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

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

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

Ethical review	Approved WMO
Status	Will not start
Health condition type	Plasma cell neoplasms
Study type	Interventional

Summary

ID

NL-OMON37444

Source
ToetsingOnline

Brief title
Daratumumab in combination with bortezomib and dexamethasone

Condition

- Plasma cell neoplasms
- Plasma cell neoplasms

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

Research involving
Human

Sponsors and support

Primary sponsor: Genmab
Source(s) of monetary or material Support: Sponsor- Genmab A/S

Intervention

Keyword: Daratumumab, multiple myeloma, phaseI/II, relapsed -refractory

Outcome measures

Primary outcome

The primary variable for this trial will be the incidence of AEs

Secondary outcome

Secondary variables are:

* The rate of response according to the International Uniform Response

Criteria21

* PK variables (AUC, Cmax, minimum or trough concentration in plasma [Cmin],

time to Cmax [Tmax], apparent clearance [CL], volume of distribution [V], and

t1/2)

* Time to progression

* Duration of response

* Progression-free 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 bortezomib and dexamethasone in subjects with relapsed or refractory MM

Study design

In this Phase I/II safety trial of daratumumab in combination with bortezomib and low-dose dexamethasone, a standard Phase I 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 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

Intervention

Skeletal Survey
A whole-body X ray or CT scan, including the cranium, is required. Additional surveys (X ray, CT scan, or magnetic resonance imaging scan) may be performed at the investigator*s discretion (eg, to confirm response, to evaluate new symptoms or bone pain).
Blood and Urine sapmples will be taken for testing: Biochemistry, hematology, HIV, Hepatitis B and Cytomegalovirus Serology, Pregnancy,Bone Marrow Assessments ,Serum Immunoglobulin A, M, and G (M component), Urinalysis for M component ,Serum Free Light Chain Ratio Prognostic Factors: Pharmacokinetic/Pharmacodynamic Assessments of Daratumumab Concentration in Serum

Study burden and risks

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Contacts

Public
Genmab

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DK
Scientific
Genmab

Bredgade 34
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- (Part 1) Have relapsed MM after receiving a minimum of 2 and a;maximum of 4 prior lines of therapy and be eligible for treatment with Bor/Dex. Subjects must be naive to Bortezomib

treatment;- (Part 2) Have relapsed MM after receiving a minimum of 1 and a;maximum of 3 prior lines of therapy, but not have MM that is refractory to the last treatment, and be eligible for treatment with Bor/Dex. ;- Have measurable levels of M-component, defined as serum Mcomponent 1.0 g/dL and/or urine M-component 200 mg/24-hour;sample.;- Be older than or be 18 years of age.;- ECOG performance status (0-2).;- Following receipt of verbal and written information about the study, the patient must provide signed informed consent before any study related activity is carried out.

Exclusion criteria

- Have previously received an allogenic stem cell transplant.;- Have received auto SCT within 12 weeks before the first infusion.;- Have received chemotherapy or any experimental drug or therapy;within 3 weeks before the first infusion.;- Have received bortezomib, lenalidomide, or thalidomide within 2 weeks before the first infusion.;- Have MM that is refractory to bortezomib, defined as not having a minimum clinical response of MR for at least 2 months during the last treatment with bortezomib).;- Must not be known to be seropositive for HIV

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	4
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	dexamethasone
Registration:	Yes - NL intended use
Product type:	Medicine

Brand name:	HuMax-CD38
Generic name:	Daratumumab

Ethics review

Approved WMO Date:	16-02-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	01-08-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	14-09-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	28-12-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	EUCTR2011-005692-16-NL
CCMO	NL39334.041.12