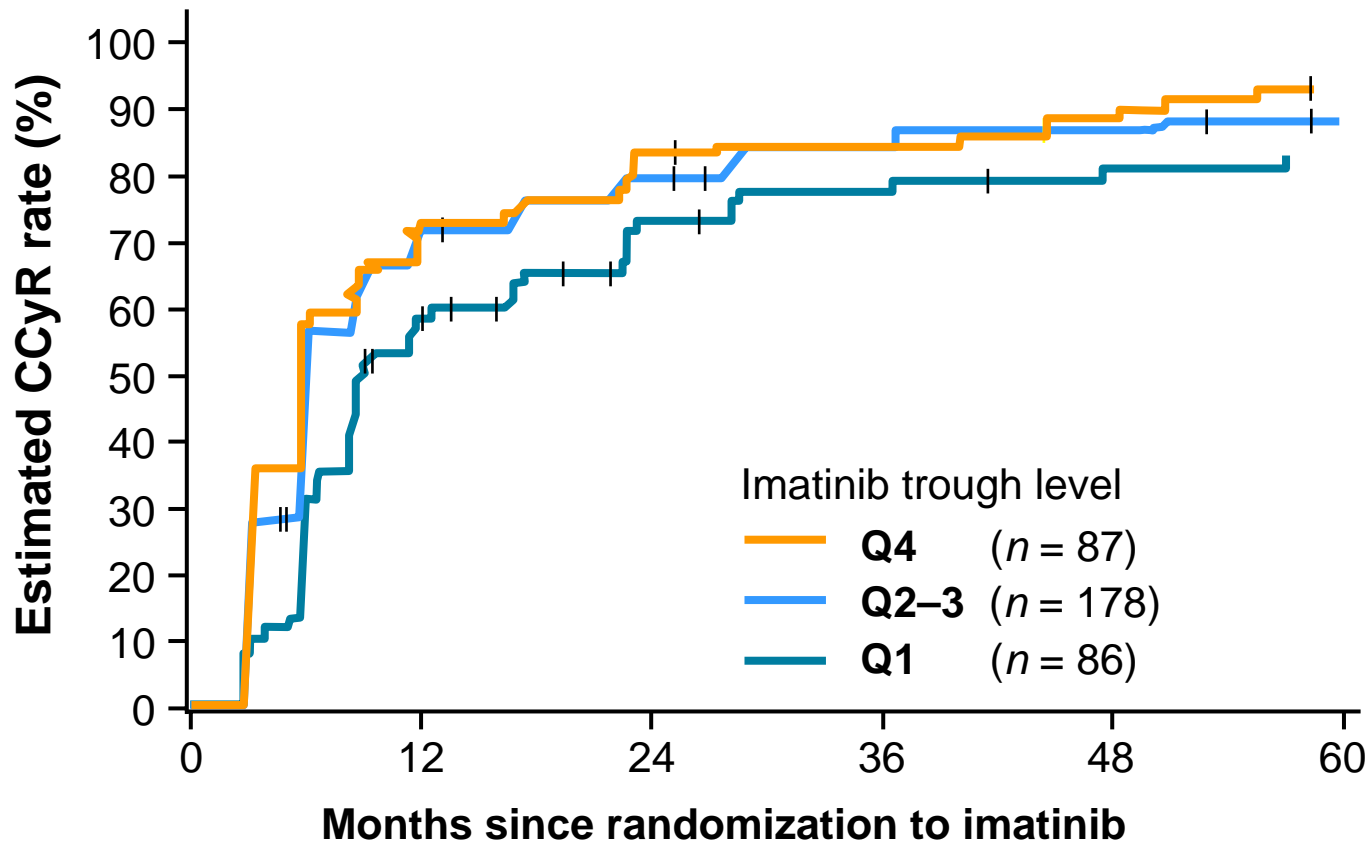


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Larson et al. *Blood* 2008;111:4022–8.

