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Trial record **1 of 1** for: CACZ885I2202

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Dose Finding, Safety and Efficacy of Monthly Subcutaneous Canakinumab Administration in Metformin Monotherapy Treated Type 2 Diabetic Patients

This study has been terminated.

(Numerically modest lowering of HbA1c with canakinumab in combination with metformin was inadequate to continue patients with T2DM into Period IV of this study.)

Sponsor:
Novartis

Information provided by (Responsible Party):
Novartis

ClinicalTrials.gov Identifier:
NCT00900146

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History of Changes

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Results First Received: November 22, 2011

Study Type:	Interventional
Study Design:	Allocation: Randomized; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor); Primary Purpose: Treatment
Condition:	Diabetes Mellitus, Type 2
Interventions:	Drug: Canakinumab Drug: Metformin Drug: Placebo

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
Study consisted of four periods: screening (Period I), dose-finding (Period II), intermediate (Period III),and long-term continuation (Period IV). Eligible patients were randomized for 4-month treatment of Period II. Intermediate period continued until primary analysis was completed and optimal dose was selected. Study got terminated in Period III.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
A total of 556 patients were randomized in Period II. 5 patients one in each 5, 15, 50mg Canakinumab arms and 2 in Placebo were randomized in error, but never received study treatment. All tables reflect the 551 treated patients.

Reporting Groups

	Description
Canakinumab 5 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 5 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 15 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 15 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a

	daily injection of insulin glargine as add-on therapy.
Canakinumab 50 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 50 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 150 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 150 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Placebo + Metformin	In 4 month dose finding period as well as during intermediate period, patients received one injection of canakinumab matching placebo monthly and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations).

Participant Flow for 2 periods

Period 1: Dose Finding: Period II (4 Months)

	Canakinumab 5 mg + Metformin	Canakinumab 15 mg + Metformin	Canakinumab 50 mg + Metformin	Canakinumab 150 mg + Metformin	Placebo + Metformin
STARTED	**93**	**95**	**92**	**92**	**179**
Full Analysis Set (FAS)/Safety	**93**	**95**	**92**	**92**	**179**
COMPLETED	**88**	**93**	**87**	**90**	**167** [1]
NOT COMPLETED	**5**	**2**	**5**	**2**	**12**
Withdrawal by	**2**	**2**	**5**	**1**	**9**

Subject					
Lost to Follow-up	**2**	**0**	**0**	**1**	**3**
Administrative problems	**1**	**0**	**0**	**0**	**0**

[1] Placebo also included 1 patient with no study completion page.

Period 2: Intermediate: Period III

	Canakinumab 5 mg + Metformin	Canakinumab 15 mg + Metformin	Canakinumab 50 mg + Metformin	Canakinumab 150 mg + Metformin	Placebo + Metformin
STARTED	**87**	**93**	**84**	**90**	**167**
Safety Set	**86**	**92**	**84**	**90**	**166**
COMPLETED	**0**	**0**	**0**	**0**	**0**
NOT COMPLETED	**87**	**93**	**84**	**90**	**167**
Withdrawal by Subject	**0**	**1**	**0**	**0**	**3**
Lost to Follow-up	**2**	**0**	**0**	**0**	**1**
Administrative problems	**85**	**92**	**84**	**90**	**163**

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 5 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 5 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 15 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 15 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 50 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 50 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 150 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 150 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.

Placebo + Metformin	In 4 month dose finding period as well as during intermediate period, patients received one injection of canakinumab matching placebo monthly and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations).
Total	Total of all reporting groups

Baseline Measures

	Canakinumab 5 mg + Metformin	Canakinumab 15 mg + Metformin	Canakinumab 50 mg + Metformin	Canakinumab 150 mg + Metformin	Placebo + Metformin	Total
Number of Participants [units: participants]	**93**	**95**	**92**	**92**	**179**	**551**
Age [1] [units: years] Mean (Standard Deviation)	**53.5 (10.27)**	**55.5 (9.70)**	**53.0 (9.29)**	**53.7 (10.36)**	**54.3 (10.15)**	**54.1 (9.99)**
Gender [units: participants]						
Female	**38**	**46**	**47**	**35**	**74**	**240**
Male	**55**	**49**	**45**	**57**	**105**	**311**

[1] Baseline measures were based on the full analysis set (FAS) which included all randomized patients except for mis-randomized patients. Mis-randomized patients referred to patients who are not qualified for randomization but who were inadvertently randomized into the study and did not receive study drug.

Outcome Measures

Hide All Outcome Measures

1. Primary: Number of Participants With Adverse Events (AEs), Serious Adverse Events, Death and Clinical Significant AEs During 4 Months (Period II) [Time Frame: 4 months (Period II)]

Measure Type	Primary

Measure Title	Number of Participants With Adverse Events (AEs), Serious Adverse Events, Death and Clinical Significant AEs During 4 Months (Period II)
Measure Description	Adverse events are defined as any unfavorable and unintended diagnosis, symptom, sign (including an abnormal laboratory finding), syndrome or disease which either occurs during study, having been absent at baseline, or, if present at baseline, appears to worsen. Serious adverse events are any untoward medical occurrences that result in death, are life threatening, require (or prolong) hospitalization, cause persistent or significant disability/incapacity, result in congenital anomalies or birth defects, or are other conditions which in judgment of investigators represent significant hazards.
Time Frame	4 months (Period II)
Safety Issue	Yes

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.
The safety set (SAF) included all patients who received at least one dose of study medication during Period II.

Reporting Groups

	Description
Canakinumab 5 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 5 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 15 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 15 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a

	daily injection of insulin glargine as add-on therapy.
Canakinumab 50 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 50 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 150 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 150 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Placebo + Metformin	In 4 month dose finding period as well as during intermediate period, patients received one injection of canakinumab matching placebo monthly and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations).

Measured Values

	Canakinumab 5 mg + Metformin	Canakinumab 15 mg + Metformin	Canakinumab 50 mg + Metformin	Canakinumab 150 mg + Metformin	Placebo + Metformin
Number of Participants Analyzed **[units: participants]**	**93**	**95**	**92**	**92**	**179**
Number of Participants With Adverse Events (AEs), Serious Adverse Events, Death and Clinical Significant AEs During 4 Months (Period II) **[units: Participants]**					
Any Adverse Events	**33**	**43**	**45**	**43**	**76**

Death	**0**	**0**	**0**	**0**	**0**
Serious Adverse Events	**2**	**1**	**2**	**5**	**6**

No statistical analysis provided for Number of Participants With Adverse Events (AEs), Serious Adverse Events, Death and Clinical Significant AEs During 4 Months (Period II)

2. Primary: Change From Baseline in Hemoglobin A1c (HbA1c) at Month 4 During Dose-finding Period of the Study (Period II) [Time Frame: Baseline, Month 4]

Measure Type	Primary
Measure Title	Change From Baseline in Hemoglobin A1c (HbA1c) at Month 4 During Dose-finding Period of the Study (Period II)
Measure Description	HbA1c was measured by National glycohemoglobin standardization program (NGSP) certified methodology. HbA1c is an integrated measure of average glucose concentration in plasma in the last 2-3 months. The analysis of covariance (ANCOVA) included treatment and metformin dose group as main effects and baseline HbA1c as a covariate.
Time Frame	Baseline, Month 4
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.
The full analysis set (included all randomized patients except for mis-randomized patients who randomized in error but did not receive study drug. Last observation carried forward (LOCF) method was used for patients without Month 4 HbA1c data for any reason and who used rescue medication or any other glucose lowering agents other than metformin.

Reporting Groups

	Description
Canakinumab 5 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 5 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a

	daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 15 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 15 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 50 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 50 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 150 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 150 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Placebo + Metformin	In 4 month dose finding period as well as during intermediate period, patients received one injection of canakinumab matching placebo monthly and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations).

