MULTI-CENTER, OPEN LABEL, SINGLE ARM PHASE IIIB STUDY ON SAFETY AND EFFICACY OF SUBCUTANEOUS (SC) TOCILIZUMAB (TCZ) IN MONOTHERAPY OR IN COMBINATION WITH METHOTREXATE (MTX) OR OTHER NON-BIOLOGIC DISEASE MODIFYING ANTIRHEUMATIC DRUGS (DMARDS) IN RHEUMATOID ARTHRITIS PATIENTS WITH AN INADEQUATE RESPONSE TO NON-BIOLOGIC DMARDS

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To evaluate the safety and tolerability of SC TCZ monotherapy and/or in combination with MTX or other non-biologic DMARDs comprising AEs, physical examination, vital signs, and clinical laboratory assessments, including immunogenicity, in patients...

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

Summary

ID

NL-OMON38533

Source
ToetsingOnline

Brief title
OSCAR

Condition

- Autoimmune disorders
- Joint disorders

Synonym
RA, rheumatoid arthritis

Research involving
Human

Sponsors and support

Primary sponsor: Roche Nederland B.V.
Source(s) of monetary or material Support: farmaceutische industrie

Intervention

Keyword: open-label, Rheumatoid Arthritis, subcutaneous, Tocilizumab

Outcome measures

Primary outcome

Safety Outcome Measures

1. Incidence and severity of AEs, serious adverse events, and AEs of special

interest over time up to Week 24.

2. Rates of AEs leading to dose modification or study withdrawal up to Week 24.

3. Assessment of physical examination and vital signs up to Week 24.

4. Incidence of clinically significant laboratory abnormalities following TCZ

SC administration up to Week 24.

5. Assessment of immunogenicity following SC TCZ administration up to Week 24

and 8 weeks after last dose.

6. Rates of AEs leading to dose modification of concomitant RA medication(s) up

to Week 24

Efficacy Outcome Measures

1. Change in DAS28-ESR up to week 24.

2. ACR response scores up to week 24.

3. EULAR response criteria up to week 24.

4. Change in SDAI or CDAI up to week 24.

5. Change in total TJC and total SJC over time.

6. Proportion of patients and reasons for corticosteroid and / or NSAID dose reductions and/or discontinuation over time.

Secondary outcome

Immunogenicity Outcome Measures

Anti-TCZ antibodies, TCZ levels, and soluble IL-6 receptors are to be measured during the study. In addition, for any patients withdrawn due to hypersensitivity reaction (serious or non serious), these will be collected at the time of the event and at least 6 weeks after the last dose

Patient-Reported Outcome Measures

1. Patient Global Assessment of disease activity visual analogue scale (VAS) up to week 24.

2. Patient Pain VAS up to week 24

3. Health Assessment Questionnaire-Disability Index up to week 24.

4. Patient compliance (patient diary cards and return records) up to week 24.

5. Patient reported assessment of RA medication intolerance utilizing an

intolerance specific questionnaire derived from the Methotrexate Intolerance

Severity Score up to Week 24, if applicable.

Study description

Background summary

RA is a progressive auto immune disease characterized by inflammation and irreversible damages to the joints. IL-6 had been implicated to be linked with RA. Tocilizumab is a humanized anti-body and proven to decrease IL-6 activity. A subcutaneous dosing regimen may be more convenient for many patients, because the ability to administer the medication themselves at home. This last topic is the main purpose for executing this study.

Study objective

To evaluate the safety and tolerability of SC TCZ monotherapy and/or in combination with MTX or other non-biologic DMARDs comprising AEs, physical examination, vital signs, and clinical laboratory assessments, including immunogenicity, in patients with active rheumatoid arthritis (RA) for a study period of 24 weeks.

Study design

This is a multi-center, open-label single-arm study to evaluate the safety and tolerability of TCZ, administered as monotherapy and/or in combination with MTX or other non-biologic DMARDs TCZ 162 mg will be administered qw by SC injection as a single fixed dose and irrespective of body weight for the treatment duration of 24 weeks
Dosages of non-biologic DMARDs should remain stable during the 24-week study, unless in the opinion of the Investigator, there are strong medical grounds, for example intolerance or other safety issues, for discontinuation of these medications.
Dosages of oral corticosteroids and NSAIDs should remain stable during the first 16 weeks of the study, unless in the opinion of the Investigator, there are strong medical grounds, for example intolerance or other safety issues, for discontinuation of these medications. From week 16 onwards, the dosage can then be decreased according to daily practice and according to the schedule the Investigators deemes appropriate.

Intervention

Patients will be injected with subcutaneous Tocilizumab, the first time at the hospital, after that another 23 times by themselves at home, or by a specialized nurse if that is required.

Study burden and risks

burden:
subcutaneous medication injection, firts time in hospital therafter 23 times at home
physical exam, including joint scores and vital functions (9x)
blood draw (9x) and urine voiding (8x), filling out 3 types of questionnaires and pain scores (9x)
ECG (1x)
thorax x-ray (1x)
pregnancy test, if applicable (9x)
joint counts (9x)

risks:
- injection problems during subcutaneous administration of the study medication
- risk on hematoma due to vena punction for blood draw
- unknown adverse events of the study medication, for known adverse events see SPC tocilizumab

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

Patients must meet the following criteria for study entry:;1. Able and willing to give written informed consent and comply with the requirements of the study protocol.;2. Patients at least 18 years of age.;3. Patients with a diagnosis of active RA according to the revised (1987) ACR criteria or EULAR/ACR (2010) criteria.;4. Oral corticosteroids (<=10 mg/day prednisone or equivalent) and NSAIDs (up to the maximum recommended dose) are permitted if on a stable dose regimen for >=4 weeks prior to Baseline.;5. Permitted non-biologic DMARDs are allowed if at a stable dose for at least 4 weeks prior to Baseline.;6. Receiving treatment on an outpatient basis, not including TCZ.;7. Females of childbearing potential and males with female partners of childbearing potential may participate in this study only if using a reliable means of contraception (e.g., physical barrier [patient or partner], contraceptive pill or patch, spermicide and barrier, or intrauterine device) during the study and for at least 3 months following the last dose of TCZ.;8. If female of childbearing potential, the patient must have a negative pregnancy test at the Screening and Baseline visits.;9. Patients that are conventional DMARD inadequate responders (IR), or are biological DMARD-IR with a maximum of an inadequate response to not more than one biological DMARD.;10. Have moderate to severe RA (DAS28 >= 3.2, >= 1 swollen joint).

