Nilotinib plus pegylated interferon alpha2b in CML.

Gepubliceerd: 03-12-2012 Laatst bijgewerkt: 18-08-2022

Nilotinib plus PegIFN will increase depth of response in CML patients who have stable responses above 0.01%.

Ethische beoordeling	Niet van toepassing
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON29139

Bron
NTR

Verkorte titel
NordDutchCML009

Aandoening

CML in chronic phase;suboptimal response or stable detectable molecular response after at least 2 years of imatinib treatment

Ondersteuning

Primaire sponsor: VU University Medical Center, Amsterdam
Overige ondersteuning: sponsor, Novartis, MSD.

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

1. The proportion of patients with confirmed MR4.0 IS at Month 12;
The predictive value for response of:

2. Relative and absolute numbers of CD4+ and CD8+ T cells, NK cells, NKT cells, B cells and regulatory T cells (CD4+, CD25+, FoxP3+), as measured by flow cytometry assay pre- and post-treatment;
3. The presence and frequency of BCR-ABL-, WT1, Prame- or PR1-specific cytotoxic T-cells as measured by flow cytometry using tetramer technique;
4. The cytotoxic capacity of lymphocytes, as measured by killing activity of NK cells, IFN ã production by and granzyme B staining of T cells after stimulation, all performed pre- and post treatment;
5. Plasma cytokine profiles, as measured by the Luminex multiplex array system pre- and post-treatment;
6. Phosphoproteomic profiles pre- and post-treatment;
7. The frequency of residual leukemic stem cells, as detected by flow cytometry using phospho-CRKL activity as a read-out of BCR-ABL activity.

Toelichting onderzoek

Achtergrond van het onderzoek

Study phase: Phase II.

Patient population:

Patients with suboptimal molecular response or stable detectable molecular residual disease after ≥2 years of treatment with imatinib (i.e. BCR ABL level between 0.01% and 1% IS).

Study objective:

To assess the effect of switching CML patients, who have been treated with imatinib ¡Ý2 years and who have stable detectable molecular residual disease between 0.01-1.0% (IS), to the combination of Nilotinib and PegIFN, in terms of the proportion of patients who achieve confirmed MR4.0.

Study design:

Single arm, open label, multicenter study to assess the efficacy, safety and tolerability of nilotinib 300 mg BID, alone and in combination with PegIFN 25 - 40 ¦Ìg/week in patients not in CMR. Patients will be treated with nilotinib 300 mg BID at the beginning of the study to establish the tolerability before adding PegIFN. Combination treatment will be continued until

Month 12, which is followed by monotherapy phase of nilotinib 300 mg BID.
Overall study duration for the individual patient is 24 months.

Doel van het onderzoek

Nilotinib plus PegIFN will increase depth of response in CML patients who have stable responses above 0.01%.

Onderzoeksopzet

Total expected study duration is 3 years.

Study start (FPFV): Jan 2013;

Recruitment end (LPFV): Jan 2014;

Study end (LPLV): Jan 2016;

Completion of Clinical Study Report (CSR): June 2016;

Publication date: June 2016.

Onderzoeksproduct en/of interventie

Patients will be treated with nilotinib 300 mg BID at the beginning of the study to establish the tolerability before adding PegIFN. Combination treatment will be continued until Month 12, which is followed by monotherapy phase of nilotinib 300 mg BID for 12 months.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Patients at least 18 years of age;

2. At diagnosis chronic myeloid leukemia in chronic phase;

3. Documented complete cytogenetic response by bone marrow (standard cytogenetics) or peripheral blood BCR ABL <1% IS;

4. Persistent disease demonstrated by two PCR positive tests (i.e. BCR ABL level between 0.01% and 1% IS) which have been performed during the past 9 months and more than 10 weeks apart. One of these should be performed within 1 month of registration;

5. Treatment with imatinib for at least 2 years with 400 mg and at a stable dose (i.e. the dose has not changed in the previous 6 months);