Measured Values

	Canakinumab 5 mg + Metformin	Canakinumab 15 mg + Metformin	Canakinumab 50 mg + Metformin	Canakinumab 150 mg + Metformin	Placebo + Metformin
Number of Participants Analyzed [units: participants]	**92**	**94**	**89**	**91**	**175**
Change From Baseline in Hemoglobin A1c (HbA1c) at Month 4 During Dose-finding Period of the Study (Period II) [units: percentage of hemoglobin A1c] Least Squares Mean (Standard Error)	**-0.19 (0.072)**	**-0.29 (0.071)**	**-0.31 (0.073)**	**-0.25 (0.071)**	**-0.13 (0.053)**

No statistical analysis provided for Change From Baseline in Hemoglobin A1c (HbA1c) at Month 4 During Dose-finding Period of the Study (Period II)

3. Primary: Change From Baseline in Dynamic Phase Secreted Insulin Per Unit of Glucose Concentration (Φd) Over 4 Months (Period III) [Time Frame: Baseline, Over Month 4]

Measure Type	Primary
Measure Title	Change From Baseline in Dynamic Phase Secreted Insulin Per Unit of Glucose Concentration (Φd) Over 4 Months (Period III)
Measure Description	This was planned as interim analysis and was not conducted because the study was terminated in period III.
Time Frame	Baseline, Over Month 4
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.
The benefit of canakinumab for the treatment of patients with type 2 diabetes mellitus in combination with metformin was inadequate to continue patients into Period IV in the present study, and therefore decided to terminate the study during Period III.

Reporting Groups

	Description

Canakinumab 5 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 5 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 15 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 15 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 50 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 50 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 150 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 150 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Placebo + Metformin	In 4 month dose finding period as well as during intermediate period, patients received one injection of canakinumab matching placebo monthly and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by

	local regulations).

Measured Values

	Canakinumab 5 mg + Metformin	Canakinumab 15 mg + Metformin	Canakinumab 50 mg + Metformin	Canakinumab 150 mg + Metformin	Placebo + Metformin
Number of Participants Analyzed **[units: participants]**	**0**	**0**	**0**	**0**	**0**
Change From Baseline in Dynamic Phase Secreted Insulin Per Unit of Glucose Concentration (Φd) Over 4 Months (Period III) **[units: pmol/min/m2/mmol* hour/L]** **Least Squares Mean (Standard Error)**					

No statistical analysis provided for Change From Baseline in Dynamic Phase Secreted Insulin Per Unit of Glucose Concentration (Φd) Over 4 Months (Period III)

4. Secondary: Change From Baseline in C-peptide Area Under Curve (AUC 0-4 Hours) Following Meal Test (Period II) [Time Frame: Baseline, Month 4]

Measure Type	Secondary
Measure Title	Change From Baseline in C-peptide Area Under Curve (AUC 0-4 Hours) Following Meal Test (Period II)
Measure Description	A standard liquid mixed-meal challenge was done at baseline and Month 4. Patients completed each standard meal challenge with measurement of C-peptide prior to and after a liquid mixed meal. Sampling times were -20, -10, and -1, 10, 20, 30, 60, 90, 120, 150, 180 and 240 minutes relative to start of meal. C-peptide levels over 4 hrs were shown as Area Under the Curve,(AUC). AUC was calculated as: x=1 AUC ΣAx n Where Ax = AUC for the 240 min.interval, and X = 1 for the 1st interval. The analysis of covariance included baseline C-peptide AUC 0-4 hours as a covariate.
Time Frame	Baseline, Month 4
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.

The full analysis set included all randomized patients except for mis-randomized patients who inadvertently randomized into study and did not receive study drug. Last observation carried forward method was used for patients without Month 4 data for any reason and who used rescue medication or any other glucose lowering agents other than metformin.

Reporting Groups

	Description
Canakinumab 5 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 5 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 15 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 15 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 50 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 50 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 150 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 150 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local

	regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Placebo + Metformin	In 4 month dose finding period as well as during intermediate period, patients received one injection of canakinumab matching placebo monthly and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations).

Measured Values

	Canakinumab 5 mg + Metformin	Canakinumab 15 mg + Metformin	Canakinumab 50 mg + Metformin	Canakinumab 150 mg + Metformin	Placebo + Metformin
Number of Participants Analyzed [units: participants]	**81**	**87**	**83**	**91**	**153**
Change From Baseline in C-peptide Area Under Curve (AUC 0-4 Hours) Following Meal Test (Period II) [units: nmol*hour/L] Least Squares Mean (Standard Error)	**-0.399 (0.1444)**	**-0.388 (0.1394)**	**-0.834 (0.1425)**	**-0.610 (0.1396)**	**-0.588 (0.1070)**

No statistical analysis provided for Change From Baseline in C-peptide Area Under Curve (AUC 0-4 Hours) Following Meal Test (Period II)

5. Secondary: Change From Baseline in Prandial Plasma Glucose Area Under Curve (AUC0-4 Hours) Following Meal Test (Period II) [Time Frame: Baseline, Month 4]

Measure Type	Secondary
Measure Title	Change From Baseline in Prandial Plasma Glucose Area Under Curve (AUC0-4 Hours) Following Meal Test (Period II)
Measure Description	A standard liquid mixed-meal challenge was done at baseline and Month 4. Patients completed each standard meal challenge with measurement of glucose prior to and after a liquid mixed meal. Sampling times were -20, -10, and -1, 10, 20, 30, 60, 90, 120, 150, 180 and 240 minutes relative to the start of meal. Glucose levels over 4 hrs were shown as Area Under the Curve,(AUC). AUC was

	calculated as: x=1 AUC ΣAx n Where Ax = AUC for the 240 min.interval, and X = 1 for the 1st interval. The model of analysis of covariance included baseline plasma glucose AUC 0-4 hours as a covariate.
Time Frame	Baseline, Month 4
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.
The full analysis set included all randomized patients except for mis-randomized patients who inadvertently randomized into study and did not receive study drug. Last observation carried forward method was used for patients without Month 4 data for any reason and who used rescue medication or any other glucose lowering agents other than metformin.

Reporting Groups

	Description
Canakinumab 5 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 5 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 15 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 15 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 50 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 50 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local

	regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 150 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 150 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Placebo + Metformin	In 4 month dose finding period as well as during intermediate period, patients received one injection of canakinumab matching placebo monthly and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations).

Measured Values

	Canakinumab 5 mg + Metformin	Canakinumab 15 mg + Metformin	Canakinumab 50 mg + Metformin	Canakinumab 150 mg + Metformin	Placebo + Metformin
Number of Participants Analyzed **[units: participants]**	**79**	**83**	**82**	**84**	**147**
Change From Baseline in Prandial Plasma Glucose Area Under Curve (AUC0-4 Hours) Following Meal Test (Period II) **[units: mmol*hour/L]** **Least Squares Mean (Standard Error)**	**-0.999 (0.8094)**	**-1.012 (0.7917)**	**-2.103 (0.7928)**	**1.618 (0.7791)**	**-0.851 (0.6053)**

No statistical analysis provided for Change From Baseline in Prandial Plasma Glucose Area Under Curve (AUC0-4 Hours) Following Meal Test (Period II)

6. Secondary: Change From Baseline in Insulin Area Under Curve (AUC 0-4 Hours) Following Meal Test (Period II) [Time Frame: Baseline, Month 4]

Measure Type	Secondary
Measure Title	Change From Baseline in Insulin Area Under Curve (AUC 0-4 Hours) Following Meal Test (Period II)
Measure Description	A standard liquid mixed-meal challenge was done at baseline and Month 4. Patients completed each standard meal challenge with measurement of insulin prior to and after a liquid mixed meal. Sampling times were -20, -10, and -1, 10, 20, 30, 60, 90, 120, 150, 180 and 240 minutes relative to the start of meal. Insulin levels over 4 hrs were shown as Area Under the Curve,(AUC). AUC was calculated as: x=1 AUC ΣAx n Where Ax = AUC for the 240 min.interval, and X = 1 for the 1st interval. Model of analysis of covariance included baseline insulin AUC 0-4 hours as covariate.
Time Frame	Baseline, Month 4
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.
The full analysis set included all randomized patients except for mis-randomized patients who inadvertently randomized into study and did not receive study drug. Last observation carried forward method was used for patients without Month 4 data for any reason and who used rescue medication or any other glucose lowering agents other than metformin.