Patient not responding as well as expected

Estimated cumulative CCyR rates according to imatinib trough levels



At 5 years, Q1 vs others, $p = 0.005$, and $p = 0.01$ overall

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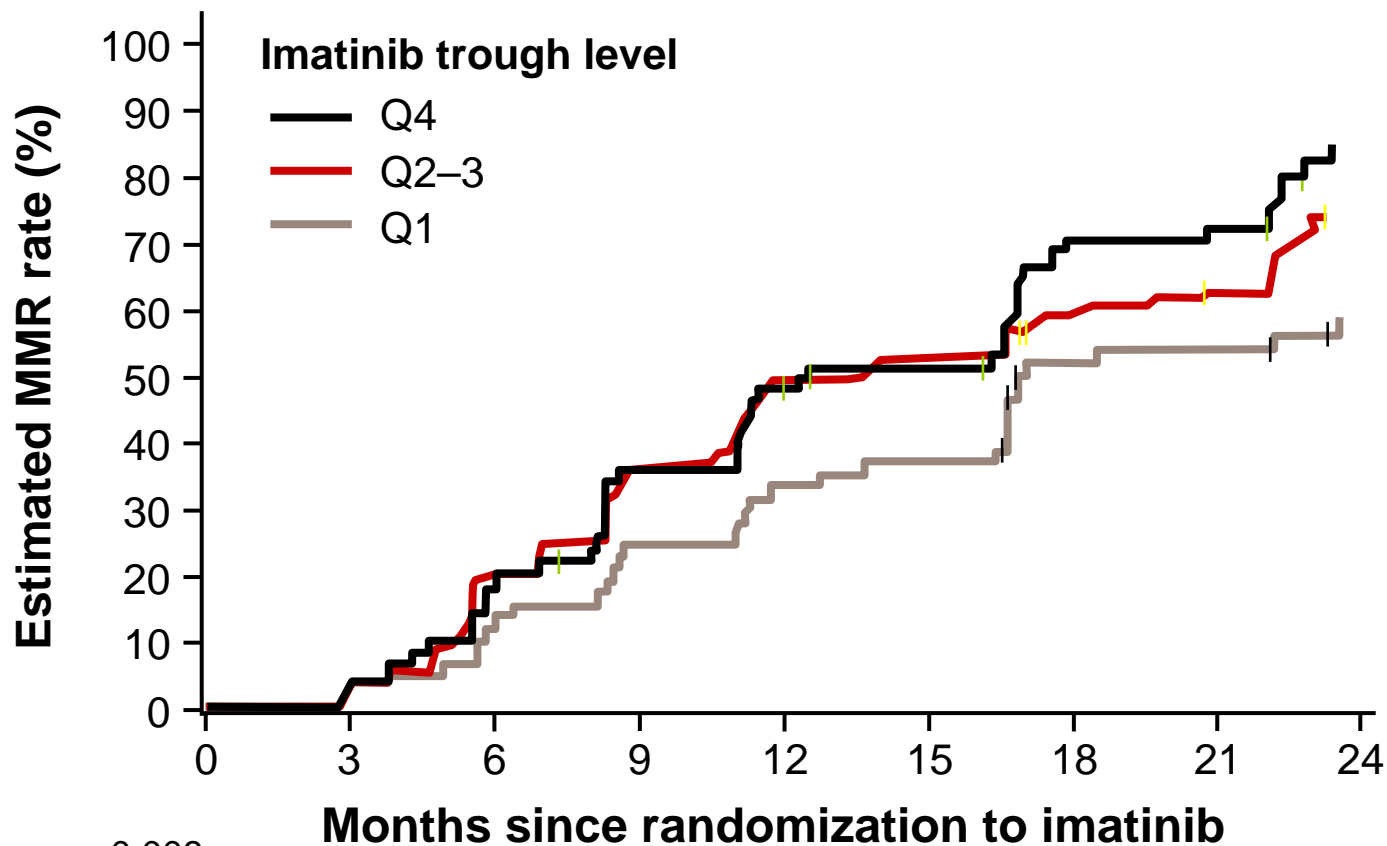


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Larson *et al.* *Blood* 2008;111:4022–8.

Patient not responding as well as expected

Estimated cumulative MMR rates according to imatinib trough levels



Q1 vs others, $p = 0.008$,
and $p = 0.02$ overall

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Larson *et al.* *Blood* 2008;111:4022-8.

Patient not responding as well as expected

- A correlation has been demonstrated between imatinib blood levels and clinical response^{1,2}
- In some patients, unexpectedly poor response may be due to inadequate imatinib plasma concentrations
- If the imatinib blood level is low, dose escalation may improve response

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1. Picard *et al.* *Blood* 2007;109:3496.
2. Larson *et al.* *Blood* 2008;111:4022.

