Patient-guided dose reduction of tyrosine kinase inhibitors in chronic myeloid leukaemia (RODEO): a prospective, multicentre, single-arm study

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Primary: To assess the proportion of patients with intervention failure at 12 months after dose reduction, defined as patients who have restarted their initial dose due to (expected) loss of major molecular response.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Haematological disorders NEC
Study type	Interventional

Summary

ID

NL-OMON52067

Source
ToetsingOnline

Brief title
RODEO

Condition

- Haematological disorders NEC

Synonym
chronic leukemia, chronic myeloid leukemia, CML

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: chronic myeloid leukaemia, dose reduction, tyrosine kinase inhibitors

Outcome measures

Primary outcome

The primary objective of this study is to assess the proportion of patients with treatment failure at 12 months after first dose reduction, defined as patients who have restarted their initial dose due to (expected) loss of MMR.

Secondary outcome

- The proportion of patients with intervention failure at 6 months after dose reduction and study end
- Change in outcomes at pre-defined timepoints after dose reduction with regards to:
o the proportion of patients with (patient-reported) side effects, including number of side effects (per patient and total) and severity of side effects using the EORTC QLQc30-CML24 and EORTC symptom list
o Patients* health-related quality of life using the Euroqol EQ-5D-5L
o Patients* beliefs about medicines using the Beliefs about Medicine Questionnaire (BMQ)
o Medication adherence using the Medication Adherence Report Scale (MARS-5)
o Healthcare consumption and productivity loss using the iMTA Medical

Cost Questionnaire (MCQ) and Productivity Cost Questionnaire (PCQ)

- Patient involvement during shared decision making will be assessed among

patients using the SDMQ9 and among healthcare providers using the SDMQ-doc

- Patients* level of distress and remorse will be assessed using the Decision

Regret Scale (DRS) and the Decision Conflict scale (DCS)

Study description

Background summary

Tyrosine kinase inhibitors have proven to be safe and effective in the treatment of chronic myeloid leukaemia. Despite their effectiveness, TKIs are also associated with adverse events that can decrease patients* quality of life and increase healthcare utilization and costs. Recent studies have indicated that dose reduction of TKIs can benefit optimal use by maintaining therapy efficacy while reducing adverse events and medication costs and increasing quality of life. These studies have used a one-size fits all approach and dose reduction was initiated by the healthcare provider. However, the choice for dose reduction can be considered as a preference sensitive decision as the preferred treatment option is dependent on personal needs and preferences of each individual (e.g. treatment goal and the extent of dose reduction). Thus, a patient-centred approach is needed to meet these needs and preferences.

Study objective

Primary: To assess the proportion of patients with intervention failure at 12 months after dose reduction, defined as patients who have restarted their initial dose due to (expected) loss of major molecular response.

Study design

prospective, multicentre, single-arm study

Intervention

The intervention is a patient*guided dose reduction. Patients will receive personalised, lower TKI doses, using an online patient decision aid and decide upon during a shared decision making consult.

Study burden and risks

A lower dose might be as therapeutically effective as standard dose. We expect that no more than 19% of the patients will experience intervention failure after dose reduction. Moreover, we expect that patients who restart their initial dose will regain MMR or better again. Furthermore, it is possible to expect some benefits with regards to patient-reported side effects, QoL, attitudes towards medication (intake), medication adherence due to lower TKI dose. Also, with this personalised approach, one can expect that patients* level of distress and remorse concerning their choice for dose reduction is low. However, investigating whether this will be true is an essential aspect of this study and will be assessed by collecting patient-reported data.

Reducing the dose induces the risk to lose molecular response. To accurately monitor the risk of loss of molecular response, an extra BCR-ABL1 analysis will be performed 6 weeks after each dose reduction and 3-monthly thereafter according to European guidelines [1]. All BCR-ABL results are seen and authorized by the treating internist-haematologist. An increase in the BCR-ABL1 transcript levels and possible loss of response is therefore noticed immediately. Literature show that in case of loss of MMR, resuming standard dose allows for MMR achievement within 4 months. Therefore, dose reduction does not endanger patients.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Aged >= 18 years
- Diagnosed with chronic phase CML
- treated with a TKI (imatinib, bosutinib, dasatinib, nilotinib, ponatinib, there are no restrictions regarding using a lower than standard dose at inclusion, or previously having switched from TKI due to toxicity
- major molecular response (MMR) or better for an uninterrupted period of at least 6 months at inclusion date
- Able and willing to participate
- Has provided written informed consent

Exclusion criteria

- Inability to understand the nature and extent of the trial and the procedures required (left at the discretion of the treating physician)
- Previous loss of MMR on a reduced TKI dose due to intolerability
- Molecular or cytogenetic failure to previous TKI
- Previous allogeneic hematopoietic stem cell transplantation
- CML in accelerated phase or blast crisis
- Pregnancy or lactation
- Life expectancy <= 1 year

Study design

Design

Study phase:	4
Study type:	Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	17-06-2022
Enrollment:	140
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Busolif
Generic name:	Bosutinib
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Glivec
Generic name:	Imatinib
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Iclusig
Generic name:	Ponatinib
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Sprycel
Generic name:	Dastinib
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Tasigna
Generic name:	Nilotinib
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	21-02-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-05-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-06-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-09-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-10-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2021-006581-20-NL
CCMO	NL78123.091.21