PERSISTENCE OF MAJOR MOLECULAR REMISSION IN CHRONIC MYELOID LEUKEMIA AFTER a second stop of TKI TREATMENT in patients who failed an initial stop attempt : a multicenter prospective trial

Published: 18-12-2017
Last updated: 12-04-2024

Assessment of treatment-free remission (persistence of MMR) after second attempt of TKI discontinuation in patients who failed a relapsed in the EURO-SKI study or under EURO-SKI like conditions. Patients must have received at least three years of...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON46534

Source
ToetsingOnline

Brief title
DASTOP2 trial

Condition

- Leukaemias
- Leukaemias

Synonym
Chronic myeloid leukemia

Research involving
Human

Sponsors and support

Primary sponsor: Uppsala University Hospital
Source(s) of monetary or material Support: Bristol-Myers Squibb,Universiteit ziekenhuis van Uppsala en farmaceutische industrie.,University Hospital Uppsala

Intervention

Keyword: 2nd stop, Chronic phase, CML, Stop dasatinib

Outcome measures

Primary outcome

The proportion of patients maintaining MMR at 6 and 12 months after discontinuing TKI a second time (survival without loss of major molecular response, MMR, defined as BCR-ABL1 > 0.1% on IS at one time point).

Secondary outcome

Assessment of:

1. Clinical and biological factors correlating with persistence of MMR or better after second TKI stop (BCR-ABL level before 2nd stop, Sokal score, gender, duration and type of TKI-treatment, duration of first TKI-stop, immunological biomarkers)

2. Number of patients who re-achieved stable MR4, and were offered study participation;.and Overall and progression-free survival and the occurrence of a restart of TKI without prior molecular relapse.

3. Time to reachievement of MR4 after second loss of MMR.

4. Adverse events related to second TKI stop, clinical and biological factors correlated to development of these AEs.

Study description

Background summary

In the EURO-SKI study, more than 800 patients with undetectable or low level disease defined by MR4 or better, were included and stopped their treatment. At EHA 2016, an analysis of 750 patients was presented. More than 55% of patients remained in treatment free remission after 12 months, with loss of MMR defined as trigger for re-treatment. In this study, almost all patients had used imatinib before stopping. Second generation TKIs induce faster and deeper molecular remissions, which may result in higher rates of successful discontinuation.

Previously, a small study where patients failing a first stop in the STIM-study were retreated with imatinib and then subjected to a second stop attempt after having been in CMR at least 1 year has been reported. In this study 4 out of 16 patients (25%) remained in MMR with a median follow-up of 32 months (15-53 months), and no hematological relapses or progressions to AP/BC were observed.

The induction of faster and deeper responses by 2nd gen TKIs makes it tempting to use these drugs in patients who relapsed after a discontinuation attempt by imatinib. The first-line studies of nilotinib (ENESTnd) and dasatinib (DASISION), comparing these drugs with imatinib in newly diagnosed patients, clearly showed that 2GTKIs induce faster and deeper molecular responses than imatinib.

Study objective

Assessment of treatment-free remission (persistence of MMR) after second attempt of TKI discontinuation in patients who failed a relapsed in the EURO-SKI study or under EURO-SKI like conditions. Patients must have received at least three years of further TKI treatment of which the two last years should be dasatinib. The patients must have been in MR4 for at least one year.

Study design

Multicenter phase 2 study, prospective, open label, uncontrolled.

Intervention

- Dasatinib treatment phase for 24 months.
- Treatment- Free Remission (TFR) phase, if patient had re-achieved a MR4 for at least 1 year.
- Follow up for 3 years.

Study burden and risks

As no treatment is given after the discontinuation, it is possible to expect some quality of life benefit, especially in patients that have suffered side effects on TKI treatment.

As explained in this study stopping TKI in patients in CMR induces a risk of molecular relaps of CML. Data from the EURO-SKI study show that in case of relapse, resuming TKI allows controlling the disease again. Data from the EURO-SKI study shows that it is safe and no patients progressed to AP/BC.
In this study, close monitoring of residual disease by RT-PCR after stopping TKI will allow early detection of possible molecular relapse.

As has been seen after stopping imatinib for the first time, myalgia and arthralgia, may also be expected to occur at a second stop trial.
In general, this is a benign phenomenon, not requiring therapy. However, in a few cases, it has been necessary to treat this pain syndrome with corticosteroids. These may also have adverse effects, like mood disorders, induction of diabetes mellitus, osteoporosis and immune suppression.

Contacts

Public
Uppsala University Hospital

Dag Hammarskölds väg 20
Uppsala 75185
SE
Scientific
Uppsala University Hospital

Dag Hammarskölds väg 20
Uppsala 75185
SE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. CML in chronical phase (CP) under TKI treatment after failing a prior attempt to stop treatment within EURO-SKI or outside the study but according to EURO-SKI trial procedures. For the latter group this requires at least 3 years of TKI treatment (first line or second line due to intolerance to first line) before first stop, and MR4 for at least one year before stopping.
2. Treated with TKI for at least one year after having failed a prior attempt to stop TKI. Previous TKI can be any.
3. Typical BCR/ABL1 transcript (b3a2 and/or b2a2) must have been confirmed at diagnosis or later during the disease course.
4. 18 years or older

Exclusion criteria

1. Previous hematological relapse after first stop of TKI.
2. Previous AP/BC at any time in the history of the disease.
3. Restart of TKI without loss of MMR after first stop
4. Current participation in another clinical study.
5. Previous or planned allogeneic stem cell transplantation.
6. Patients with contra-indications to dasatinib therapy due to comorbidities.
7. Subjects with acute hepatitis B virus (HBV) infections.
8. Uncontrolled or significant cardiovascular disease.
9. Pulmonary arterial hypertension.
10. Pleural or pericardial effusions of any grade at study entry are excluded
11. History of significant bleeding disorder unrelated to CML
12. Hypersensitivity to dasatinib and excipients of dasatinib tablets.

Study design

Design

Study type: Interventional
Masking: Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	20-11-2018
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Sprycel
Generic name:	Dasatinib
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	18-12-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	10-10-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	EUCTR2016-004106-34-NL
CCMO	NL62339.029.17