Blood level testing (BLT)

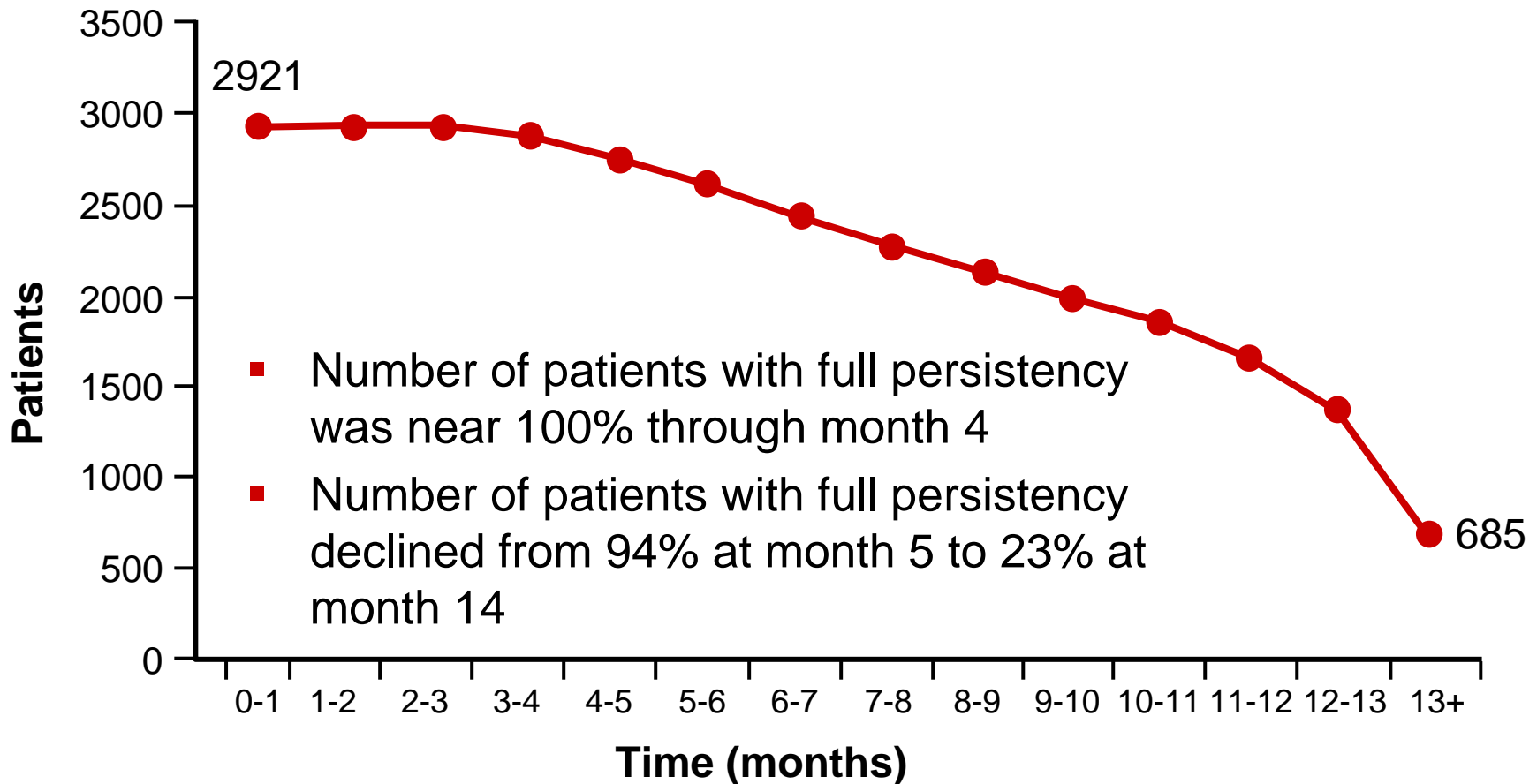
- A physician may want to consider imatinib BLT if a patient is
 - Not responding to imatinib as well as expected
 - **Thought not to be adhering to their imatinib regimen**
 - Thought to be experiencing drug–drug interactions
 - Experiencing side effects that are unusually severe for the prescribed dosage

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Suspected poor adherence



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Tsang *et al. J Clin Oncol.* 2006;24:330s. Abstract 6119.



