An open-label study assessing the addition of subcutaneous golimumab (GLM) to conventional disease-modifying antirheumatic drug (DMARD) therapy in biologic-naÃ¯ve subjects with rheumatoid arthritis (Part 1), followed by a randomized study assessing the value of combined intravenous and subcutaneous GLM administration aimed at inducing and maintaining remission (Part 2).

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Part 1: To assess the safety and effectiveness of subcutaneous golimumab 50 mg (SC-GLM50), administered by autoinjection once monthly during 6 months, when combined with different DMARD regimens used in daily rheumatology. Part 2: In subjects who...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON36401

Source
ToetsingOnline

Brief title
GO-MORE

Condition

- Autoimmune disorders
- Joint disorders

Synonym
arthritis, Rheumatoid Arthritis

Research involving
Human

Sponsors and support

Primary sponsor: Merck Sharp & Dohme (MSD)
Source(s) of monetary or material Support: Schering Plough Research Institute (SPRI)

Intervention

Keyword: combined intravenous-subcutaneous treatment, golimumab, rheumatoid arthritis, safety and efficacy

Outcome measures

Primary outcome

Part 1:

The proportion of subjects achieving DAS28-ESR EULAR response.

Part 2:

1. Proportion of subjects who are in DAS28-ESR remission at the start of month

11 (visit 10).

2. Proportion of subjects who are in DAS28-ESR remission at the end of month 12

(visit 11).

Secondary outcome

Deel 1:

1. Disease activity measured with composite scoring indices (DAS28-CRP,

DAS28-ESR and SDAI) and their subcomponents.

2. Proportion of subjects achieving EULAR moderate and good response using the

DAS28-CRP.

3. Proportion of subjects achieving low disease activity and remission states

according to cutoffs applicable to the aforementioned composite indices.

Part 2:

1. AUC for DAS28-ESR versus time between the end of month 6 en the end of month

12.

2. Time to DAS28-ESR remission.

3. DAS28-ESR remission rates at every trial visit.

4. Proportion of subjects achieving low disease activity based on DAS28-ESR and

SDAI levels.

Study description

Background summary

Golimumab (GLM) is a fully human anti-TNF-alfa monoclonal antibody that is administered subcutaneously once monthly.
GLM (50 mg, SC) has been registered by the European Authorities on October, 1st 2009.
The knowledge related to the safety profile of GLM can change over time through expanded use in terms of patient characteristics and the number of patients exposed. As a lot new agents, upon introduction to the market, have usually been studied only in a limited number of highly selcted patient patient populations, it is important to continue to investigate and document the safety and effectiveness of GLM, aiming at increasing the knowledge base of GLM in the daily clinical practice setting.

Study objective

Part 1: To assess the safety and effectiveness of subcutaneous golimumab 50 mg (SC-GLM50), administered by autoinjection once monthly during 6 months, when combined with different DMARD regimens used in daily rheumatology.

Part 2: In subjects who have responded to the treatment administered in part 1 (i.e., from baseline to the end of month 6(but have not achieved remission at the end of month 6, to stud ywhether a strategy of using intravenous golimumab at 2 mg/kg body weight (IV-GLM2) to induce remission, followed by SC-GLM50 to retain remission, is superior to continuing a SC-GLM50 regimen.

Study design

This is an open-label, multinational, multicenter, prospective trial of GLM in biologic-naive subjects with RA who have active disease despite taking a conventional DMARD regiman.
In total approximately 3150 patients will participate in part 1 of the study and approximately 500 patients in part 2 of the study.

Part 1: subjects will be asked to continue their DMARD regimen under wich their disease is not sufficiently controlled and will receive subcutaneous GLM (50 mg) by autoinjection once monthly.
Patients will be treated during 6 months (i.e. a total of six doses), for which they will have to visit the hospital 5 times.
During these visits physical examination (including bloodpressure and heartrate) and RA specific assessments (TJC28 and SJC28) will be performed, blood samples taken (clinical chemistry, hematology, ESR, RA and inflammatory factors) and questionnaires completed (HAQ, EQ-5D and evaluation of the patients regarding illness and treatment).

Patients who only participate in part 1 of the trial (they are not eligible for part 2 of the trial, or enrollment in part 2 may already been closed) and live in a country where GLM is commercially available and reimburable, the subject will end his/her participation in the trial at the end of month 6.
In case GLM is not (yet) available and the investigator feels the subject would benefit from continued GLM use, then the sponsor will provide GLM free of charge for an additional 6 months (part 1 extension phase). The subject will attend a final visit for safety follow up at the end of month 12.

