Bortezomib and Tipifarnib in MDS.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26222

Source
NTR

Brief title
PMDS17

Health condition

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

Sponsors and support

Primary sponsor: Radboud University Nijmegen Medical Centre
Source(s) of monetary or material Support: Ortho-Biotech a division of Janssen-Cilag BV.

Intervention

Outcome measures

Primary outcome

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).

Secondary outcome

1. Erythroid response according to revised IWG criteria (Cheson, 2006);

2. Platelet response according to revised IWG criteria;

3. Neutrophil response according to revised IWG criteria;

4. Marrow response in terms of complete remission, partial remission, stable disease, failure, relapse or disease progression according to revised IWG criteria;

5. Cytogenetic response according to revised IWG criteria;

6. Duration of hematological (erythroid, platelet and neutrophil), marrow and cytogenetic response and improvement;

7. Progression or transformation to leukemia according to FAB classification;

8. Time to relapse after complete remission, partial remission, stable disease, failure, relapse, disease progression or AML transformation (according to revised IWG criteria), censored at death;

9. Survival.

Study description

Background summary

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.

Study 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.

Study design

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.

Intervention

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.

Contacts

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Eligibility criteria

Inclusion criteria

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.

Exclusion criteria

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.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	07-06-2007
Enrollment:	18
Type:	Anticipated

Ethics review

Positive opinion

Date:	29-06-2011
Application type:	First submission

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

Study results

Summary results
N/A