6. No other current or planned anti leukemia therapies;

7. ECOG Performance status 0,1, or 2;

8. Adequate organ function as defined by:

A. Total bilirubin <1.5 x ULN. Does not apply to patients with isolated hyperbilirubinemia (e.g. Gilbert's disease) grade <3;

B. ASAT and ALAT <2.5 x ULN;

C. Serum amylase and lipase = or < 1.5 x ULN;

D. Alkaline phosphatase =< 2.5 x ULN;

E. Creatinine clearance >30 ml/min;

F. Mg++, K+ >= LLN.

9. Life expectancy of more than 12 months in the absence of any intervention;

10. Patient has given written informed consent to participate in the study.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Prior accelerated phase or blast crisis;

2. Patient has received another investigational agent within last 6 months;

3. Previous treatment with nilotinib or dasatinib;

4. Prior stem cell transplantation;

5. Impaired cardiac function including any one of the following:

A. Inability to monitor the QT/QTc interval on ECG;

B. Long QT syndrome or a known family history of long QT syndrome;

C. Clinically significant resting brachycardia (<50 beats per minute);

D. QTc >450 msec on baseline ECG (using the QTcF formula). If QTcF >450 msec and electrolytes are not within normal ranges, electrolytes should be corrected and then the patient re screened for QTc;

E. Myocardial infarction within 12 months prior to starting study;

F. Other clinically significant uncontrolled heart disease (e.g. unstable angina, congestive heart failure or uncontrolled hypertension);

G. History of or presence of clinically significant ventricular or atrial tachyarrhythmias.

6. Known atypical BCR ABL transcript not quantifiable by standard RQ PCR;

7. History of active malignancy during the past 5 years with the exception of basal carcinoma of the skin or carcinoma in situ of cervix uteri or breast;

8. Acute liver disease or cirrhosis;

9. Previous or active acute or chronic pancreatic disease;

10. Another severe and/or life threatening medical disease;

11. History of significant congenital or acquired bleeding disorder unrelated to cancer;

12. Impairment of gastrointestinal (GI) function or GI disease that may significantly alter the absorption of study drug;

13. Patients actively receiving therapy with strong CYP3A4 inhibitors and the treatment cannot be either discontinued or switched to a different medication prior to starting study drug;

14. Patients who are currently receiving treatment with any medications that have the potential to prolong the QT interval and the treatment cannot be either discontinued or switched to a different medication prior to starting study drug;

15. Patients who are:

A. Pregnant;

B. Breast feeding;

C. Of childbearing potential without a negative pregnancy test prior to baseline;

D. Male or female of childbearing potential unwilling to use contraceptive precautions throughout the trial (post menopausal women must be amenorrheic for at least 12 months to be considered of non childbearing potential).

16. Interruption of imatinib therapy for a cumulative period in excess of 21 days in the preceding 3 months;

17. Major toxicity on imatinib in past 3 months;

18. History of non compliance, or other inability to grant informed consent;

19. Past or present history of alcohol abuse, use of illicit drugs, or severe psychiatric disorders, including depression;

20. Known hypersensitivity to any interferon preparation;

21. Autoimmune hepatitis or a history of autoimmune disease;

22. Pre existing thyroid disease unless it can be controlled with conventional treatment;

23. Epilepsy and/or compromised central nervous system (CNS) function;

24. HCV/HIV patients;

25. Poorly controlled diabetes mellitus(i.e. HbA1c >9.0) or clinically relevant diabetic complications such as neuropathy, retinopathy, nephropathy, coronary or peripheral vascular

disease.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	15-01-2013
Aantal proefpersonen:	60
Type:	Werkelijke startdatum

Ethische beoordeling

Niet van toepassing

Soort:	Niet van toepassing

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL3574
NTR-old	NTR3732
Ander register	EudraCT : 2012-004321-25
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A