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Blood level testing (BLT)

- A physician may want to consider imatinib BLT if a patient is
 - Not responding to imatinib as well as expected
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 - **Thought to be experiencing drug–drug interactions**
 - Experiencing side effects that are unusually severe for the prescribed dosage

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Drug–drug interactions

Because imatinib is metabolized by cytochrome P450 (CYP) 3A4 and CYP3A5, substances that inhibit or induce CYP3A4/5 may result in altered metabolism and consequently altered plasma concentrations of imatinib

Aprepitant

Clarithromycin / erythromycin

Cyclosporin

Itraconazole

Pimozide

Grapefruit juice

**CYP3A4/5 inhibitors:
may INCREASE imatinib
plasma concentration**

Barbiturates

Carbamazepine

Dexamethasone

Phenytoin

St John's wort

**CYP3A4/5 inducers:
may DECREASE imatinib
plasma concentration**

Glivec® [Summary of Product Characteristics]. Basel, Switzerland: Novartis Pharma AG. Available at: <http://www.glivec.com/content/tools/espc.jsp>.

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Blood level testing (BLT)

- A physician may want to consider imatinib BLT if a patient is
 - Not responding to imatinib as well as expected
 - Thought not to be adhering to their imatinib regimen
 - Thought to be experiencing drug–drug interactions
 - **Experiencing side effects that are unusually severe for the prescribed dosage**

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Unusually severe side effects

- High imatinib trough blood levels have been observed in some patients suffering from unusual severe toxicity¹
- Particular adverse events may be linked with high imatinib plasma concentrations²
- Imatinib blood level testing can help decision-making on how to manage patients with unusually severe side effects
- If the imatinib blood concentration is higher than expected, reducing the dose of imatinib may be a logical strategy

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1. Blasdel *et al.* *Blood* 2007;110:1699.

2. Larson *et al.* *Blood* 2008;111:4022.

Objectives of the EUTOS for CML Pharmacological Monitoring project

- Expand availability of imatinib BLT to a European level
 - Free of charge at a central facility (Bordeaux University Hospital)
- Establish monitoring facilities in respective countries, using a standardized monitoring protocol
 - Quality control performed by Bordeaux team
- Construct a dosing database to
 - Verify / define the therapeutic threshold (around 1000 ng/mL)

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Pharmacological Monitoring Working Group

- François Guilhot (France)
- François Xavier Mahon (France)
- Peter Schuld – Novartis

- Mathieu Molimard (France) is providing technical support

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Easy access to BLT

- A laboratory kit has been created to
 - Facilitate sample submission
 - Ensure all samples arrive in quality and time
- This may be requested from Novartis
- An e-mail address for investigators seeking technical advice has been set up
 - imatinib@chu-bordeaux.fr
 - Mailbox is checked regularly by the Bordeaux team

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Current status (Sep 2008)

- Central facility in Bordeaux is accepting sample from around Europe
- A binder of supporting information has been completed, providing information for physicians wishing to use the central BLT service in Bordeaux
- Control rounds for national laboratories have been initiated, and the first national laboratories have been validated

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Summary

- A physician may want to consider imatinib BLT if a patient is
 - Not responding to imatinib as well as expected
 - Thought not to be adhering to their imatinib regimen
 - Thought to be experiencing drug–drug interactions
 - Experiencing side effects that are unusually severe
- Through EUTOS for CML, imatinib BLT is available free of charge at a central facility in Bordeaux
- Quality-controlled national facilities are being established throughout Europe
- Please contact Professor Mahon (Bordeaux) or Dr Schuld (Novartis) for further information

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Spread of Excellence

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Objectives

- To bring the other EUTOS for CML projects together into a clearly defined offering for physicians
- To ensure all physicians receive high-quality medical education and resources that support them in caring for patients with CML

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Spread of Excellence Working Group

- Francisco Cervantes (Spain)
- Rüdiger Hehlmann (Germany)
- Fabrizio Pane (Italy)
- Susanne Saussele (Germany)
- Lara Montrucchio – Novartis

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Core resource

- Materials to support local implementation of the EUTOS for CML project
- Contents include
 - An introduction to EUTOS for CML
 - BLT and RQ-PCR backgrounders and case-based monographs
 - Media materials (sample releases, media backgrounders)

