Bortezomib and Tipifarnib in MDS.

Gepubliceerd: 29-06-2011 Laatst bijgewerkt: 18-08-2022

The primary objective is to assess the safety of treatment with escalating dosages of VELCADE in combination with ZARNESTRA in subjects with Intermediate-2 or high risk MDS according to the IPSS classification.

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON26222

Bron
NTR

Verkorte titel
PMDS17

Aandoening

Myelodysplastic syndrome, Tipifarnib (ZARNESTRA), Bortezomib (VELCADE).

Ondersteuning

Primaire sponsor: Radboud University Nijmegen Medical Centre
Overige ondersteuning: Ortho-Biotech a division of Janssen-Cilag BV.

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Safety (type, frequency, and severity [National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 3.0] of adverse events, and relationship of adverse events to VELCADE in combination with ZARNESTRA).

Toelichting onderzoek

Achtergrond van het onderzoek

Study phase: Phase I.

Objective:

The primary objective is to assess the safety of treatment with escalating dosages of VELCADE in combination with ZARNESTRA in subjects with Intermediate-2 or high risk MDS according to the IPSS classification.

The secondary objectives of this study are to determine:

1. Hematological improvement (International Working Group [IWG] criteria) after treatment of VELCADE in combination with ZARNESTRA;

2. The efficacy in terms of the number of patients with CR or PR after treatment of VELCADE in combination with ZARNESTRA.

Doel van het onderzoek

The primary objective is to assess the safety of treatment with escalating dosages of VELCADE in combination with ZARNESTRA in subjects with Intermediate-2 or high risk MDS according to the IPSS classification.

Onderzoeksopzet

Screening: Up to 28 days prior to initiation of treatment.

Treatment phase: Four cycles of four weeks. The patient may receive 2 additional cycles if a PR is achieved after 4 cycles. Subjects will visit the hospital at day 1, 8, 15, 22 of each cycle. All subjects will be monitored for adverse events throughout the study and for 30 days after administration of the last dose of VELCADE.

Post-treatment phase: Subjects will visit the hospital on day 28 of the last treatment cycle for an end-of-treatment visit and on day 30 after the last day of treatment.

After completion of the study patients will return to regular medical care.

Onderzoeksproduct en/of interventie

A phase I clinical trial in which the study subjects with MDS will receive 4 courses consisting of:

1. Starting cohort: Cohort 1: Cohort of 3 patients with a four-weekly cycle of ZARNESTRA 200 mg bid (days 1-21) combined with VELCADE 1.0 mg/m2/day intravenously on days 8, 15, and 22 every 4 weeks;

2. Cohort 2: Cohort of 3 patients with a four-weekly cycle of ZARNESTRA 200 mg bid (days 1-21) combined with VELCADE 1.3 mg/m2/day intravenously on days 8, 15, and 22 every 4 weeks;

3. Cohort 3: 2 parallel cohorts of 6 patients each with a 4-weekly cycle of ZARNESTRA 200 mg bid (days 1-21) combined with VELCADE 1.6 mg/m2/day intravenously on days 8, 15, and 22 every 4 weeks versus ZARNESTRA 300 mg bid (days 1-21) combined with VELCADE 1.3 mg/m2/day intravenously on days 8, 15, and 22 every 4 weeks;

4. Cohort –1, consisting of 3 patients with a four-weekly cycle of ZARNESTRA 200 mg bid (days 1-14) combined with VELCADE 1.0 mg/ m2/day on days 8, 15, and 22 every 4 weeks. This cohort will start if intolerable toxicity occurs in the first cohort;

5. Cohort –2, consisting of 3 patients with a four-weekly cycle of ZARNESTRA 200 mg bid (days 1-14) combined with VELCADE 0.7 mg/ m2/day on day 8,15 and 22 every 4 weeks. This cohort will start if intolerable toxicity occurs in cohort -1.

