An Open label, International, Multicenter, Dose Escalating Phase I/II Trial Investigating the Safety of Daratumumab in Combination with Lenalidomide and Dexamethasone in Patients with Relapsed or Relapsed and Refractory Multiple Myeloma

Published: 16-02-2012
Last updated: 26-04-2024

* To establish the safety profile of daratumumab when given in combination with lenalidomide and dexamethasone in subjects with relapsed or relapsed and refractory MM

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Plasma cell neoplasms
Study type	Interventional

Summary

ID

NL-OMON47233

Source
ToetsingOnline

Brief title
GEN503:Daratumumab in combination with lenalidomide and dexamethason

Condition

- Plasma cell neoplasms
- Plasma cell neoplasms

Synonym
"Kahler's disease", "Malignant growth of plasma cells"

Research involving
Human

Sponsors and support

Primary sponsor: Janssen-Cilag
Source(s) of monetary or material Support: Sponsor

Intervention

Keyword: Daratumumab, Multiple Myeloma, Phase I/II, Relapsed-refractory

Outcome measures

Primary outcome

The main variable for this study, the incidence of side effects.

Secondary outcome

Secondary end points are:

- The rate of response

- Pharmacokinetic parameters

- The time to progression

- Duration of response

- Survival

Study description

Background summary

Multiple myeloma (MM) is a plasma cell disorder, characterized by uncontrolled, malignant proliferation and accumulation of plasma cells. In the majority of patients, the malignant plasma cells produce a monoclonal protein (M protein or paraprotein).
Multiple myeloma accounts for approximately 1% of all malignancies and 10% of all hematologic malignancies, with a higher frequency in African Americans where it accounts for 20% of all hematologic malignancies. At present, there is no cure available.

Treatments include combination chemotherapy, proteasome inhibition, immunomodulatory drugs, high-dose chemotherapy, and autologous stem cell transplantation (auto SCT).

Study objective

* To establish the safety profile of daratumumab when given in combination with lenalidomide and dexamethasone in subjects with relapsed or relapsed and refractory MM

Study design

In this Phase I/II safety trial of daratumumab in combination with lenalidomide and low-dose dexamethasone (Len/Dex), a standard Phase 1 *3 + 3* design is appropriate to adequately observe DLTs associated with the regimen while not exposing an undue number of subjects to doses that may be subtherapeutic. The dose escalation part of the trial (Part 1) will be followed by a cohort expansion part (Part 2) in which subjects will be enrolled into 2 cohorts of 16 subjects each at the MTD (or maximum tested dose) determined during Part 1. Part 2 of this trial will allow for a greater degree of experience with the combination therapy at what is expected to be a therapeutic dose of daratumumab and Len/Dex.

Intervention

Skeletal survey:
X-rays or CT scan of the entire body, including the skull, is required.
Additional studies (X-ray, CT scan or
MRI) can be performed, this is at the discretion of the investigator (eg to confirm the response to new
symptoms or pain in the bones to be evaluated).
Blood and urine analysis will be performed to determine the following values**: biochemistry, hematology, Hepatitis B and
Cytomegalovirus Serology, pregnancy, Serum immunoglobulin A, M and G (M-component) Urinalysis for Mcomponent
Serum free light chain ratio and pharmacokinetic / pharmacodynamic study of the concentration daratumumab
the serum.
bone marrow examination

Study burden and risks

Skeletal survey:
X-rays or CT scan of the entire body, including the skull, is required.
Additional studies (X-ray, CT scan or
MRI) can be performed, this is at the discretion of the investigator (eg to

confirm the response to new
symptoms or pain in the bones to be evaluated).
Blood and urine analysis will be performed to determine the following
values**: biochemistry, hematology, Hepatitis B and
Cytomegalovirus Serology, pregnancy, Serum immunoglobulin A, M and G
(M-component) Urinalysis for Mcomponent
Serum free light chain ratio and pharmacokinetic / pharmacodynamic study of
the concentration daratumumab
the serum.
bone marrow examination

Contacts

Public
Janssen-Cilag

Turnhoutseweg 30
Beerse 2340
NL
Scientific
Janssen-Cilag

Turnhoutseweg 30
Beerse 2340
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Before entering Phase 1 of the study, subjects must:
1. Have relapsed multiple myeloma after receiving a minimum of 2 and a maximum of 4 prior lines of therapy and be eligible for treatment with Len/Dex.
2. Have measurable levels of M component, defined as serum M component* 1.0 g/dL and/or urine M component * 200 mg/24 hour sample.
3. Be * 18 years of age.
4. Have an Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1, or 2 (Attachment 1).
5. Have a life expectancy of * 3 months.
6. Provide signed informed consent after receipt of oral and written information about the study and before any study-related activity is performed.;Before entering Phase 2 of the study, subjects must:
1. - Have received at least 1 prior line of therapy for multiple myeloma (refer to Attachment 2).
- Have achieved a response (PR or better) to at least one prior regimen.
- Have documented evidence of progressive disease (PD) as defined by the IMWG criteria on or after their last regimen.
2. Have measurable levels of M component, defined as serum M component * 1.0 g/dL and/or urine M component * 200 mg/24 hour sample.
3. Be * 18 years of age.
4. Have an ECOG performance status score of 0, 1, or 2 (Attachment 1).
5. Have a life expectancy of * 3 months.
6. Provide signed informed consent after receipt of oral and written information about the study and before any study-related activity is performed.

Exclusion criteria

1. Have previously received an allogenic stem cell transplant.
2. Have received auto SCT within 12 weeks before the first infusion.
3. Have received antimyeloma treatment, radiotherapy, or any experimental drug or therapy within 2 weeks before the first infusion.
4.Have discontinued lenalidomide due to any treatment-related adverse event or be refractory to any dose of lenalidomide.
Refractory to lenalidomide is defined as either:
- Subjects whose disease progresses within 60 days of lenalidomide, or
- Subjects whose disease is nonresponsive while on any dose of lenalidomide. Nonresponsive disease is defined as either failure to achieve at least an MR or development of PD while on lenalidomide.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-06-2013
Enrollment:	5
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Darzalex
Generic name:	Daratumumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Dexamethasone
Generic name:	Dexamethasone
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Revlimid
Generic name:	Lenalidomide
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	16-02-2012
Application type:	First submission

Review commission:	METC NedMec
Approved WMO Date:	01-08-2012
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	14-09-2012
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-12-2012
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-01-2013
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-04-2013
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-09-2013
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	20-09-2013
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-05-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-05-2014
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	23-06-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-07-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-08-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-01-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-03-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-07-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-09-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-09-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-12-2015
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	03-02-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-04-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-04-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-12-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	18-01-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	31-05-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	08-06-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-01-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-02-2018
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	26-02-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-03-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	20-06-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-01-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	31-01-2019
Application type:	Amendment
Review commission:	METC NedMec

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	EUCTR2011-005709-62-NL
ClinicalTrials.gov	NCT01615029
CCMO	NL39344.041.12