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Trial record **1 of 1** for: CACZ885A2204

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Safety and Efficacy of Intravenous ACZ885 and Oral Methotrexate Therapy in Patients With Early Rheumatoid Arthritis

This study has been completed.

Sponsor:
Novartis

Information provided by (Responsible Party):
Novartis

ClinicalTrials.gov Identifier:
NCT00487825

First received: June 18, 2007
Last updated: July 24, 2012
Last verified: July 2012
History of Changes

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Results First Received: January 24, 2011

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor); Primary Purpose: Treatment
Condition:	Rheumatoid Arthritis
Interventions:	Drug: Canakinumab (investigational) Drug: Placebo Drug: Methotrexate (MTX)

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
A 26-week, phase II, multi-center, randomized, double-blind, placebo-controlled study to assess the response to treatment and to determine a biomarker profile in responders to Canakinumab plus MTX as com-pared to MTX alone in early rheumatoid arthritis patients. Study starting 16-Mar 2007 and ending 19 Dec 2008.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
Canakinumab + Methotrexate	Canakinumab, human anti-interleukin-1beta monoclonal antibody plus Methotrexate (MTX). Intravenous (IV) Infusion of 600mg canakinumab on Day 1, 15 continuing every 4 weeks up to week 26. Methotrexate is given as variable dosing regimen of 7.5 mg–15 mg weekly.
Methotrexate	Methotrexate is given as variable dosing regimen of 7.5 mg–15 mg weekly. Intravenous (IV) Placebo Solution, given in the same mode of administration as the canakinumab solution.

Participant Flow: Overall Study

	Canakinumab + Methotrexate	Methotrexate
STARTED	52 [1]	26
COMPLETED	46	21
NOT COMPLETED	6	5
Adverse Event	2	2
Lack of Efficacy	1	1
not specified	3	2

[1] "Started" indicates Intent-to-treat population (ITT)

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Canakinumab + Methotrexate	Canakinumab, human anti-interleukin-1beta monoclonal antibody plus Methotrexate (MTX). Intravenous (IV) Infusion of 600mg canakinumab on Day 1, 15 continuing every 4 weeks up to week 26. Methotrexate is given as variable dosing regimen of 7.5 mg–15 mg weekly.
Methotrexate	Methotrexate is given as variable dosing regimen of 7.5 mg–15 mg weekly. Intravenous (IV) Placebo Solution, given in the same mode of administration as the canakinumab solution.
Total	Total of all reporting groups

Baseline Measures

	Canakinumab + Methotrexate	Methotrexate	Total
Number of Participants [units: participants]	52	26	78
Age [units: Years] Mean (Standard Deviation)	51.6 (12.78)	49.7 (14.15)	50.9 (13.9)
Gender [units: participants]			
Female	45	18	63
Male	7	8	15

Outcome Measures

Hide All Outcome Measures

1. Primary: Response to Intravenous Canakinumab and Oral Methotrexate (MTX) Compared to MTX Alone as Determined by 50% Improvement in Symptoms According to the American College of Rheumatology Criteria (ACR50) [Time Frame: 6, 14, and 26 weeks of treatment]

Measure Type	Primary
Measure Title	Response to Intravenous Canakinumab and Oral Methotrexate (MTX) Compared to MTX Alone as Determined by 50% Improvement in Symptoms According to the American College of Rheumatology Criteria (ACR50)
Measure Description	A patient was considered as improved according to the ACR50 criteria if she/he had at least a 50 % improvement in both the tender and the swollen 28-joint count, and in at least 3 of the following 5 measures: • Patient's pain assessment (Visual Analogue Scale (VAS) 100 mm) • Patient's global assessment of disease activity (VAS 100 mm) • Physician's global assessment of disease activity (VAS 100 mm) • Patient self-assessed disability (Health Assessment Questionnaire (HAQ) score) • Acute phase reactant (high sensitivity C-reactive Protein (hsCRP))
Time Frame	6, 14, and 26 weeks of treatment
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent-to-treat population (ITT)

Reporting Groups

	Description
Canakinumab + Methotrexate	Canakinumab, human anti-interleukin-1beta monoclonal antibody plus Methotrexate (MTX). Intravenous (IV) Infusion of 600mg canakinumab on Day 1, 15 continuing every 4 weeks up to week 26. Methotrexate is given as variable dosing regimen of 7.5 mg-15 mg weekly.
Methotrexate	Methotrexate is given as variable dosing regimen of 7.5 mg-15 mg weekly. Intravenous (IV) Placebo Solution, given in the same mode of administration as the canakinumab solution.

