A Randomized, Double-blind, Placebo-controlled Study to Assess the Efficacy and Safety of CNTO 328 (Anti-IL-6 Monoclonal Antibody) Plus Best Supportive Care Compared With Best Supportive Care in Subjects With Multicentric Castleman*s Disease

Published: 20-10-2009
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Primary Objective:The primary objective of this study is to demonstrate that CNTO 328 in combination with BSC is superiorto BSC in terms of objective response (complete response [CR] + partial response [PR]) among subjectswith multicentric Castleman…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lymphomas NEC
Study type	Interventional

Summary

ID

NL-OMON36768

Source
ToetsingOnline

Brief title
CNTO328MCD2001

Condition

- Lymphomas NEC
- Immune disorders NEC

- Haematopoietic neoplasms (excl leukaemias and lymphomas)

Synonym
angiofollicular hyperplasia, Castleman's disease, lymphoproliferative disease

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Castleman's disease, CNTO328, siltuximab

Outcome measures

Primary outcome

The primary efficacy endpoint will be objective tumor response (CR + PR)

modified to allow assessment of

measurable cutaneous lesions, as measured by Cheson criteria (Cheson et al,

2007; positron-emission

tomography [PET] scan data, if obtained, will not be taken into account).

Other efficacy endpoints include:

• Duration of tumor response (whenever possible, disease progression documented

by the appearance

of new lesions should be confirmed by histologic examination of the new lesions)

• Time to treatment failure

• Change in hemoglobin from baseline to the average of the last 8 weeks of

treatment (through

Week 18)

• Proportion of subjects who are able to discontinue corticosteroids

Patient-reported outcome (PRO) endpoints include:

• Change from baseline in fatigue measured by the Functional Assessment of

Chronic Illness

Therapy-Fatigue (FACIT-F)

• Change from baseline in physical function assessed by the Medical Outcome

Study Short-Form-36

(SF-36) Physical Component Summary (PCS)

• Change from baseline in patient-reported symptom severity measured with the

MCD Symptom

Scale

Secondary outcome

PHARMACOKINETIC EVALUATIONS

Pharmacokinetic endpoints include:

• Cmin

• Cmax

If sufficient data are available, other pharmacokinetic parameters, including

but not limited to t1/2,

AUC(t1-t2), CL, and V may be calculated.

PHARMACODYNAMIC BIOMARKER EVALUATIONS

Assays to be performed include:

• Tissue and blood gene expression profiling

• Immunohistochemistry and serum analysis of proteins relevant to the IL-6

signaling pathway (eg,

hepcidin, CRP)

SAFETY EVALUATIONS

• AEs and AEs >= Grade 3

• SAEs

• Infusion reactions

• Clinically significant abnormal laboratory parameters

• Antibodies to CNTO 328

Study description

Background summary

CNTO 328 is a chimeric (murine-human) IgG1* mAb that specifically binds human IL-6 with high affinity
and prevents its interaction with the IL-6 receptor, glycoprotein (GP) 80 (Seideman and Peritt, 2002). The
chimeric antibody contains the variable region of a murine anti-human IL-6 mAb and the constant region
from a human immunoglobulin gamma (IgG) 1 molecule. The mechanism of action of CNTO 328 is
neutralization of IL-6 bioactivity, which can be measured indirectly by C-reactive protein (CRP)
suppression.

Hypothesis:
The primary hypothesis is that CNTO 328 + BSC will demonstrate a higher overall response rate than
placebo + BSC, and provide durable clinical benefit with an acceptable benefit/risk profile.

Study objective

Primary Objective:
The primary objective of this study is to demonstrate that CNTO 328 in

combination with BSC is superior
to BSC in terms of objective response (complete response [CR] + partial response [PR]) among subjects
with multicentric Castleman*s disease (MCD).

Secondary Objectives:
The secondary objectives of this study are:
• To demonstrate additional measures of efficacy (duration of tumor response; time to treatment
failure; change in hemoglobin levels; ability to discontinue corticosteroids; and improvement in
fatigue, physical function, and other disease-related symptoms)
• To study the safety of prolonged dosing
• To determine the pharmacokinetics of CNTO 328 among subjects with MCD
• To determine a baseline hepcidin value predictive of a >= 2 g/dL increase in hemoglobin

Study design

This is a A Randomized, Double-blind, Placebo-controlled Study

Intervention

Subjects will receive CNTO 328 (11 mg/kg) or placebo by a 1-hour IV infusion every 3 weeks. Subjects will be randomly assigned to 2 treatment groups:
• Treatment Group A: Placebo + BSC
• Treatment Group B: CNTO 328 + BSC

Study burden and risks

See page 22 and 23 of the protocol for description of potential risks. Also, see informed consent for detailed description of all requirements for the patients.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Measurable and symptomatic MCD proven by biopsy.
- Pretreatment clinical laboratory values meeting these criteria within 4 weeks before treatment:
a. Absolute neutrophil count (ANC) >= 1.0 x 109/L
b. Platelets >= 75 x 109/L
c. ALT within 2.5 x ULN; total bilirubin within 2.5 x ULN; unfractionated alkaline phosphatase within
2.5 x ULN; if unfractionated alkaline phosphatase is above 2.5 x ULN, subjects will be eligible if alkaline phosphatase liver fraction is within 2.5 x ULN
d. Serum creatinine <= 3.0 mg/dL
- ECOG Performance Status of 0, 1, or 2
- Corticosteroids dose that does not exceed 1 mg/kg/day of prednisone (or equivalent, and has remained stable or decreased over the 4 weeks before
enrollment

Exclusion criteria

1. HIV or HHV-8 positive
2. Previous lymphoma
3. Malignancies
4. Concurrent medical condition or disease that is likely to interfere with study procedures or results
5. Use of disallowed therapies: other concomitant anti-tumor therapies for Castleman*s

disease

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-05-2010
Enrollment:	2
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	CNTO328-siltuximab
Generic name:	CNTO328-siltuximab

Ethics review

Approved WMO

Date:	20-10-2009
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	01-12-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-03-2010
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-06-2010
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-08-2010
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-10-2010
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-02-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-03-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-04-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	30-08-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-11-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-12-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2009-012380-34-NL
CCMO	NL29786.078.09