Reporting Groups

	Description
Canakinumab 5 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 5 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 15 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 15 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a

	daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 50 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 50 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 150 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 150 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Placebo + Metformin	In 4 month dose finding period as well as during intermediate period, patients received one injection of canakinumab matching placebo monthly and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations).

Measured Values

	Canakinumab 5 mg + Metformin	Canakinumab 15 mg + Metformin	Canakinumab 50 mg + Metformin	Canakinumab 150 mg + Metformin	Placebo + Metformin
Number of Participants Analyzed [units: participants]	**68**	**73**	**70**	**77**	**133**
Change From Baseline in Insulin Area Under Curve (AUC 0-4 Hours) Following Meal Test (Period II) [units: pmol*hour/L]	**18.623 (28.5445)**	**66.237 (27.4053)**	**-14.016 (27.9738)**	**-20.583 (26.5602)**	**0.121 (20.7195)**

Least Squares Mean (Standard Error)					

No statistical analysis provided for Change From Baseline in Insulin Area Under Curve (AUC 0-4 Hours) Following Meal Test (Period II)

7. Secondary: Change From Baseline in 2-hour Glucose Level Following Meal Test (Period II) [Time Frame: Baseline, Month 4]

Measure Type	Secondary
Measure Title	Change From Baseline in 2-hour Glucose Level Following Meal Test (Period II)
Measure Description	A standard liquid mixed-meal challenge was done at baseline and Month 4. Patients fasted overnight after 10 pm on day prior to scheduled visit. Study visits should occur before 10 am. Patients completed each standard meal challenge with measurement of glucose prior to and after a liquid mixed meal. The sampling times were -20, -10, and -1, 10, 20, 30, 60, 90, 120, 150, 180 and 240 minutes relative to the start of meal. The analysis of covariance included treatment and metformin dose group as main effects and baseline 2-hour glucose level as covariate.
Time Frame	Baseline, Month 4
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.
The full analysis set included all randomized patients except for mis-randomized patients who inadvertently randomized into study and did not receive study drug. Last observation carried forward method was used for patients without Month 4 data for any reason and who used rescue medication or any other glucose lowering agents other than metformin.

Reporting Groups

	Description
Canakinumab 5 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 5 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was

	completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 15 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 15 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 50 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 50 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 150 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 150 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Placebo + Metformin	In 4 month dose finding period as well as during intermediate period, patients received one injection of canakinumab matching placebo monthly and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations).

Measured Values

	Canakinumab 5	Canakinumab 15	Canakinumab 50	Canakinumab 150	Placebo +

	mg + Metformin	mg + Metformin	mg + Metformin	mg + Metformin	Metformin
Number of Participants Analyzed [units: participants]	**79**	**85**	**83**	**84**	**151**
Change From Baseline in 2-hour Glucose Level Following Meal Test (Period II) [units: mmol/L] Least Squares Mean (Standard Error)	**-0.427 (0.2537)**	**-0.239 (0.2457)**	**-0.777 (0.2471)**	**0.262 (0.2445)**	**-0.347 (0.1873)**

No statistical analysis provided for Change From Baseline in 2-hour Glucose Level Following Meal Test (Period II)

8. Secondary: Change From Baseline in Peak Glucose Level Following Meal Test (Period II) [Time Frame: Baseline, Month 4]

Measure Type	Secondary
Measure Title	Change From Baseline in Peak Glucose Level Following Meal Test (Period II)
Measure Description	A standard liquid mixed-meal challenge was done at baseline and Month 4. Patients fasted overnight after 10 pm on day prior to scheduled visit. Study visits should occur before 10 am. Patients completed each standard meal challenge with measurement of glucose prior to and after a liquid mixed meal. The sampling times were -20, -10, and -1, 10, 20, 30, 60, 90, 120, 150, 180 and 240 minutes relative to the start of meal. The analysis of covariance included treatment and metformin dose group as main effects and baseline peak glucose level as covariate.
Time Frame	Baseline, Month 4
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.
The full analysis set included all randomized patients except for mis-randomized patients who inadvertently randomized into study and did not receive study drug. Last observation carried forward method was used for patients without Month 4 data for any reason and who used rescue medication or any other glucose lowering agents other than metformin.

Reporting Groups

	Description
Canakinumab 5 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 5 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 15 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 15 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 50 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 50 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 150 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 150 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.

Placebo + Metformin	In 4 month dose finding period as well as during intermediate period, patients received one injection of canakinumab matching placebo monthly and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations).

Measured Values

	Canakinumab 5 mg + Metformin	Canakinumab 15 mg + Metformin	Canakinumab 50 mg + Metformin	Canakinumab 150 mg + Metformin	Placebo + Metformin
Number of Participants Analyzed [units: participants]	**81**	**85**	**83**	**87**	**152**
Change From Baseline in Peak Glucose Level Following Meal Test (Period II) [units: mmol/L] Least Squares Mean (Standard Error)	**-0.386 (0.2302)**	**-0.380 (0.2257)**	**-0.565 (0.2270)**	**0.381 (0.2208)**	**-0.339 (0.1711)**

No statistical analysis provided for Change From Baseline in Peak Glucose Level Following Meal Test (Period II)

9. Secondary: Change From Baseline in Peak C-peptide Following Meal Test (Period II) [Time Frame: Baseline, Month 4]

Measure Type	Secondary
Measure Title	Change From Baseline in Peak C-peptide Following Meal Test (Period II)
Measure Description	A standard liquid mixed-meal challenge was done at baseline and Month 4. Patients fasted overnight after 10 pm on the day prior to scheduled visit. Study visits should occur before 10 am. Patients completed each standard meal challenge with measurement of C-peptide prior to and after a liquid mixed meal. Sampling times were -20, -10, and -1, 10, 20, 30, 60, 90, 120, 150, 180 and 240 minutes relative to the start of meal. The analysis of covariance included treatment and metformin dose group as main effects and baseline peak C-peptide level as a covariate.
Time Frame	Baseline, Month 4
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.

The full analysis set included all randomized patients except for mis-randomized patients who inadvertently randomized into study and did not receive study drug. Last observation carried forward method was used for patients without Month 4 data for any reason and who used rescue medication or any other glucose lowering agents other than metformin.

Reporting Groups

	Description
Canakinumab 5 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 5 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 15 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 15 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 50 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 50 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 150 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 150 mg Canakinumab injected in the clinic

	at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Placebo + Metformin	In 4 month dose finding period as well as during intermediate period, patients received one injection of canakinumab matching placebo monthly and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations).

