Een wetenschappelijk onderzoek met nieuwe middelen, Ibrutinib en Venetoclax, bij patiënten met chronische lymfatische leukemie (CLL), waarbij de ziekte na eerdere behandeling is teruggekeerd of eerdere behandeling onvoldoende respons heeft opgeleverd.

Gepubliceerd: 01-03-2017 Laatst bijgewerkt: 15-05-2024

Ethische beoordeling	Goedgekeurd WMO
Status	Werving gestopt
Type aandoening	Leukemieën
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON23972

Bron
NTR

Verkorte titel
Vision

Aandoening

- Leukemieën

Aandoening

Chronic Lymfocytic Leukemia (CLL)

Betreft onderzoek met
Mensen

Ondersteuning

Primaire sponsor:	HOVON Data Center
Secundaire sponsoren:	Nordic CLL group
Overige ondersteuning:	HOVON, Abbvie, Janssen

Onderzoeksproduct en/of interventie

Toelichting

Uitkomstmaten

Primaire uitkomstmaten

(Only considered for arm B of the study)

- Proportion of patients fulfilling the criteria for progression free survival (PFS) at 12 months after stopping therapy (27 months after starting treatment) for patients randomized to stop treatment (arm B of the study), reinitiated treatment due to MRD positivity not considered progression (see section 13.1 for details).

Toelichting onderzoek

Achtergrond van het onderzoek

Study aim:

The aim of the current trial is to evaluate if combination treatment with venetoclax + ibrutinib in patients with relapsed or refractory chronic lymphocytic leukemia (RR CLL) can lead to MRD negativity, which may induce long lasting remissions for MRD-negative patients randomized to stopping treatment after 15 months.

Study design:

Phase-II trial, prospective, multicenter, open-label, randomized. Patient population:

Fit (CIRS ¡Ü 6) and unfit (CIRS >6) patients with a creatinine clearance ¡Ý 30 ml/min with previously treated CLL with or without TP53 aberrations requiring treatment

Intervention:

All patients receive ibrutinib + venetoclax (with delayed start and ramp up of venetoclax from cycle 3) for the 15 cycles.

Patients not achieving MRD negativity after cycle 12 (PB) AND/OR cycle 15 (PB+BM) continue on ibrutinib maintenance (non-randomized group). Patients achieving MRD negativity after cycle 12 (PB) AND cycle 15 (PB+BM) are randomized 1:2 between ibrutinib maintenance (arm A) and stopping treatment (observation, arm B).

Patients randomized to arm B who become MRD positive or have symptomatic CLL according to IWCLL critera during the observation period reinitiate treatment with both ibrutinib and venetoclax for 12 cycles and continue ibrutinib treatment until toxicity or progression.

Only patients randomized for observation (arm B) are considered for the primary endpoint without formal comparison between arms.

Onderzoeksopzet

- Before enrollment: within 28 days before registration, as specified in 10.2

- After each cycle until end of cycle 15

- Weekly during venetoclax ramp up in cycle 3

- After cycle 15: every 3 months, whether in the maintenance or the treatment cessation group, until month 51 (15 months + 3 years)

- Thereafter every 6 months until 7 years after registration or until progression, whatever comes first.

Onderzoeksproduct en/of interventie

All patients receive ibrutinib + venetoclax (with delayed start and ramp up of venetoclax from cycle 3) for the 15 cycles. Patients not achieving MRD negativity after cycle 12 (PB) AND/OR cycle 15 (PB+BM) continue on ibrutinib maintenance (non-randomized group). Patients achieving MRD negativity after cycle 12 (PB) AND cycle 15 (PB+BM) are randomized 1:2 between ibrutinib maintenance (arm A) and stopping treatment (observation, arm B).

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Contactpersonen

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Deelname eisen

Leeftijd
Volwassenen (18-64 jaar)
Volwassenen (18-64 jaar)
65 jaar en ouder
65 jaar en ouder

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

♦ Documented CLL or SLL requiring treatment according to IWCLL criteria after either being refractory to first line therapy or relapse after initial therapy.

♦ Age at least 18 years.

♦ Adequate bone marrow function defined as:

- Absolute neutrophil count (ANC) >0.75 x 109/L

- Platelet count >30,000 /¡ÌL 30 x 109/L.