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Core resource

**Using Molecular Monitoring
to Optimize Therapy for
Chronic Myeloid Leu**

A Case-Based Review

EUTOS for CML
European Treatment and Outcome Study

**Imatinib
PCR testing fo**

Setting the standards
future of oncolo

CML
European Treatment and Outcome Study

**Using imatinib
blood level testing to
optimize therapy**

A case-based review

EUTOS for CML
European Treatment and Outcome Study

NOVARTIS
ONCOLOGY

**Imatinib
blood level testing**

A new initiative in the era of
targeted therapy for Ph+ CML

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NOVARTIS
ONCOLOGY



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Pharmacological Monitoring resource

- Physician information pack to support the EUTOS for CML Pharmacological Monitoring project
- Available on EUTOS for CML website
- Contains
 - An introduction to the EUTOS for CML Pharmacological Monitoring service
 - Patient information leaflet
 - Monitoring request form and guidance notes
 - Background information
 - Case-based monograph

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Pharmacological Monitoring resource

Pharmacological monitoring laboratories: Guidelines for participation

Background

The European Treatment and Outcome Study for chronic myeloid leukemia (EUTOS for CML) is a scientific collaboration between the European LeukemiaNet (ELN) and Novartis. Its main purpose is to support the optimization of treatment for CML.

There are multiple projects planned within the EUTOS for CML program. One of these is a pharmacological monitoring project, designed to increase the provision of plasma imatinib monitoring, free of charge, across Europe. The guidelines below are intended for laboratories that wish to offer this monitoring service.

Organizational structure

- The Pharmacological Monitoring project will be overseen by a Steering Committee, initially consisting of Prof. Francois Guilhot (Université de Poitiers, Poitiers, France), Prof. Francois-Xavier Mahon (Université Victor Segalen, Bordeaux, France), and Dr Peter Schulz (Novartis).
- The Steering Committee will lead the implementation of the Pharmacological Monitoring project. In particular, it will be responsible for nominating and certifying laboratories for participation within the project.
- It is anticipated that 1-2 laboratories will be selected per participating country. However, numbers may vary at the discretion of the Steering Committee.

Frequently asked questions

What is EUTOS for CML?

The European Treatment and Outcome Study for CML (EUTOS for CML) is a unique scientific collaboration between the European LeukemiaNet (ELN) and Novartis. It aims to use the strengths of the two organizations – the clinical expertise and experience of the ELN, allied to Novartis' outreach potential and funding provision – to help physicians optimize the treatment of CML.

Why do we need the EUTOS for CML program?

Strategies for the management of CML have evolved rapidly over the past few years, and Europe has played a leading role in this process. The EUTOS for CML program has been created to help keep Europe at the forefront of this advancement in the coming years. Ultimately, the program will foster continued improvements in outcomes for European patients with CML.

What projects are being run within the EUTOS for CML program?

There are four key projects:

- CML registry – expanding the existing European registry to facilitate the collection of baseline, treatment and outcome data from representative samples of European patients with CML.
- Molecular monitoring – promoting quality-controlled, standardized monitoring of therapeutic outcomes at the molecular level.

- Pharmacological monitoring – increasing the availability of therapeutic drug monitoring.
- Spread of excellence – promoting continuing medical education and awareness of CML.

Pharmacological monitoring Why monitor blood levels of imatinib?

Trough plasma levels of imatinib have been associated with molecular responses, with a level of around 1000 ng/L molecular response.¹

However, at a given dose, trough plasma levels of imatinib vary between patients. There are several potential causes, including plasma drug–drug interactions, and patient-related factors such as adherence.

Hence, if a patient is not responding to imatinib as expected, it is essential to determine whether imatinib blood levels should not be assumed that the patient has become resistant to the drug.

What is the purpose of the EUTOS for CML monitoring project?

The aims of the project are to increase the availability of standardized imatinib monitoring across Europe. To achieve this, the project will:

INFORMATION FOR PATIENTS

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Imatinib plasma level determination

IMATINIB (GLIVEC®) MONITORING REQUEST

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CENTRE HOSPITALIER UNIVERSITAIRE DE BORDEAUX
LABORATOIRE DE PHARMACOLOGIE CLINIQUE ET TOXICOLOGIQUE
Dr N. Molinard
Centre Hospitalier Pellegrin – Tropic
Plateau Technique 24 étage – 33076 Bordeaux Cedex, France
Tél : +33 (0)5 56 79 55 91 – Fax : +33 (0)5 56 79 55 95

Patient's identity:
Label with identifying number
Or
Signature

Details of the clinical unit:
Telephone:
Fax:
E-mail address (optional)

* (Imatinib), as part of your

assessment performed by the Department of
Clinical Pharmacology at the University of Bordeaux,
will be used to measure the

effectiveness of your treatment and your disease will be

monitored. Your participation in this study will not in any way influence the

care you receive or the results of your examinations on your part.