Measured Values

	Canakinumab 5 mg + Metformin	Canakinumab 15 mg + Metformin	Canakinumab 50 mg + Metformin	Canakinumab 150 mg + Metformin	Placebo + Metformin
Number of Participants Analyzed [units: participants]	**84**	**89**	**84**	**89**	**154**
Change From Baseline in Peak C-peptide Following Meal Test (Period II) [units: nmol/L] Least Squares Mean (Standard Error)	**-0.075 (0.0524)**	**-0.115 (0.0509)**	**-0.227 (0.0523)**	**-0.207 (0.0506)**	**-0.212 (0.0394)**

No statistical analysis provided for Change From Baseline in Peak C-peptide Following Meal Test (Period II)

10. Secondary: Change From Baseline in Peak Insulin Level Following Meal Test (Period II) [Time Frame: Baseline, Month 4]

Measure Type	Secondary
Measure Title	Change From Baseline in Peak Insulin Level Following Meal Test (Period II)
Measure Description	A standard liquid mixed-meal challenge was done at baseline and Month 4. Patients fasted overnight after 10 pm on day prior to scheduled visit. Study visits should occur before 10 am. Patients completed each standard meal challenge with measurement of insulin prior to and after a liquid mixed meal. The sampling times were -20, -10, and -1, 10, 20, 30, 60, 90, 120, 150, 180 and 240 minutes relative to the start of meal. The analysis of covariance included treatment and metformin dose group as main effects and

	baseline 2-hour insulin level as covariate.
Time Frame	Baseline, Month 4
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.
The full analysis set included all randomized patients except for mis-randomized patients who inadvertently randomized into study and did not receive study drug. Last observation carried forward method was used for patients without Month 4 data for any reason and who used rescue medication or any other glucose lowering agents other than metformin.

Reporting Groups

	Description
Canakinumab 5 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 5 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 15 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 15 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 50 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 50 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a

	daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 150 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 150 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Placebo + Metformin	In 4 month dose finding period as well as during intermediate period, patients received one injection of canakinumab matching placebo monthly and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations).

Measured Values

	Canakinumab 5 mg + Metformin	Canakinumab 15 mg + Metformin	Canakinumab 50 mg + Metformin	Canakinumab 150 mg + Metformin	Placebo + Metformin
Number of Participants Analyzed [units: participants]	**76**	**81**	**82**	**84**	**148**
Change From Baseline in Peak Insulin Level Following Meal Test (Period II) [units: pmol/L] Least Squares Mean (Standard Error)	**13.1 (14.40)**	**26.0 (14.00)**	**2.0 (13.88)**	**-7.0 (13.61)**	**1.7 (10.59)**

No statistical analysis provided for Change From Baseline in Peak Insulin Level Following Meal Test (Period II)

11. Secondary: Change From Baseline in Insulin Secretion Rates Relative to Glucose AUC (0-2 Hours) at Month 4 Following Meal Test (Period II) [Time Frame: Baseline, Month 4]

Measure Type	Secondary
Measure Title	Change From Baseline in Insulin Secretion Rates Relative to Glucose AUC (0-2 Hours) at Month 4 Following Meal Test (Period II)
Measure Description	Change in Insulin Secretion Rate stimulated by Liquid mixed-meal challenge. A standard liquid mixed-meal challenge was done at baseline and Month 4. Blood samples were taken prior to and after meal for glucose and insulin at sample times: -20, -10, -1 and 10, 20, 30, 60, 90, 120, 180, and 240 minutes relative to the start of the meal. The model of analysis of covariance included baseline Insulin secretion rate relative to glucose AUC at 0-2 hours as a covariate.
Time Frame	Baseline, Month 4
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.
The full analysis set included all randomized patients except for mis-randomized patients who inadvertently randomized into study and did not receive study drug. Last observation carried forward method was used for patients without Month 4 data for any reason and who used rescue medication or any other glucose lowering agents other than metformin.

Reporting Groups

	Description
Canakinumab 5 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 5 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 15 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 15 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief

	visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 50 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 50 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 150 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 150 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Placebo + Metformin	In 4 month dose finding period as well as during intermediate period, patients received one injection of canakinumab matching placebo monthly and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations).

Measured Values

	Canakinumab 5 mg + Metformin	Canakinumab 15 mg + Metformin	Canakinumab 50 mg + Metformin	Canakinumab 150 mg + Metformin	Placebo + Metformin
Number of Participants Analyzed **[units: participants]**	**77**	**83**	**81**	**82**	**149**
Change From Baseline in Insulin Secretion Rates Relative to Glucose AUC (0-2 Hours) at Month 4 Following Meal Test (Period II) **[units: pmol/min/m²/mmol *hour/L]**	**-0.369 (0.6922)**	**-0.331 (0.6705)**	**-1.761 (0.6744)**	**-2.428 (0.6681)**	**-1.635 (0.5084)**

Least Squares Mean (Standard Error)					

No statistical analysis provided for Change From Baseline in Insulin Secretion Rates Relative to Glucose AUC (0-2 Hours) at Month 4 Following Meal Test (Period II)

12. Secondary: Change From Baseline in 2 Hour Insulin Secretion Rate Derived Based on Glucose and C-peptide Following at Month 4 Following Meal Test (Period II) [Time Frame: Baseline, Month 4]

Measure Type	Secondary
Measure Title	Change From Baseline in 2 Hour Insulin Secretion Rate Derived Based on Glucose and C-peptide Following at Month 4 Following Meal Test (Period II)
Measure Description	A standard liquid mixed-meal challenge was done at baseline and Month 4. A 2 hour insulin secretion rate using deconvolution was performed. The deconvolution was an algorithm that analyzed the insulin secretion rate relative to glucose and C-peptide combined. Blood samples were taken prior to and after meal at sample times: -20, -10, -1 and 10, 20, 30, 60, 90, 120, 180, and 240 minutes relative to the start of the meal. The analysis of covariance included treatment and metformin dose group as main effects and baseline 2 hour Insulin secretion rate as a covariate.
Time Frame	Baseline, Month 4
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.
The full analysis set included all randomized patients except for mis-randomized patients who inadvertently randomized into study and did not receive study drug. Last observation carried forward method was used for patients without Month 4 data for any reason and who used rescue medication or any other glucose lowering agents other than metformin.

Reporting Groups

	Description
Canakinumab 5 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 5 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local

	regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 15 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 15 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 50 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 50 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 150 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 150 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Placebo + Metformin	In 4 month dose finding period as well as during intermediate period, patients received one injection of canakinumab matching placebo monthly and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations).

Measured Values

	Canakinumab 5 mg + Metformin	Canakinumab 15 mg + Metformin	Canakinumab 50 mg + Metformin	Canakinumab 150 mg + Metformin	Placebo + Metformin
Number of Participants Analyzed [units: participants]	80	88	83	86	152
Change From Baseline in 2 Hour Insulin Secretion Rate Derived Based on Glucose and C-peptide Following at Month 4 Following Meal Test (Period II) [units: pmol/min/m²] Least Squares Mean (Standard Error)	-17.022 (10.4317)	-9.607 (9.9815)	-31.296 (10.2302)	-38.515 (10.0176)	-24.812 (7.6980)

No statistical analysis provided for Change From Baseline in 2 Hour Insulin Secretion Rate Derived Based on Glucose and C-peptide Following at Month 4 Following Meal Test (Period II)

13. Secondary: Change From Baseline in Peak Plasma Glucose Level (7-point Glucose Testing) at Month 4(Period II) [Time Frame: Baseline, Month 4]

Measure Type	Secondary
Measure Title	Change From Baseline in Peak Plasma Glucose Level (7-point Glucose Testing) at Month 4(Period II)
Measure Description	Patients were asked to check their glucose level (7 times) using their glucose meter on one of the seven days prior to the Meal Challenge Visits (Period II: baseline, Month 4. Patient was instructed to test at following timepoints: fasting before breakfast, 2 hours after starting breakfast, before lunch, 2 hours after starting lunch, before dinner, 2 hours after dinner and at bedtime. The patient documented the results in their Study Diary. The analysis of covariance included treatment and metformin dose group as main effects and baseline peak plasma glucose level as a covariate.
Time Frame	Baseline, Month 4
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.