Measured Values

	Canakinumab + Methotrexate	**Methotrexate**
Number of Participants Analyzed [units: participants]	**52**	**26**
Response to Intravenous Canakinumab and Oral Methotrexate (MTX) Compared to MTX Alone as Determined by 50% Improvement in Symptoms According to the American College of Rheumatology Criteria (ACR50) [units: Participants]		
ACR50 6 weeks after first dosing	**10**	**5**
ACR50 14 weeks after first dosing	**19**	**9**
ACR50 26 weeks after first dosing	**24**	**11**

No statistical analysis provided for Response to Intravenous Canakinumab and Oral Methotrexate (MTX) Compared to MTX Alone as Determined by 50% Improvement in Symptoms According to the American College of Rheumatology Criteria (ACR50)

2. Secondary: Response to Intravenous (IV) Canakinumab and Oral Methotrexate (MTX) Therapy (ACR20, 70, 90) Compared to MTX Alone [Time Frame: At 6 weeks, 14 weeks, and 26 weeks]

Measure Type	Secondary
Measure Title	Response to Intravenous (IV) Canakinumab and Oral Methotrexate (MTX) Therapy (ACR20, 70, 90) Compared to MTX Alone
Measure Description	A patient was considered as improved according to the criteria of ACR 20 equaling at least 20%, ACR70 = 70%, and

	ACR90 = 90% improvement in the tender and the swollen 28-joint count, and in at least 3 of the following 5 measures: • Patient's pain assessment (Visual Analogue Scale (VAS) 100 mm) • Patient's global assessment of disease activity (VAS 100 mm) • Physician's global assessment of disease activity (VAS 100 mm) • Patient self-assessed disability (Health Assessment Questionnaire (HAQ) score) • Acute phase reactant (high sensitivity C-reactive Protein (hsCRP))
Time Frame	At 6 weeks, 14 weeks, and 26 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent-to-treat population (ITT)

Reporting Groups

	Description
Canakinumab + Methotrexate	Canakinumab, human anti-interleukin-1beta monoclonal antibody plus Methotrexate (MTX). Intravenous (IV) Infusion of 600mg canakinumab on Day 1, 15 continuing every 4 weeks up to week 26. Methotrexate is given as variable dosing regimen of 7.5 mg-15 mg weekly.
Methotrexate	Methotrexate is given as variable dosing regimen of 7.5 mg-15 mg weekly. Intravenous (IV) Placebo Solution, given in the same mode of administration as the canakinumab solution.

Measured Values

	Canakinumab + Methotrexate	**Methotrexate**
Number of Participants Analyzed [units: participants]	**52**	**26**
Response to Intravenous (IV) Canakinumab and Oral Methotrexate (MTX) Therapy (ACR20, 70, 90) Compared to MTX Alone [units: Participants]		
ACR20 6 weeks after first dosing	**32**	**13**
ACR20 14 weeks after first dosing	**38**	**16**
ACR20 26 weeks after first dosing	**39**	**20**
ACR70 6 weeks after first dosing	**1**	**3**
ACR70 14 weeks after first dosing	**6**	**3**
ACR70 26 weeks after first dosing	**17**	**9**
ACR90 6 weeks after first dosing	**0**	**0**
ACR90 14 weeks after first dosing	**1**	**0**
ACR90 26 weeks after first dosing	**4**	**2**

No statistical analysis provided for Response to Intravenous (IV) Canakinumab and Oral Methotrexate (MTX) Therapy (ACR20, 70, 90) Compared to MTX Alone

3. Secondary: Percentage of Participants Achieving a Good European League Against Rheumatism (EULAR) Response (Based on the Disease Activity Score (DAS28)) at 26 Weeks [Time Frame: At 26 weeks]

Measure Type	Secondary

Measure Title	Percentage of Participants Achieving a Good European League Against Rheumatism (EULAR) Response (Based on the Disease Activity Score (DAS28)) at 26 Weeks
Measure Description	At each visit (including baseline) the DAS28 is derived as: DAS28 = 0.56*√ (tender28) + 0.28 * √ (swollen28) + 0.36 * loge(CRP+1) + 0.014*PGDA+ 0.96; where tender28 is the tender 28-joint count, swollen28 is the swollen 28-joint count, PGDA is the patient's global assessment of disease activity. Patients can be scored on a range of 0 to 10. When current DAS < 3.2, good response is defined as >1.2 improvement in DAS from baseline and non-response is improvement of ≤0.6. When current DAS >5.1, non-response is improvement of >0.6 but ≤1.2 . All others are moderate responses.
Time Frame	At 26 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intention to treat (ITT) population

Reporting Groups

	Description
Canakinumab + Methotrexate	Canakinumab, human anti-interleukin-1beta monoclonal antibody plus Methotrexate (MTX). Intravenous (IV) Infusion of 600mg canakinumab on Day 1, 15 continuing every 4 weeks up to week 26. Methotrexate is given as variable dosing regimen of 7.5 mg–15 mg weekly.
Methotrexate	Methotrexate is given as variable dosing regimen of 7.5 mg–15 mg weekly. Intravenous (IV) Placebo Solution, given in the same mode of administration as the canakinumab solution.