Your participation in this study will not in any way influence the

care you receive or the results of your examinations on your part.

Monitoring Request Form: Explanatory notes

Send the sample and Monitoring Request Form to this address.

Give details of the patient's name and personal details.

Tick the box or boxes that most closely match your reasons for wanting to monitor the blood imatinib level in this patient.

Give details of the patient's current treatment regimen, any incidents that occurred during sampling that could affect the results, and any BCR-ABL mutations the patient is known to have.

Note down the contact information for your facility or unit, so that we can contact you with any queries, and with the results of the imatinib blood-level testing.

Give details of the exact time and date at which the blood sample was drawn, and the time and date of the last dose of imatinib taken by the patient prior to sampling. Sampling should be done 24 ± 3 hours after the last dose.

Tick the boxes that match the most recently measured cytogenetic and molecular responses observed in the patient (if available).

Shipment instructions:

Plasma should be transported below +25°C by an approved carrier. To obtain free transport documents contact glivec@bordeaux.eutocml.com specifying both the number required and your full contact details.

EUTOS for CML



European Treatment and Outcome Study

Additional materials

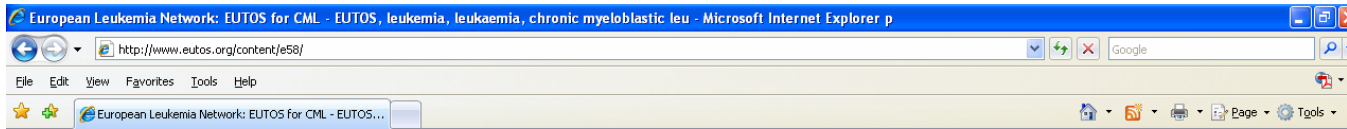
- Dedicated ELN booth for display at major congresses
 - Highlighting further the EUTOS for CML initiative and its place within the ELN
- Dedicated EUTOS for CML website (www.eutos.org) with direct links to the ELN and Novartis websites
 - Contains an overview of collaboration, materials, news, details of events and relevant contact information
- ELN recommendations summary card
- ELN newsletters

EUTOS for CML



European Treatment and Outcome Study

Additional materials



European Treatment and Outcome Study **Registry** Molecular Monitoring Pharmacology

- About the alliance
- Objectives
- News
- Contact
- Members only
- Press & Media
- Links
- Calendar

← EUTOS Home

EUTOS for CML

EUTOS for CML is a unique collaboration between the European LeukemiaNet and Novartis Oncology in Europe

News	Events
<p>2008/07/08: Update of the Spread of Excellence activities, July 2008</p> <p>2008/06/19: Meeting on targeted CML therapy: 17-19 October 2008, Cannes, France</p>	<p>Fr 2008/09/12 - Tu 2008/09/13 33rd ESMO Congress of the European Society of Medical Oncology</p> <p>Th 2008/09/18 - Sa 2008/09/20 3rd Conference on MYELOPROLIFERATIVE DISORDERS</p> <p>Su 2008/10/05 - Th 2008/10/09 ASTRO 50th Annual Meeting of the American Society of Therapeutic Radiology and Oncology</p> <p>Fr 2008/10/10 - We 2008/10/14 Gemeinsame Jahrestagung der DGHO, ÖGH und SÖGH</p> <p>Th 2008/10/30 - Tu 2008/11/04 7th Conference on CELL AND DISEASE: ADVANCED THERAPEUTIC INTERVENTIONS AND DRUG DEVELOPMENT</p>

EUTOS for CML

European Treatment and Outcome Study

A collaboration between ELN and Novartis to promote

- European CML registry
- Molecular monitoring
- Pharmacological monitoring
- Spread of excellence

CML REGISTRY

- Determine demographics and geographical variations
- Evaluate quality-controlled outcomes and implementations of ELN recommendations
- Develop a comprehensive prognostic model