The full analysis set included all randomized patients except for mis-randomized patients who inadvertently randomized into study and did not receive study drug. Last observation carried forward method was used for patients without Month 4 data for any reason and who used rescue medication or any other glucose lowering agents other than metformin.

Reporting Groups

	Description
Canakinumab 5 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 5 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 15 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 15 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 50 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 50 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 150 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 150 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a

	daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Placebo + Metformin	In 4 month dose finding period as well as during intermediate period, patients received one injection of canakinumab matching placebo monthly and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations).

Measured Values

	Canakinumab 5 mg + Metformin	Canakinumab 15 mg + Metformin	Canakinumab 50 mg + Metformin	Canakinumab 150 mg + Metformin	Placebo + Metformin
Number of Participants Analyzed [units: participants]	**81**	**85**	**82**	**86**	**152**
Change From Baseline in Peak Plasma Glucose Level (7-point Glucose Testing) at Month 4(Period II) [units: mmol/L] Least Squares Mean (Standard Error)	**-0.549 (0.2669)**	**-0.129 (0.2610)**	**-0.421 (0.2653)**	**-0.333 (0.2578)**	**-0.212 (0.1975)**

No statistical analysis provided for Change From Baseline in Peak Plasma Glucose Level (7-point Glucose Testing) at Month 4(Period II)

14. Secondary: Change From Baseline in Average Plasma Glucose Level (7-point Glucose Testing) at Month 4 (Period II) [Time Frame: Baseline, Month 4]

Measure Type	Secondary
Measure Title	Change From Baseline in Average Plasma Glucose Level (7-point Glucose Testing) at Month 4 (Period II)
Measure Description	Patients were asked to check their glucose level (7 times) using their glucose meter on one of the seven days prior to the Meal Challenge Visits (Period II: Month 0 (Baseline), Month 4. Patient was instructed to test at following timepoints: fasting before breakfast, 2 hours after starting breakfast, before lunch, 2 hours after starting lunch, before dinner, 2 hours after dinner and at bedtime. Patient documented the results in their Study Diary. The analysis of covariance included treatment and metformin dose group as main effects and baseline average plasma glucose level as a covariate.

Time Frame	Baseline, Month 4
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.
The full analysis set included all randomized patients except for mis-randomized patients who inadvertently randomized into study and did not receive study drug. Last observation carried forward method was used for patients without Month 4 data for any reason and who used rescue medication or any other glucose lowering agents other than metformin.

Reporting Groups

	Description
Canakinumab 5 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 5 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 15 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 15 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 50 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 50 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy.

	The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 150 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 150 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Placebo + Metformin	In 4 month dose finding period as well as during intermediate period, patients received one injection of canakinumab matching placebo monthly and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations).

Measured Values

	Canakinumab 5 mg + Metformin	Canakinumab 15 mg + Metformin	Canakinumab 50 mg + Metformin	Canakinumab 150 mg + Metformin	Placebo + Metformin
Number of Participants Analyzed [units: participants]	**81**	**85**	**82**	**86**	**152**
Change From Baseline in Average Plasma Glucose Level (7-point Glucose Testing) at Month 4 (Period II) [units: mmol/L] Least Squares Mean (Standard Error)	**-0.357 (0.1626)**	**-0.218 (0.1589)**	**-0.275 (0.1614)**	**-0.040 (0.1569)**	**-0.091 (0.1203)**

No statistical analysis provided for Change From Baseline in Average Plasma Glucose Level (7-point Glucose Testing) at Month 4 (Period II)

15. Secondary: Change From Baseline in Fasting Plasma Glucose at Month 4 (Period II) [Time Frame: Baseline, Month 4]

Measure Type	Secondary

Measure Title	Change From Baseline in Fasting Plasma Glucose at Month 4 (Period II)
Measure Description	Change in Fasting Glucose Level measured from plasma taken at Baseline and at Month 4. The analysis of covariance included treatment and metformin dose group as main effects and baseline fasting plasma glucose level as a covariate.
Time Frame	Baseline, Month 4
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.
The full analysis set included all randomized patients except for mis-randomized patients who inadvertently randomized into study and did not receive study drug. Last observation carried forward method was used for patients without Month 4 data for any reason and who used rescue medication or any other glucose lowering agents other than metformin.

Reporting Groups

	Description
Canakinumab 5 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 5 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 15 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 15 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.

Canakinumab 50 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 50 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 150 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 150 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Placebo + Metformin	In 4 month dose finding period as well as during intermediate period, patients received one injection of canakinumab matching placebo monthly and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations).

Measured Values

	Canakinumab 5 mg + Metformin	Canakinumab 15 mg + Metformin	Canakinumab 50 mg + Metformin	Canakinumab 150 mg + Metformin	Placebo + Metformin
Number of Participants Analyzed [units: participants]	**89**	**93**	**88**	**90**	**172**
Change From Baseline in Fasting Plasma Glucose at Month 4 (Period II) [units: mmol/L] Least Squares Mean (Standard Error)	**0.25 (0.162)**	**-0.19 (0.159)**	**-0.29 (0.162)**	**0.19 (0.160)**	**0.01 (0.118)**

No statistical analysis provided for Change From Baseline in Fasting Plasma Glucose at Month 4 (Period II)

16. Secondary: Change From Baseline in Fasting Insulin at Month 4 (Period II) [Time Frame: Baseline, Month 4]

Measure Type	Secondary
Measure Title	Change From Baseline in Fasting Insulin at Month 4 (Period II)
Measure Description	Change in fasting insulin Level measured from blood samples taken at Baseline and at Month 4. The analysis of covariance included treatment and metformin dose group as main effects and baseline fasting insulin level as a covariate.
Time Frame	Baseline, Month 4
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.
The full analysis set included all randomized patients except for mis-randomized patients who inadvertently randomized into study and did not receive study drug. Last observation carried forward method was used for patients without Month 4 data for any reason and who used rescue medication or any other glucose lowering agents other than metformin.

Reporting Groups

	Description
Canakinumab 5 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 5 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 15 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 15 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was

	completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 50 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 50 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 150 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 150 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Placebo + Metformin	In 4 month dose finding period as well as during intermediate period, patients received one injection of canakinumab matching placebo monthly and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations).

Measured Values

	Canakinumab 5 mg + Metformin	Canakinumab 15 mg + Metformin	Canakinumab 50 mg + Metformin	Canakinumab 150 mg + Metformin	Placebo + Metformin
Number of Participants Analyzed [units: participants]	**75**	**81**	**77**	**83**	**143**
Change From Baseline in Fasting Insulin at Month 4 (Period II) [units: pmol/L] Least Squares Mean (Standard Error)	**4.3 (4.74)**	**7.2 (4.57)**	**7.0 (4.67)**	**4.4 (4.47)**	**-0.4 (3.50)**

No statistical analysis provided for Change From Baseline in Fasting Insulin at Month 4 (Period II)

17. Secondary: Change From Baseline in Homeostatic Model Assessment B (HOMA2 B) Beta Cell Function (%B) at Month 4 (Period II) [Time Frame: Baseline, Month 4]

Measure Type	Secondary
Measure Title	Change From Baseline in Homeostatic Model Assessment B (HOMA2 B) Beta Cell Function (%B) at Month 4 (Period II)
Measure Description	The homeostatic model assessment (HOMA) is a method used to quantify insulin resistance and beta (β)-cell function. HOMA2-B is a computer model that uses fasting plasma insulin and glucose concentrations to estimate steady state beta cell function (%B) as a percentage of a normal reference population (normal young adults). Time profile of postprandial glucose, insulin and C-peptide were assessed as measures of β-cell response to stimulation. The analysis of covariance included treatment and metformin dose group as main effects and baseline HOMA-B as a covariate.
Time Frame	Baseline, Month 4
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.
The full analysis set included all randomized patients except for mis-randomized patients who inadvertently randomized into study and did not receive study drug. Last observation carried forward method was used for patients without Month 4 data for any reason and who used rescue medication or any other glucose lowering agents other than metformin.