Measured Values

	Canakinumab + Methotrexate	**Methotrexate**
Number of Participants Analyzed [units: participants]	**52**	**26**
Percentage of Participants Achieving a Good European League Against Rheumatism (EULAR) Response (Based on the Disease Activity Score (DAS28)) at 26 Weeks [units: Percentage of Participants]		
Good responders	**46.2**	**30.8**
Mild responders	**28.8**	**42.3**
Non responders	**17.3**	**11.5**

No statistical analysis provided for Percentage of Participants Achieving a Good European League Against Rheumatism (EULAR) Response (Based on the Disease Activity Score (DAS28)) at 26 Weeks

4. Secondary: The Number of Participants in Clinical Remission Based on Disease Activity Score (DAS)28 and Simplified Disease Activity Index (SDAI) [Time Frame: At 6 weeks, 14 weeks and 24 weeks]

Measure Type	Secondary
Measure Title	The Number of Participants in Clinical Remission Based on Disease Activity Score (DAS)28 and Simplified Disease Activity Index (SDAI)
Measure Description	At each visit (including baseline) the DAS28 and SDAI variables were derived using the following formulas: DAS28 = 0.56*√ (tender28) + 0.28 * √ (swollen28) + 0.36 * loge(CRP+1) + 0.014*PGDA+ 0.96; SDAI = tender28 + swollen28 + CRP + (PGDA / 10) + (EGDA / 10) where tender28 is the tender 28-joint count, swollen28 is the swollen 28-joint count, CRP is C-reactive protein, PGDA is the patient's global assessment of disease activity and EGDA is the physician's global assessment of disease activity.

	The Number of Participants in clinical remission is defined as the DAS28 ≤ 2.6 or SDAI ≤ 3.3.
Time Frame	At 6 weeks, 14 weeks and 24 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intention to treat (ITT) population

Reporting Groups

	Description
Canakinumab + Methotrexate	Canakinumab, human anti-interleukin-1beta monoclonal antibody plus Methotrexate (MTX). Intravenous (IV) Infusion of 600mg canakinumab on Day 1, 15 continuing every 4 weeks up to week 26. Methotrexate is given as variable dosing regimen of 7.5 mg–15 mg weekly.
Methotrexate	Methotrexate is given as variable dosing regimen of 7.5 mg–15 mg weekly. Intravenous (IV) Placebo Solution, given in the same mode of administration as the canakinumab solution.

Measured Values

	Canakinumab + Methotrexate	Methotrexate
Number of Participants Analyzed [units: participants]	**52**	**26**
The Number of Participants in Clinical Remission Based on Disease Activity Score (DAS)28 and Simplified Disease Activity Index (SDAI) [units: Participants]		
After 6 weeks	**6**	**3**
After 14 weeks	**13**	**3**
After 26 weeks	**20**	**6**

No statistical analysis provided for The Number of Participants in Clinical Remission Based on Disease Activity Score (DAS)28 and Simplified Disease Activity Index (SDAI)

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	26 weeks plus a follow-up period of 3 months
Additional Description	No text entered.

Reporting Groups

	Description
Canakinumab + Methotrexate	Canakinumab, human anti-interleukin-1beta monoclonal antibody plus Methotrexate (MTX). Intravenous (IV) Infusion of 600mg canakinumab on Day 1, 15 continuing every 4 weeks up to week 26. Methotrexate is given as variable dosing regimen of 7.5 mg–15 mg weekly.
Methotrexate	Methotrexate is given as variable dosing regimen of 7.5 mg–15 mg weekly. Intravenous (IV) Placebo Solution, given in the same mode of administration as the canakinumab solution.

Serious Adverse Events

	Canakinumab + Methotrexate	Methotrexate

Total, serious adverse events		
# participants affected / at risk	**1/52 (1.92%)**	**2/26 (7.69%)**
Gastrointestinal disorders		
Lip oedema † 1		
# participants affected / at risk	**1/52 (1.92%)**	**0/26 (0.00%)**
Upper gastrointestinal haemorrhage † 1		
# participants affected / at risk	**0/52 (0.00%)**	**1/26 (3.85%)**
General disorders		
Non-cardiac chest pain † 1		
# participants affected / at risk	**0/52 (0.00%)**	**1/26 (3.85%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA

Other Adverse Events

Hide Other Adverse Events

Time Frame	26 weeks plus a follow-up period of 3 months
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Canakinumab + Methotrexate	Canakinumab, human anti-interleukin-1beta monoclonal antibody plus Methotrexate (MTX). Intravenous (IV) Infusion of 600mg canakinumab on Day 1, 15 continuing every 4 weeks up to week 26. Methotrexate is given as variable dosing regimen of 7.5 mg–15 mg weekly.
Methotrexate	Methotrexate is given as variable dosing regimen of 7.5 mg–15 mg weekly. Intravenous (IV) Placebo Solution, given in the same mode of administration as the canakinumab solution.