Two additional cycles may be given if a PR is reached. If after 2 additional cycles, so after a total of 6 cycles, there is still a PR, therapy will not be continued. In case of a CR occurring after the third or fourth cycle, 2 additional cycles may be given.

Contactpersonen

Publiek

Radboud University Nijmegen Medical Centre
Department of Haematology 489
Theodoor Craanenlaan 1
Trial Data Center
Nijmegen 6525 GH

The Netherlands
+31 (0)24 3614794

Wetenschappelijk

Radboud University Nijmegen Medical Centre
Department of Haematology 489
Theodoor Craanenlaan 1
Trial Data Center
Nijmegen 6525 GH
The Netherlands
+31 (0)24 3614794

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. MDS (including the non-proliferative form of CMML, i.e. CMML with a WBC count < 12,0 x 109) /L with < 30% blast cells in the bone marrow and with < 5% circulating blasts);

2. IPSS: Intermediate Risk-2 or High Risk;

3. Age at the time of obtaining informed consent >18 years;

4. WHO performance status 0-2;

5. Receiving no treatment for MDS other than supportive care.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. IPSS: Low risk and Intermediate-1 category;

2. Candidates for allogeneic stem cell transplantation;

3. Having received a stem cell transplantation (allogeneic or autologous);

4. Vitamine B-12 and folic acid deficiency;

5. HIV-1 positivity;

6. Has known or suspected hypersensitivity or intolerance to VELCADE or ZARNESTRA, or heparin or to Boron or Mannitol;

7. Clinically relevant liver (AST/ALT > 1.5 ULN and bilirubin > 2 mg/dl) or renal insufficiency (ECC <50%);

8. Significant, vascular, pulmonary, gastrointestinal, endocrine, rheumatologic, or metabolic disturbances;

9. Uncontrolled diabetes (if receiving anti-diabetic agents, subjects must be on a stable dose for at least 3 months before first dose of study drug);

10. Uncontrolled or severe cardiovascular disease including myocardial infarction within 6 months of enrollment, New York Heart Association (NYHA) Class III or IV heart failure (Attachment 5, NYHA Classification of Cardiac Disease), uncontrolled angina, clinically significant pericardial disease, or cardiac amyloidosis;

11. Pregnant or breastfeeding;

12. Peripheral neuropathy or neuropathic pain Grade 2 or higher as defined by NCI CTCAE version 3;

13. Receipt of extensive radiation therapy, systemic chemotherapy, or other antineoplastic therapy within 8 weeks before enrollment;

14. Serious medical or psychiatric illness likely to interfere with participation in this clinical study;

15. Use of enzyme-inducing anticonvulsants (e.g. phenytoin, phenobarbital, carbamazepine). Use of valproate because it acts as a histone deacetylase inhibitor. However, subjects may use other non-enzyme inducing anticonvulsants such as gabapentin or topiramate;

16. Necessity of immunosuppressive drugs, anti-apoptotic agents other than Velcade or Zarnestra, systemic corticosteroids or systemic retinoids, or any cancer therapy other than Velcade or Zarnestra during the treatment portion of this study;

17. Prior exposure to farnesyltransferase inhibitors or proteasome inhibitors;

18. Have received an experimental drug or used an experimental medical device within 8 weeks before the planned start of treatment. Concurrent participation in non-treatment studies is allowed, if it will not interfere with participation in this study;

19. Hematopoietic growth factor therapy or other disease modulating therapy, including the chronic use of systemic corticosteroids or any use of systemic retinoids within 8 weeks before randomization;

20. Known allergy to imidazol derivatives such as clotrimazole, ketoconazole, miconazole,

econazole, fenticonazole, isoconazole, sulconazole, ticonazole or terconazole;

21. Pregnant or lactating females
22. Having a desire to have children.

Onderzoeksopzet

Opzet

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

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	07-06-2007
Aantal proefpersonen:	18
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	29-06-2011
Soort:	Eerste indiening

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	NL2818
NTR-old	NTR2959
Ander register	METC : 2006/189
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A