Reporting Groups

	Description
Canakinumab 5 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 5 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief

	visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 15 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 15 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 50 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 50 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 150 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 150 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Placebo + Metformin	In 4 month dose finding period as well as during intermediate period, patients received one injection of canakinumab matching placebo monthly and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations).

Measured Values

	Canakinumab 5 mg +	**Canakinumab 15 mg +**	**Canakinumab 50 mg +**	**Canakinumab 150 mg +**	**Placebo +**

	Metformin	Metformin	Metformin	Metformin	Metformin
Number of Participants Analyzed **[units: participants]**	**75**	**79**	**77**	**83**	**143**
Change From Baseline in Homeostatic Model Assessment B (HOMA2 B) Beta Cell Function (%B) at Month 4 (Period II) **[units: percentage of beta cell function]** **Least Squares Mean (Standard Error)**	**-1.067 (6.0549)**	**2.259 (5.9304)**	**8.215 (5.9727)**	**6.217 (5.7307)**	**-2.182 (4.4846)**

No statistical analysis provided for Change From Baseline in Homeostatic Model Assessment B (HOMA2 B) Beta Cell Function (%B) at Month 4 (Period II)

18. Secondary: Change From Baseline in Homeostatic Model Assessment Insulin Resistance (HOMA2 IR) at Month 4 (Period II) [Time Frame: Baseline, Month 4]

Measure Type	Secondary
Measure Title	Change From Baseline in Homeostatic Model Assessment Insulin Resistance (HOMA2 IR) at Month 4 (Period II)
Measure Description	The homeostatic model assessment (HOMA) is a method used to quantify insulin resistance and beta (β)-cell function. HOMA2-IR is a computer model that uses fasting plasma insulin and glucose concentrations to estimate insulin resistance which is the reciprocal of insulin sensitivity (%S)(100/%S)as a percentage of a normal reference population (normal young adults). The analysis of covariance included treatment and metformin dose group as main effects and baseline HOMA2 IR as a covariate.
Time Frame	Baseline, Month 4
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.
The full analysis set included all randomized patients except for mis-randomized patients who inadvertently randomized into study and did not receive study drug. Last observation carried forward method was used for patients without Month 4 data for any reason and who used rescue medication or any other glucose lowering agents other than metformin.

Reporting Groups

	Description
Canakinumab 5 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 5 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 15 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 15 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 50 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 50 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 150 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 150 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a

	daily injection of insulin glargine as add-on therapy.
Placebo + Metformin	In 4 month dose finding period as well as during intermediate period, patients received one injection of canakinumab matching placebo monthly and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations).

Measured Values

	Canakinumab 5 mg + Metformin	Canakinumab 15 mg + Metformin	Canakinumab 50 mg + Metformin	Canakinumab 150 mg + Metformin	Placebo + Metformin
Number of Participants Analyzed [units: participants]	**75**	**81**	**77**	**83**	**143**
Change From Baseline in Homeostatic Model Assessment Insulin Resistance (HOMA2 IR) at Month 4 (Period II) [units: percentage of insulin resistance] Least Squares Mean (Standard Error)	**0.245 (0.3107)**	**0.517 (0.2990)**	**0.255 (0.3054)**	**0.252 (0.2925)**	**0.013 (0.2286)**

No statistical analysis provided for Change From Baseline in Homeostatic Model Assessment Insulin Resistance (HOMA2 IR) at Month 4 (Period II)

19. Secondary: Change From Baseline in Quantitative Insulin Sensitivity Check Index (QUICKI) at Month 4 (Period II) [Time Frame: Baseline, Month 4]

Measure Type	Secondary
Measure Title	Change From Baseline in Quantitative Insulin Sensitivity Check Index (QUICKI) at Month 4 (Period II)
Measure Description	The Quantitative Insulin Sensitivity Check Index (QUICKI) score, measures insulin sensitivity which is the inverse of insulin resistance. The score is calculated by the equation: 1 /(log(fasting insulin µU/mL) + log(fasting glucose mg/dL)). In normal subjects, the mean score ± SE is 0.366 ± 0.029. The analysis of covariance included treatment and metformin dose group as main effects and baseline QUICKI as a covariate.
Time Frame	Baseline, Month 4
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.

The full analysis set included all randomized patients except for mis-randomized patients who inadvertently randomized into study and did not receive study drug. Last observation carried forward method was used for patients without Month 4 data for any reason and who used rescue medication or any other glucose lowering agents other than metformin.

Reporting Groups

	Description
Canakinumab 5 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 5 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 15 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 15 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 50 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 50 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 150 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 150 mg Canakinumab injected in the clinic

	at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Placebo + Metformin	In 4 month dose finding period as well as during intermediate period, patients received one injection of canakinumab matching placebo monthly and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations).

Measured Values

	Canakinumab 5 mg + Metformin	Canakinumab 15 mg + Metformin	Canakinumab 50 mg + Metformin	Canakinumab 150 mg + Metformin	Placebo + Metformin
Number of Participants Analyzed [units: participants]	**75**	**81**	**77**	**83**	**143**
Change From Baseline in Quantitative Insulin Sensitivity Check Index (QUICKI) at Month 4 (Period II) [units: units on a scale] Least Squares Mean (Standard Error)	**-0.001 (0.0017)**	**0.000 (0.0016)**	**-0.003 (0.0017)**	**-0.001 (0.0016)**	**0.000 (0.0013)**

No statistical analysis provided for Change From Baseline in Quantitative Insulin Sensitivity Check Index (QUICKI) at Month 4 (Period II)

20. Secondary: Change From Baseline in High-sensitivity C-reactive Protein (hsCRP) at Month 4 (Period II) [Time Frame: Baseline, Month 4]

Measure Type	Secondary
Measure Title	Change From Baseline in High-sensitivity C-reactive Protein (hsCRP) at Month 4 (Period II)
Measure Description	The change from baseline in hsCRP (on the logarithmic scale) at Month 4 was measured for this analysis. The analysis of covariance included treatment and metformin dose group as main effects and baseline hsCRP as a covariate.
Time Frame	Baseline, Month 4

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.
The full analysis set included all randomized patients except for mis-randomized patients who inadvertently randomized into study and did not receive study drug. Last observation carried forward method was used for patients without Month 4 data for any reason and who used rescue medication or any other glucose lowering agents other than metformin.

Reporting Groups

	Description
Canakinumab 5 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 5 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 15 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 15 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 50 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 50 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief

	visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 150 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 150 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Placebo + Metformin	In 4 month dose finding period as well as during intermediate period, patients received one injection of canakinumab matching placebo monthly and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations).

Measured Values

	Canakinumab 5 mg + Metformin	Canakinumab 15 mg + Metformin	Canakinumab 50 mg + Metformin	Canakinumab 150 mg + Metformin	Placebo + Metformin
Number of Participants Analyzed **[units: participants]**	**89**	**93**	**87**	**91**	**168**
Change From Baseline in High-sensitivity C-reactive Protein (hsCRP) at Month 4 (Period II) **[units: log (mg/L)]** **Least Squares Mean (Standard Error)**	**-0.19 (0.037)**	**-0.32 (0.036)**	**-0.44 (0.037)**	**-0.40 (0.036)**	**-0.08 (0.027)**

No statistical analysis provided for Change From Baseline in High-sensitivity C-reactive Protein (hsCRP) at Month 4 (Period II)

21. Secondary: Percentage Change From Baseline in Fasting Lipids Profile at Month 4 (Period II) [Time Frame: Baseline, Month 4]

Measure Type	Secondary
Measure Title	Percentage Change From Baseline in Fasting Lipids Profile at Month 4 (Period II)

Measure Description	The fasting lipid profiles included triglycerides, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), calculated very low-density lipoprotein (VLDL), non-HDL cholesterol. Percentage change was measured as [(value at month 4 – baseline value)/baseline value]*100%. The analysis of covariance model included treatment and metformin dose group as main effects and baseline triglycerides, total cholesterol, LDL, HDL, VLDL and non-HDL as covariates.
Time Frame	Baseline, Month 4
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.
The full analysis set included all randomized patients except for mis-randomized patients who randomized in error, did not receive study drug. LOCF method was used for patients without Month 4 data for any reason and who used rescue drug or any other glucose lowering agents other than metformin. 'n' = patients with baseline and endpoints data.