- Hemoglobin >8.0 g/dL (5 mmol/L)

Unless directly attributable to CLL infiltration of the bone marrow, proven by bone marrow biopsy

♦ Creatinine clearance (CrCL) ¡Ý 30ml/min calculated according to the modified formula of Cockcroft and Gault or directly measured with 24hr urine collection.

♦ Adequate liver function as indicated

- Serum aspartate transaminase (AST) or alanine transaminase (ALT) ¡Ü 3.0 x upper limit of normal (ULN)

- Bilirubin ¡Ü1.5 x ULN (unless bilirubin rise is due to Gilbert's syndrome or of non-hepatic origin)

- Prothrombin time (PT)/International normal ratio (INR) <1.5 x ULN and PTT (activated partial thromboplastin time [aPTT]) <1.5 x ULN (unless abnormalities are related to coagulopathy or bleeding disorder).

♦ Negative serological testing for hepatitis B (HBsAg negative and anti-HBc negative; patients positive for anti-HBc may be included if PCR for HBV DNA is negative and HBV-DNA PCR is performed every month until 12 months after last dose), negative testing for hepatitis C RNA within 42 days prior to registration.

♦ WHO/ECOG performance status 0-3 (appendix C), stage 3 only if attributable to CLL.

♦ Negative pregnancy test at study entry (for women of childbearing potential).

♦ Male and female subjects of reproductive potential must agree to use both a highly effective method of birth control (e.g. implants, injectables, combined oral contraceptives, some intrauterine devices [IUDs], complete abstinence , or sterilized partner) and a barrier method (e.g., condoms, cervical ring, sponge, etc.) during the period of therapy and for 90 days after the last dose of study drug.

♦ Ability and willingness to provide written informed consent and to adhere to the study visit schedule and other protocol requirements.

♦ Written informed consent.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

♦ Any prior therapy with ibrutinib and/or venetoclax.

♦ Transformation of CLL (Richter¡¯s transformation).

♦ Patients with a history of confirmed progressive multifocal leukoencephalopathy (PML).

♦ Malignancies other than CLL currently requiring systemic therapies or not being treated in curative intention before or showing signs of progression after curative treatment.

♦ Known allergy to xanthine oxidase inhibitors and/or rasburicase.

♦ Known bleeding disorders (e.g., von Willebrand¡¯s disease or hemophilia).

♦ Uncontrolled or active infection.

♦ Patients requiring treatment with a strong cytochrome P450 (CYP) 3A inhibitor (see appendix K). or anticoagulant therapy with warfarin or phenoprocoumon or other vitamin K antagonists. Please note: Patients being treated with NOACs can be included, but must be properly informed about the potential risk of bleeding under treatment with ibrutinib.

♦ History of stroke or intracranial hemorrhage within 6 months prior to registration.

♦ Major surgery within 28 days prior to registration.

♦ Use of investigational agents which might interfere with the study drug within 28 days prior to registration.

♦ Vaccination with live vaccines within 28 days prior to registration

♦ Steroid therapy within 7 days prior to registration, with the exception of inhaled steroids for asthma, topical steroids, steroids up to 25 mg of prednisolone daily to control autoimmune phenomenon¡¯s, or replacement/stress corticosteroids.

♦ Pregnant women and nursing mothers.

♦ Any psychological, familial, sociological and geographical condition potentially hampering compliance with the study protocol and follow-up schedule.

Onderzoeksopzet

Opzet

Fase onderzoek:	2
Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd

Blindering:	Open / niet geblindeerd
Controle:	Geen controle groep
Doel:	Behandeling / therapie

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	12-07-2017
Aantal proefpersonen:	230
Type:	Werkelijke startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nee

Ethische beoordeling

Goedgekeurd WMO

Datum:	23-06-2017
Soort:	Eerste indiening
Toetsingscommissie:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 53008
Bron: ToetsingOnline

Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL6110
NTR-old	NTR6249
protocolNR	016-002599-29 : HO141 CLL
CCMO	NL59487.018.16
EudraCT	2016-002599-29
ClinicalTrials.gov	NCT03226301
OMON	NL-OMON53008

Resultaten

Samenvatting resultaten
N/A