Exclusion criteria

A patient will be excluded if the answer to any of the following statements is *yes*:;General:;1. Major surgery (including joint surgery) within 8 weeks prior to Screening or planned major surgery within 6 months following baseline.;2. Rheumatic autoimmune disease other than RA, including systemic lupus erythematosis, mixed connective tissue disorder, scleroderma, polymyositis, or significant systemic involvement secondary to RA (e.g., vasculitis, pulmonary fibrosis or Felty*s syndrome). Secondary Sjögren*s syndrome with RA is permitted.;3. Functional Class IV as defined by the ACR Classification of Functional Status in Rheumatoid Arthritis.;4. Diagnosis of juvenile idiopathic arthritis or juvenile RA and/or RA before the age of 16.;5. Prior history of or current inflammatory joint disease other than RA (e.g., gout, Lyme disease, seronegative spondyloarthropathy including reactive arthritis, psoriatic arthritis, and arthropathy of inflammatory bowel disease).;6. Patients with lack of peripheral venous access.;Excluded Previous or Concomitant Therapy:;7. Exposure to TCZ

(either intravenous [IV] or SC) at any time prior to Baseline.;8. Treatment with any investigational agent within 4 weeks (or five half-lives of the investigational drug, whichever is longer) of Screening.;9. Previous treatment with any cell-depleting therapies, including investigational agents or approved therapies, some examples are CAMPATH, anti-CD4, anti-CD5, anti-CD3, anti CD19, and anti-CD20.;10. Treatment with IV gamma globulin, plasmapheresis within 6 months of Baseline.;11. Treatment with more than one biologic DMARD;12. Intraarticular or parenteral corticosteroids within 4 weeks prior to Baseline.;13. Immunization with a live/attenuated vaccine within 4 weeks prior to Baseline.;14. Any previous treatment with alkylating agents such as chlorambucil, or with total lymphoid irradiation.;Exclusions for General Safety:;15. History of severe allergic or anaphylactic reactions to human, humanized, or murine monoclonal antibodies.;16. Evidence of serious uncontrolled concomitant cardiovascular, nervous system, pulmonary (including obstructive pulmonary disease), renal, hepatic, endocrine (including uncontrolled diabetes mellitus), or gastrointestinal (GI) disease.;17. History of diverticulitis, diverticulosis requiring antibiotic treatment, or chronic ulcerative lower GI disease such as Crohn*s disease, ulcerative colitis, or other symptomatic lower GI conditions that might predispose to perforation.;18. Known active current or history of recurrent bacterial, viral, fungal, mycobacterial, or other infections (including but not limited to tuberculosis [TB] and atypical mycobacterial disease, hepatitis B and C, and herpes zoster, but excluding fungal infections of nail beds).;19. Any major episode of infection requiring hospitalization or treatment with IV antibiotics within 4 weeks of Screening or oral antibiotics within 2 weeks of Screening.;20. Active TB requiring treatment within the previous 3 years. Patients should be screened for latent TB and, if positive, treated following local practice guidelines prior to initiating TCZ. Patients treated for TB with no recurrence in 3 years are permitted.;21. Current liver disease as determined by the Investigator.;22. Positive hepatitis B surface antigen or hepatitis C antibody.;23. Primary or secondary immunodeficiency (history of or currently active).;24. Evidence of active malignant disease, malignancies diagnosed within the previous 10 years (including hematological malignancies and solid tumors, except basal and squamous cell carcinoma of the skin or carcinoma in situ of the cervix uteri that has been excised and cured), or breast cancer diagnosed within the previous 20 years.;25. Pregnant women or nursing (breast feeding) mothers.;26. Patients with reproductive potential not willing to use an effective method of contraception.;27. History of alcohol, drug, or chemical abuse within 1 year prior to Screening.;28. Neuropathies or other conditions that might interfere with pain evaluation.;Laboratory Exclusion Criteria (at Screening):;29. Serum creatinine >1.4 mg/dL (124 µmol/L) in female patients and >1.6 mg/dL (141 µmol/L) in male patients.;30. Alanine aminotransferase or aspartate aminotransferase >1.5 times upper limit of normal (ULN).;31. Total bilirubin >ULN.;32. Platelet count <100 x 109/L (100,000/mm3).;33. Hemoglobin <85 g/L (8.5 g/dL; 5.3 mmol/L).;34. White blood cells <3.0 x 109/L (3000/mm3).;35. Absolute neutrophil count <2.0 x 109/L (2000/mm3).;36. Absolute lymphocyte count <0.5 x 109/L (500/mm3).

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-01-2014
Enrollment:	150
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	RoActemra
Generic name:	tocilizumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	08-10-2013
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	24-10-2013
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	21-01-2014
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-03-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-05-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-06-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-07-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-11-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-03-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2013-000342-19-NL
Other	ML28702/OSCAR
CCMO	NL44026.056.13