Reporting Groups

	Description
Canakinumab 5 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 5 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 15 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 15 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.

Canakinumab 50 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 50 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 150 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 150 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Placebo + Metformin	In 4 month dose finding period as well as during intermediate period, patients received one injection of canakinumab matching placebo monthly and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations).

Measured Values

	Canakinumab 5 mg + Metformin	Canakinumab 15 mg + Metformin	Canakinumab 50 mg + Metformin	Canakinumab 150 mg + Metformin	Placebo + Metformin
Number of Participants Analyzed [units: participants]	**93**	**95**	**92**	**92**	**179**
Percentage Change From Baseline in Fasting Lipids Profile at Month 4 (Period II) [units: percent change] Least Squares Mean (Standard Error)					
Total cholesterol (n = 91, 93, 88, 91, 172)	**3.163 (1.5364)**	**3.922 (1.5188)**	**5.334 (1.5542)**	**6.265 (1.5234)**	**2.697 (1.1334)**
Triglycerides (n = 91, 93, 88, 91, 172)	**16.127 (4.3130)**	**7.903 (4.2688)**	**19.937 (4.3684)**	**18.795 (4.2786)**	**7.009 (3.1813)**

LDL (n = 90, 90, 85, 87, 165)	2.624 (2.4606)	4.741 (2.4582)	2.705 (2.5137)	5.938 (2.4752)	5.129 (1.8351)
HDL (n = 91, 93, 88, 91, 172)	1.438 (1.6619)	5.346 (1.6441)	8.074 (1.6853)	6.780 (1.6494)	3.963 (1.2303)
VLDL (n= 90, 90, 85, 87, 165)	15.646 (3.9196)	6.711 (3.9118)	16.533 (3.9986)	16.618 (3.9373)	7.370 (2.9203)
Non-HDL (n = 91, 93, 88, 91, 172)	4.25 (2.022)	4.40 (1.999)	5.17 (2.046)	7.25 (2.005)	3.04 (1.491)

No statistical analysis provided for Percentage Change From Baseline in Fasting Lipids Profile at Month 4 (Period II)

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	Patients have been exposed up to 15 months (median exposure however was at about 6 months)
Additional Description	The data reported below in the safety tables are from the pooled Phase II and Phase III data.

Reporting Groups

	Description
Canakinumab 5 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 5 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 15 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 15 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a

	daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 50 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 50 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 150 mg + Metformin	Experimental: Canakinumab 150 mg + Metformin In 4-Month Dose-finding period, patients visited the clinic monthly and had 150 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Placebo + Metformin	In 4 month dose finding period as well as during intermediate period, patients received one injection of canakinumab matching placebo monthly and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations).

Serious Adverse Events

	Canakinumab 5 mg + Metformin	Canakinumab 15 mg + Metformin	Canakinumab 50 mg + Metformin	Canakinumab 150 mg + Metformin	Placebo + Metformin
Total, serious adverse events					
# participants affected / at risk	**3/93 (3.23%)**	**1/95 (1.05%)**	**5/92 (5.43%)**	**7/92 (7.61%)**	**8/179 (4.47%)**
Cardiac disorders					

Acute left ventricular failure [†1]					
# participants affected / at risk	**0/93 (0.00%)**	**0/95 (0.00%)**	**0/92 (0.00%)**	**0/92 (0.00%)**	**1/179 (0.56%)**
Angina pectoris [†1]					
# participants affected / at risk	**0/93 (0.00%)**	**0/95 (0.00%)**	**0/92 (0.00%)**	**1/92 (1.09%)**	**0/179 (0.00%)**
Angina unstable [†1]					
# participants affected / at risk	**0/93 (0.00%)**	**0/95 (0.00%)**	**0/92 (0.00%)**	**0/92 (0.00%)**	**1/179 (0.56%)**
Atrial fibrillation [†1]					
# participants affected / at risk	**0/93 (0.00%)**	**0/95 (0.00%)**	**0/92 (0.00%)**	**1/92 (1.09%)**	**0/179 (0.00%)**
Cardiac failure congestive [†1]					
# participants affected / at risk	**0/93 (0.00%)**	**0/95 (0.00%)**	**0/92 (0.00%)**	**0/92 (0.00%)**	**1/179 (0.56%)**
Coronary artery disease [†1]					
# participants affected / at risk	**0/93 (0.00%)**	**0/95 (0.00%)**	**0/92 (0.00%)**	**0/92 (0.00%)**	**1/179 (0.56%)**
Myocardial infarction [†1]					
# participants affected / at risk	**0/93 (0.00%)**	**0/95 (0.00%)**	**0/92 (0.00%)**	**0/92 (0.00%)**	**1/179 (0.56%)**
Gastrointestinal disorders					
Colonic polyp [†1]					
# participants affected / at risk	**0/93 (0.00%)**	**0/95 (0.00%)**	**1/92 (1.09%)**	**0/92 (0.00%)**	**0/179 (0.00%)**
Inguinal hernia [†1]					
# participants affected / at risk	**0/93 (0.00%)**	**0/95 (0.00%)**	**0/92 (0.00%)**	**0/92 (0.00%)**	**1/179 (0.56%)**
General disorders					
Oedema peripheral [†1]					
# participants affected / at risk	**0/93 (0.00%)**	**0/95 (0.00%)**	**0/92 (0.00%)**	**0/92 (0.00%)**	**1/179 (0.56%)**

Hepatobiliary disorders					
Cholecystitis †1					
# participants affected / at risk	**0/93 (0.00%)**	**0/95 (0.00%)**	**1/92 (1.09%)**	**0/92 (0.00%)**	**1/179 (0.56%)**
Infections and infestations					
Breast abscess †1					
# participants affected / at risk	**0/93 (0.00%)**	**0/95 (0.00%)**	**0/92 (0.00%)**	**1/92 (1.09%)**	**0/179 (0.00%)**
Cellulitis †1					
# participants affected / at risk	**0/93 (0.00%)**	**0/95 (0.00%)**	**1/92 (1.09%)**	**0/92 (0.00%)**	**0/179 (0.00%)**
Gastroenteritis †1					
# participants affected / at risk	**0/93 (0.00%)**	**0/95 (0.00%)**	**0/92 (0.00%)**	**1/92 (1.09%)**	**0/179 (0.00%)**
Gastroenteritis bacterial †1					
# participants affected / at risk	**0/93 (0.00%)**	**0/95 (0.00%)**	**0/92 (0.00%)**	**1/92 (1.09%)**	**0/179 (0.00%)**
Graft infection †1					
# participants affected / at risk	**0/93 (0.00%)**	**0/95 (0.00%)**	**0/92 (0.00%)**	**0/92 (0.00%)**	**1/179 (0.56%)**
Pneumonia †1					
# participants affected / at risk	**0/93 (0.00%)**	**0/95 (0.00%)**	**0/92 (0.00%)**	**0/92 (0.00%)**	**1/179 (0.56%)**
Urosepsis †1					
# participants affected / at risk	**1/93 (1.08%)**	**0/95 (0.00%)**	**0/92 (0.00%)**	**0/92 (0.00%)**	**0/179 (0.00%)**
Injury, poisoning and procedural complications					
Multiple fractures †1					
# participants affected / at risk	**0/93 (0.00%)**	**0/95 (0.00%)**	**1/92 (1.09%)**	**0/92 (0.00%)**	**0/179 (0.00%)**