MOLECULAR MONITORING

- Provide quality-controlled outcome data
- Distribute standardized RD-PCR for BCR-ABL quantification and mutation detection
- Determine prognostic significance of mutations

PHARMACOLOGICAL MONITORING

- Provide standardized imatinib blood level testing throughout Europe
- Establish national reference centers
- Define imatinib therapeutic threshold and toxic dose

SPREAD OF EXCELLENCE

- Promote implementation of ELN guidelines
- Promote information and communication by website, newsletters, CME, symposia

ELN LeukemiaNet[®] European

• EU-funded Network of Excellence
• www.leukemianet.eu

SCOPE

The ELN brings together

- 92 national leukemia study groups
- 87 interdisciplinary partner groups
- 1000 physicians and scientists in
- 133 centres and 24 countries
- caring for ten thousands of patients

ACHIEVEMENTS

- Structures for information, communication and network management centers, and an ELN website
- European registry (CML, MDS, ELL, ALL) to gather clinical and laboratory data that will be used to improve diagnosis and management
- Clinical trials program at a European level, including studies of tyrosine kinase inhibitors in several leukemia entities
- Consensus recommendations, including management of CML, standardization of molecular monitoring, detection of mutations, etc.

CURRENT RESEARCH

- Diagnostics**
Morphology and immunology
Cytogenetics
Minimal residual disease
Gene profiling
- New Treatments**
Clinical Trials
Stem cell transplantation
Supportive care



133 CENTERS IN 24 COUNTRIES



● Lead participant
● Participant

GOALS

- Strengthen scientific and technological excellence in research and treatment of leukemias
- Promote clinical trials
- Prepare guidelines
- Spread excellence

CONTACT

Network Management Center
Tel: +49 (0)521 393 4108
E-mail: nm@leukemia-net.org
www.leukemia-net.org

JOIN

Membership is available by institution. Everybody with an interest in leukemia is welcome. Prior contact with the respective WP-leader is required.

The European Treatment Outcome Study (EUTOS) is a collaboration between the European LeukemiaNet ELN and Novartis to improve understanding of CML, promote best practise, and enhance treatment outcomes, through 4 key projects:

EUTOS for CML



European Treatment and Outcome Study

Educational events

- Events with sessions dedicated to EUTOS for CML and its subprojects
 - ELN meeting, Budapest (Oct 2007)
 - ELN meeting, Cannes (Oct 2008)
- Events based on EUTOS for CML subprojects
 - Various Registry workshops
 - BLT training day, Bordeaux (Nov 2008)

EUTOS for CML



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Public relations

- A successful EUTOS for CML launch event was held in Budapest, Hungary in October 2007
 - 12 European journalists in attendance
 - 200 journalists accessed the webcast of the meeting over the following two months
- After the launch event:
 - 20 articles were published through printed and online outlets
 - News of the collaboration reached in excess of 2 million people across 9 markets

EUTOS for CML



European Treatment and Outcome Study

Summary

- The Spread of Excellence subproject ensures that all physicians receive high quality medical education and supports the other three subprojects through information and PR
- Materials created so far include
 - EUTOS for CML website (www.eutos.org)
 - Core resource
 - Pharmacological Monitoring resource
 - Congress booth
 - ELN recommendations summary card

EUTOS for CML



European Treatment and Outcome Study

EUTOS for CML Summary

EUTOS for CML



European Treatment and Outcome Study

Summary

- EUTOS for CML is a unique collaboration between the ELN and Novartis
- It aims 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 of CML across Europe
- The four subprojects – CML Registry, Molecular Monitoring, Pharmacological Monitoring, and Spread of Excellence – support these aims

EUTOS for CML



European Treatment and Outcome Study

Highlights so far (Sep 2008)

- **Registry**
 - Research plan and core dataset agreed for in-study and out-study patients
 - Research plan in development for prospective patients
- **Molecular monitoring**
 - Laboratory standardization on schedule
- **Pharmacological monitoring**
 - Central facility in Bordeaux is accepting samples
 - Local facilities across Europe undergoing standardization
- **Educational / spread of excellence**
 - Pocket card, exhibition booth, and website completed
 - Unrestricted support for ELN educational CML symposia
 - Core resource and Pharmacological Monitoring resource finalized
 - EUTOS for CML sessions planned at key meetings

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European Treatment and Outcome Study

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