ISRCTN31181395 https://doi.org/10.1186/ISRCTN31181395

Imatinib COncentration Monitoring Evaluation: the clinical usefulness of "routine" versus "rescue" therapeutic drug monitoring (TDM) interventions in chronic myeloid leukaemia (CML) patients

Submission date 27/05/2009	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 18/08/2009	**Overall study status** Completed	
Last Edited 20/01/2015	**Condition category** Cancer	

Plain English summary of protocol
Not provided at time of registration

Study website
http://www.imatinib-monitoring.ch/

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2009-011519-19

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
EudraCT 2009-011519-19

Study information

Scientific Title
A study to compare the clinical usefulness of "routine" versus "rescue" therapeutic drug monitoring (TDM) interventions in chronic myeloid leukaemia (CML) patients: a multicentre parallel group open-label randomised clinical trial

Acronym
I-COME

Study objectives
Could a routine therapeutic drug monitoring (TDM) program of imatinib improve the clinical outcome of chronic myeloid leukaemia (CML) patients treated with imatinib (i.e. good quality of life achieved by an event free survival and lack of moderate clinical or severe laboratory adverse events), compared with a rescue recourse to TDM reserved to problematic cases (i.e. suboptimal achievement of therapeutic response or suspicion of toxicity)?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Faculty of Biology and Medicine Ethical Committee of the University of Lausanne approved on the 31st March 2009 (ref: CE 31/09)

Study design
Multicentre parallel group open-label randomised clinical trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Quality of life

Participant information sheet

Can be found at: http://www.imatinib-monitoring.ch/

Health condition(s) or problem(s) studied
Chronic myeloid leukaemia (CML)

Interventions
Each patient will achieve a one-year study period while being included in one of the two following groups:

Intervention arm:
A systematic monitoring of imatinib plasma concentrations will be performed starting from study inclusion and during the whole observation period, in order to optimise the dosage regimen. Initially, up to 3 cycles of TDM-based adjustments will serve to normalise trough plasma levels around a target of 1000 ng/ml. Since no consensual upper limit of blood level has been defined for imatinib, a dosage reduction will be primarily driven by the clinical situation and will only be proposed in case of signs of toxicity (grade 2 or 3, as defined in the primary endpoint) along with a trough plasma level significantly higher than 1000 ng/ml. The trough level will also be measured at this time in order to document a possible high imatinib concentration. Measurement of blood concentration and dosage re-adjustment will remain accessible throughout the study in case of clinical concerns ("rescue TDM").

Control arm:
The patients will continue to be treated according to the standard of care for CML (i.e. ELN recommendations), without routine measurement of imatinib concentrations. Measurement of blood concentration will however be possible in case of clinical concerns ("rescue TDM") for either unsatisfactory therapeutic response or occurrence of toxicity. However, no access to TDM determinations will be granted on introduction of interacting drugs. In the absence of clinical concerns, the control patients will simply provide two blood samples (one at inclusion, and one after 1 year of treatment), which are planned to be measured by the laboratory only at the end of the study.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
1. Percentage of patients remaining without lack of efficacy or disease progression (i.e. "event-free" according to IRSI study definition)
2. Occurrence of moderate or severe adverse events (NCI-CTC grade 2 or more oedema, fatigue, headache, nausea, diarrhoea, musculoskeletal pain and skin rash; grade 3 or more anaemia, neutropenia, thrombocytopenia and increased liver enzymes; leucopenia and vomiting will not be analysed because of their obvious correlation with neutropenia and nausea)
3. Discontinuation of treatment

Measured after one-year follow-up.

Secondary outcome measures
1. Percentage of patients achieving major molecular response (MMR) after one-year follow-up
2. Median reduction of BCR-ABL transcripts (i.e. molecular response) over one year

3. Percentage of patients achieving complete cytogenetic response (CCyR) after one-year follow-up
4. Percentage of patients remaining without moderate adverse events of any kind (NCI-CTC grade 2)
5. Percentage of patients with clinical concerns at inclusion (i.e. lack of response/progression or adverse events) and presenting an improvement over one year
6. Percentage of patients with imatinib plasma levels above 1000 ng/ml after one-year follow-up
7. Predictive performance of either total or free concentrations for the achievement of therapeutic outcomes or the occurrence of concentration-related adverse effects (PK-PD relationships using all collected samples)
8. Interaction of genetic factors or co-medication known to affect drug transport (P-gp and hOCT1) and metabolism (CYP3A) with pharmacokinetic variables and efficacy/toxicity outcomes
9. Compliance of practitioners towards dosage adaptation advice

Overall study start date
31/03/2009

Completion date
31/12/2012

Eligibility

Key inclusion criteria
1. CML patients in the chronic or accelerated phase of the disease
2. Receiving imatinib since less than 5 years
3. Aged 18 years and older, either sex

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
300

Key exclusion criteria
1. Pregnant and breastfeeding women are excluded de facto from this study
2. Less than 18 years of age

Date of first enrolment
31/03/2009

Date of final enrolment

31/12/2012

Locations

Countries of recruitment
Switzerland

Study participating centre
Division of Clinical Pharmacology and Toxicology
Lausanne
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Sponsor information

Organisation
University Hospital Centre and University of Lausanne (CHUV) (Switzerland)

Sponsor details
Division of Clinical Pharmacology and Toxicology
Hopital Beaumont 06.633
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1011

Sponsor type
Hospital/treatment centre

Website
http://www.chuv.ch/

ROR
https://ror.org/05a353079

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
University Hospital Centre and University of Lausanne (CHUV) (Switzerland) - Division of Clinical Pharmacology and Toxicology

Funder Name
Novartis Switzerland, Bern (Switzerland) - received a grant in aid

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/12/2014		Yes	No