Other Adverse Events

	Canakinumab + Methotrexate	Methotrexate
Total, other (not including serious) adverse events		
# participants affected / at risk	**36/52 (69.23%)**	**21/26 (80.77%)**
Ear and labyrinth disorders		
Vertigo † 1		
# participants affected / at risk	**2/52 (3.85%)**	**2/26 (7.69%)**
Gastrointestinal disorders		
Abdominal pain † 1		
# participants affected / at risk	**0/52 (0.00%)**	**2/26 (7.69%)**
Abdominal pain upper † 1		
# participants affected / at risk	**5/52 (9.62%)**	**0/26 (0.00%)**
Diarrhoea † 1		
# participants affected / at risk	**5/52 (9.62%)**	**6/26 (23.08%)**

Dyspepsia † [1]		
# participants affected / at risk	4/52 (7.69%)	0/26 (0.00%)
Nausea † [1]		
# participants affected / at risk	8/52 (15.38%)	9/26 (34.62%)
Vomiting † [1]		
# participants affected / at risk	4/52 (7.69%)	3/26 (11.54%)
General disorders		
Fatigue † [1]		
# participants affected / at risk	7/52 (13.46%)	2/26 (7.69%)
Nodule † [1]		
# participants affected / at risk	0/52 (0.00%)	2/26 (7.69%)
Oedema peripheral † [1]		
# participants affected / at risk	4/52 (7.69%)	2/26 (7.69%)
Infections and infestations		
Bronchitis † [1]		
# participants affected / at risk	2/52 (3.85%)	2/26 (7.69%)
Influenza † [1]		
# participants affected / at risk	3/52 (5.77%)	0/26 (0.00%)
Nasopharyngitis † [1]		
# participants affected / at risk	6/52 (11.54%)	5/26 (19.23%)
Upper respiratory tract infection † [1]		
# participants affected / at risk	4/52 (7.69%)	2/26 (7.69%)
Injury, poisoning and procedural complications		
Fall † [1]		
# participants affected / at risk	1/52 (1.92%)	2/26 (7.69%)
Musculoskeletal and connective tissue disorders		
Arthralgia † [1]		
# participants affected / at risk	2/52 (3.85%)	2/26 (7.69%)
Back pain † [1]		
# participants affected / at risk	5/52 (9.62%)	5/26 (19.23%)
Pain in extremity † [1]		
# participants affected / at risk	2/52 (3.85%)	2/26 (7.69%)
Nervous system disorders		
Dizziness † [1]		
# participants affected / at risk	4/52 (7.69%)	4/26 (15.38%)
Headache † [1]		
# participants affected / at risk	7/52 (13.46%)	2/26 (7.69%)
Psychiatric disorders		
Depression † [1]		
# participants affected / at risk	3/52 (5.77%)	2/26 (7.69%)
Sleep disorder † [1]		
# participants affected / at risk	3/52 (5.77%)	0/26 (0.00%)
Respiratory, thoracic and mediastinal disorders		

Cough † 1		
# participants affected / at risk	**4/52 (7.69%)**	**3/26 (11.54%)**
Skin and subcutaneous tissue disorders		
Alopecia † 1		
# participants affected / at risk	**5/52 (9.62%)**	**3/26 (11.54%)**
Hyperhidrosis † 1		
# participants affected / at risk	**3/52 (5.77%)**	**1/26 (3.85%)**
Rash † 1		
# participants affected / at risk	**2/52 (3.85%)**	**3/26 (11.54%)**
Vascular disorders		
Hypertension † 1		
# participants affected / at risk	**3/52 (5.77%)**	**1/26 (3.85%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data
No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.
There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.
The agreement is: ☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo. ☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo. ☑ Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed. **Restriction Description:** The terms and conditions of Novartis' agreements with its investigators may vary. However, Novartis does not prohibit any investigator from publishing. Any publications from a single-site are postponed until the publication of the pooled data (i.e., data from all sites) in the clinical trial.

Results Point of Contact:

Name/Title: Study Director
Organization: Novartis Pharmaceuticals
phone: 862-778-8300

No publications provided

Responsible Party:	Novartis
ClinicalTrials.gov Identifier:	NCT00487825 History of Changes
Other Study ID Numbers:	**CACZ885A2204**
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Results First Received:	January 24, 2011
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Health Authority:	United States: Food and Drug Administration