Part 2: subjects who responded to treatment but are not in remission at the end of part 1 will be randomized in a 1:1 ration to one of the two treatment arms.
- Arm 1 (strategy arm): IV-GLM2 (2mg / kg) will be infused to each subject at the start of month 7, then at the start of month 8 and 10, if the subject has not achieved remission at any of these infusion visits. If a subject is found to be in remission at the time of an infusion visit after month 7, that subject will receive a subcutaneous GLM (50 mg) injection, and the monthly SC-GLM50 regimen will continue until the end of month 12 unless the subject is found to have flared (i.e. remission was not retained) at the start of month

10. In this case the subject will receive an IV-GLM2 infusion at the start of month 10; SC-GLM50 injections will be resumed at the start of month 11 and continued until the end of month 12.
- Arm 2 (reference arm): the monthly SC-GLM50 regimen will be continued from the start of month 7 through the end of month 12

In this period the subject will have 6 study related visits, during which physical examination (including bloodpressure and heartrate) and RA specific assessments (TJC68 and SJC66) will be performed, blood samples taken (clinical chemistry, hematology, ESR, inflammatory factors) and questionnaires completed (HAQ, EQ-5D and evaluation of the patients regarding illness and treatment).

Intervention

During part 1 of the study golimumab will be injected once a month (50 mg) using a autoinjector. Subjects who are eligible for the extension of part 1 will be treated for an additional 6 months with SC-GLM50.

Subjects who are eligible for part 2 of the trial and are randomized to the IV arm are infused with IV-GLM 2 on month 7, 8 and 10, unless the patient is found in remission during one of the infusion visits. In that case the patient will be further treated once a month with subcetaneous GLM until month 12. In case of a flare the patient can be switched to the IV regimen again until month 10. Patients in the reference arm will be injected with SC-GLM50 on a monthly base for 6 months.

Study burden and risks

The burden for trial subjects consists of administration of GLM by means of an autoinjector or infustion (part 2).
The SC injections with the autoinjector and/or the infusion of GLM could lead to occurence of an injection- or infusion reaction.

Further burden for the trial subjects consists of regular visits to the hospital (max. 6 visits in part 1 as well as in part 2), including venapunctures, short not extended (physical examination), RA specific assessments and the completion of questionnaires.
The most important risks for the subjects are the side effects, caused by the study medication, as described in the Investigator's Brochure version May 2009.

The most common side effects, caused by the use of GLM, are the subject's higher susceptibility for infections or worsening of existing infections. Also hypertension is a common side effect of GLM use.

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

Part 1:
1. Each subject must be 18 years or older;
2. each subject must have a diagnosis of RA according to ACR criteria;
3. Each subject must have active disease (DAS28-ESR >= 3.2) despite DMARD treatment;
4. Each subject must still be taking at least one of the allowed DMARDs at a stable dose for at least 1 month prior to trial entry, and must be capable of maintaining the stable dose during the trial;
5. Each subject must be eligible for anti-TNF- alpha according to the following criteria:
a. Subject must have failed conventional treatment according to the investigator's opinion or local guidelines;
b. local guidelines regarding safety screening of anti-TNF candidates must be met;
c. the results of the anamnesis and physical examination must make the subject eligible for

anti-TNF use and trial participation according to the investigator's judgement.;Part 2:
1. Each subject must have completed part 1 of the trial;
2. Each subject must have:
a. good or moderate DAS28-ESR response to 6 months of SC-GLM50 regimen and
b. no DAS28-ESR remission (i.e. DAS28-ESR >= 2.6) at the end of that period;
3. the investigator must judge that no safety events (eg. Serious Adverse Events, serious infections, marked injection-site reaction or intolerance to drug) have occurred that could reoccur or aggravate with increased drug exposure.

Exclusion criteria

Exclusion criteria are applicable to both part 1 and 2 of the trial;1. A subject must not have a history of biologic drug use for RA;
2. A subject must not have evidence of active TB or latent TB that is untreated;
3. A subject must not have a history of lymphoproliferative disase or any unknown malignancy;
4. A subject must not have a history of moderate of severe heart faillure (NYHA class III/IV) even if medically controlled
5. A subject must not have an inflammatory rheumatic disease other than RA that might confound the evaluations of safety and toxicity;

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-01-2010
Enrollment:	90

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Simponi 2mg/kg IV
Generic name:	Golimumab 2mg/kg IV
Product type:	Medicine
Brand name:	Simponi 50mg SC
Generic name:	Golimumab 50mg SC
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	17-09-2009
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	02-12-2009
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	29-01-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	09-02-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	01-07-2010
Application type:	Amendment

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	30-07-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	16-08-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	03-08-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	24-08-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	EUCTR2009-011137-26-NL
CCMO	NL29451.003.09