Investigations					
Hepatic enzyme increased †1					
# participants affected / at risk	**0/93 (0.00%)**	**0/95 (0.00%)**	**0/92 (0.00%)**	**1/92 (1.09%)**	**0/179 (0.00%)**
Metabolism and nutrition disorders					
Dehydration †1					
# participants affected / at risk	**0/93 (0.00%)**	**0/95 (0.00%)**	**0/92 (0.00%)**	**1/92 (1.09%)**	**0/179 (0.00%)**
Hyperglycaemia †1					
# participants affected / at risk	**0/93 (0.00%)**	**0/95 (0.00%)**	**0/92 (0.00%)**	**1/92 (1.09%)**	**0/179 (0.00%)**
Musculoskeletal and connective tissue disorders					
Osteoarthritis †1					
# participants affected / at risk	**0/93 (0.00%)**	**0/95 (0.00%)**	**0/92 (0.00%)**	**0/92 (0.00%)**	**1/179 (0.56%)**
Rotator cuff syndrome †1					
# participants affected / at risk	**1/93 (1.08%)**	**0/95 (0.00%)**	**0/92 (0.00%)**	**0/92 (0.00%)**	**0/179 (0.00%)**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)					
Basal cell carcinoma †1					
# participants affected / at risk	**0/93 (0.00%)**	**0/95 (0.00%)**	**0/92 (0.00%)**	**1/92 (1.09%)**	**0/179 (0.00%)**
Nervous system disorders					
Haemorrhagic stroke †1					
# participants affected / at risk	**1/93 (1.08%)**	**0/95 (0.00%)**	**0/92 (0.00%)**	**0/92 (0.00%)**	**0/179 (0.00%)**
Ischaemic cerebral infarction †1					
# participants affected / at risk	**1/93 (1.08%)**	**0/95 (0.00%)**	**0/92 (0.00%)**	**0/92 (0.00%)**	**0/179 (0.00%)**

Renal and urinary disorders					
Calculus ureteric †1					
# participants affected / at risk	**0/93 (0.00%)**	**0/95 (0.00%)**	**1/92 (1.09%)**	**1/92 (1.09%)**	**0/179 (0.00%)**
Calculus urinary †1					
# participants affected / at risk	**0/93 (0.00%)**	**1/95 (1.05%)**	**0/92 (0.00%)**	**0/92 (0.00%)**	**0/179 (0.00%)**
Renal failure acute †1					
# participants affected / at risk	**0/93 (0.00%)**	**0/95 (0.00%)**	**1/92 (1.09%)**	**0/92 (0.00%)**	**0/179 (0.00%)**
Renal mass †1					
# participants affected / at risk	**0/93 (0.00%)**	**0/95 (0.00%)**	**0/92 (0.00%)**	**0/92 (0.00%)**	**1/179 (0.56%)**
Reproductive system and breast disorders					
Benign prostatic hyperplasia †1					
# participants affected / at risk	**1/93 (1.08%)**	**0/95 (0.00%)**	**0/92 (0.00%)**	**0/92 (0.00%)**	**0/179 (0.00%)**

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

Other Adverse Events

Hide Other Adverse Events

Time Frame	Patients have been exposed up to 15 months (median exposure however was at about 6 months)
Additional Description	The data reported below in the safety tables are from the pooled Phase II and Phase III data.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Canakinumab 5 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 5 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 15 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 15 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 50 mg + Metformin	In 4-Month Dose-finding period, patients visited the clinic monthly and had 50 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a daily injection of insulin glargine as add-on therapy.
Canakinumab 150 mg + Metformin	Experimental: Canakinumab 150 mg + Metformin In 4-Month Dose-finding period, patients visited the clinic monthly and had 150 mg Canakinumab injected in the clinic at each visit and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations). During this period, patients with consecutive morning fasting glucose >200 mg/dL were treated with a daily injection of insulin glargine as add-on therapy. The intermediate period began after patients completed their 4-month visit and lasted until the primary analysis was completed and the optimal dose was selected. Patients continued on their randomized treatment and made brief visits to the clinic every month. From this point onward, patients with consecutive HbA1c >7.5% were treated with a

	daily injection of insulin glargine as add-on therapy.
Placebo + Metformin	In 4 month dose finding period as well as during intermediate period, patients received one injection of canakinumab matching placebo monthly and continued on a stable dose of metformin ≥ 1000 mg daily (or lower dose if required by local regulations).

Other Adverse Events

	Canakinumab 5 mg + Metformin	Canakinumab 15 mg + Metformin	Canakinumab 50 mg + Metformin	Canakinumab 150 mg + Metformin	Placebo + Metformin
Total, other (not including serious) adverse events					
# participants affected / at risk	**9/93 (9.68%)**	**9/95 (9.47%)**	**15/92 (16.30%)**	**8/92 (8.70%)**	**26/179 (14.53%)**
Gastrointestinal disorders					
Diarrhoea †1					
# participants affected / at risk	**2/93 (2.15%)**	**2/95 (2.11%)**	**5/92 (5.43%)**	**0/92 (0.00%)**	**3/179 (1.68%)**
Infections and infestations					
Nasopharyngitis †1					
# participants affected / at risk	**5/93 (5.38%)**	**4/95 (4.21%)**	**9/92 (9.78%)**	**4/92 (4.35%)**	**15/179 (8.38%)**
Urinary tract infection †1					
# participants affected / at risk	**3/93 (3.23%)**	**4/95 (4.21%)**	**5/92 (5.43%)**	**5/92 (5.43%)**	**11/179 (6.15%)**

† 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 by Novartis

Publications automatically indexed to this study:

Noe A, Howard C, Thuren T, Taylor A, Skerjanec A. Pharmacokinetic and pharmacodynamic characteristics of single-dose Canakinumab in patients with type 2 diabetes mellitus. Clin Ther. 2014 Nov 1;36(11):1625-37. doi: 10.1016/j.clinthera.2014.08.004. Epub 2014 Sep 18.

Hensen J, Howard CP, Walter V, Thuren T. Impact of interleukin-1β antibody (canakinumab) on glycaemic indicators in patients with type 2 diabetes mellitus: results of secondary endpoints from a randomized, placebo-controlled trial. Diabetes Metab. 2013 Dec;39(6):524-31. doi: 10.1016/j.diabet.2013.07.003. Epub 2013 Sep 25.

Ridker PM, Howard CP, Walter V, Everett B, Libby P, Hensen J, Thuren T; CANTOS Pilot Investigative Group. Effects of interleukin-1β inhibition with canakinumab on hemoglobin A1c, lipids, C-reactive protein, interleukin-6, and fibrinogen: a phase IIb randomized, placebo-controlled trial. Circulation. 2012 Dec 4;126(23):2739-48. doi: 10.1161/CIRCULATIONAHA.112.122556. Epub 2012 Nov 5.

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Health Authority:	Argentina: Administracion Nacional de Medicamentos, Alimentos y Tecnologia Medica Belgium: Federal Agency for Medicinal Products and Health Products Germany: Paul-Ehrlich-Institut Hungary: National Institute of Pharmacy India: Drugs Controller General of India Japan: Ministry of Health, Labor and Welfare Peru: General Directorate of Pharmaceuticals, Devices, and Drugs Romania: National Medicines Agency South Africa: National Health Research Ethics Council Turkey: Ministry of Health United Kingdom: Medicines and Healthcare Products Regulatory Agency United States: Food and Drug Administration