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Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Canakinumab

Trial Indication(s)

Non-small cell lung cancer

Protocol Number

CACZ885T2301

Protocol Title

A phase III, multicenter, randomized, double blind, placebo-controlled study evaluating the efficacy and safety of canakinumab versus placebo as adjuvant therapy in adult subjects with stages AJCC/UICC v. 8 II -IIIA and IIIB (T>5cm N2) completely resected (R0) non-small cell lung cancer (NSCLC)

Clinical Trial Phase

Phase 3

Phase of Drug Development

Phase IV

Study Start/End Dates

Study Start Date: March 16, 2018 (Actual)
Primary Completion Date: March 17, 2022 (Actual)
Study Completion Date: February 07, 2023 (Actual)

Reason for Termination (If applicable)

The study did not meet the primary endpoint of disease-free survival (DFS) at the time of the primary analysis. Upon review of the results, the benefit-risk was assessed with the decision that the study would be closed. No new safety signals were observed for canakinumab. Canakinumab treatment was halted in Aug-2022 with a temporary halt of treatment submitted to the Health Authorities (HA) and Ethics Committees (EC) as applicable. The decision to temporarily halt canakinumab/placebo treatment was solely based on the lack of efficacy observed in the analysis of the primary endpoint of DFS when canakinumab was given in the specific patient population of the CACZ885T2301 study.

Study Design/Methodology

This was a phase III, multicenter, randomized, double-blind study to evaluate the efficacy and safety of canakinumab as adjuvant therapy in adult patients with stages AJCC/UICC vs. 8 II-IIIA and IIIB (T>5 cm N2) completely resected (R0) NSCLC. Approximately 1500 patients were planned to be randomized 1:1 to canakinumab, 200 mg subcutaneously (s.c.) every 3 weeks or matching placebo s.c. every 3 weeks. Patients were planned to continue their assigned treatment until they completed 18 cycles (cycle = 21 days) or experienced any one of the following: non-small cell lung cancer (NSCLC) disease recurrence as determined by Investigator; unacceptable toxicity that precluded further treatment; treatment discontinuation at the discretion of the Investigator or patient; start of a new antineoplastic therapy; death, or loss to follow-up, whichever occurred first. All patients who discontinued from the study treatment were to be followed up every 12 weeks for survival until the final OS analysis or death, loss to follow-up or withdrawal of consent for survival follow-up. However, following the decision to halt study treatment in 23-Aug-2022, the following guidance was implemented:

- Patients on treatment were to discontinue canakinumab/placebo and were required to have an end of treatment visit and complete the 130-day safety follow-up.
- Patients on safety follow-up were to be monitored until Day 130 and then were to be discontinued from the study.
- Patients in efficacy or survival follow-up were to be discontinued from the study.

Centers

290 centers in 41 countries: Greece(6), Germany(25), United Kingdom(15), Switzerland(3), Lebanon(4), Austria(4), Hong Kong(4), United States(21), France(22), India(4), Norway(4), Spain(12), Thailand(8), Japan(25), Taiwan(11), Italy(12),

Israel(2), Poland(6), Malaysia(4), Czech Republic(2), Chile(2), Jordan(1), Turkey(5), Korea, Republic of(7), Argentina(5), Bulgaria(4), Portugal(3), Russia(12), Hungary(2), Brazil(5), Panama(1), Peru(3), Philippines(1), China(26), Romania(4), Vietnam(1), Canada(5), Iceland(1), Colombia(1), Slovenia(1), Georgia(6)

Objectives

Primary Objective:

- To compare the disease-free survival (DFS) in the canakinumab vs. placebo arms as determined by local investigator assessment.

Key Secondary Objective*:*

- To compare overall survival (OS) in the canakinumab arm vs. placebo arm.

Other secondary objectives:

- To compare DFS by local investigator assessment and OS in the canakinumab vs. placebo arms in subgroups defined respectively by PD-L1 and CD8 expression levels.
- To compare lung cancer specific survival (LCSS) in the canakinumab arm vs. placebo arm.
- To characterize the safety profile of canakinumab.
- To characterize the pharmacokinetics (PK) of canakinumab therapy.
- To characterize the prevalence and incidence of immunogenicity (anti-drug antibodies [ADAs]) of canakinumab.
- To assess the effect of canakinumab versus placebo on patient-reported outcomes (PROs) (EORTC QLQ-C30 with QLQ-LC13 incorporated and EQ-5D) including functioning and health-related quality of life.

Test Product (s), Dose(s), and Mode(s) of Administration

Canakinumab or matching placebo solution for injection was provided by Novartis as ready-to-use pre-filled syringes (PFS) to be administered by study center personnel. Two strengths and respective corresponding matching placebos were supplied:

- Canakinumab 50 mg in 0.5 mL solution for injection and one placebo formulation matching the active drug formulation.

- Canakinumab 150 mg in 1 mL solution for injection and one placebo formulation matching the active drug formulation.

Statistical Methods

The primary efficacy variable of the study was DFS, defined as the time from the date of randomization to the date of the first documented disease recurrence as assessed by local investigator radiologically or death due to any cause. The primary efficacy analysis to test this hypothesis and compare the two arms involved a stratified log-rank test at an overall one-sided 2.5% level of significance. The DFS distribution was estimated using the Kaplan-Meier method. The final DFS analysis was performed when approximately 392 DFS events were documented irrespective of the accrued sample size.

The key secondary endpoint was OS, defined as the time from the date of randomization to the date of death due to any cause. If a patient was not known to have died, then OS was censored at the last date the patient was known to be alive (on or before the LPLV date). The OS distribution was estimated using the Kaplan-Meier method. OS analyses were performed by PD-L1 subgroups as determined by immunohistochemistry. OS analyses were also performed by CD8 subgroups with the median of baseline CD8 as cut-offs.

Lung cancer specific survival (LCSS) was defined as the time from the date of randomization to the date of death due to lung cancer. For patients who died due to reasons other than lung cancer, LCSS was to be censored at the death date. The LCSS distribution was estimated using the Kaplan-Meier method.

Three PRO questionnaires were assessed: EORTC QLQ-C30, with QLQ-LC13 lung cancer module, and the EQ-5D-5L. All assessments were included in the time to definitive deterioration or first deterioration analysis.

Canakinumab serum concentrations were presented descriptively at each time point.

Immunogenicity of canakinumab was characterized descriptively by tabulating ADA results at Baseline and ADA incidence on-treatment.

Assessment of safety was a secondary endpoint for this study. The safety analyses were descriptive, no hypothesis testing was performed.

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Study Population: Key Inclusion/Exclusion Criteria

Key Inclusion Criteria:

- Had completely resected (R0) NSCLC AJCC/UICC v. 8 stage IIA-IIIA and IIIB (N2 disease only) OR had NSCLC Stage IIA-IIIA, IIIB (N2 disease only) and were candidates for complete resection surgery.
- Cisplatin-based chemotherapy was mandatory for all subjects (Exception: In subjects with stage IIA disease with no nodal involvement, cisplatin-based chemotherapy could be administered if recommended by the treating physician). When required, a minimum of two cycles of cisplatin-based chemotherapy was mandatory, after which additional therapies could be given based upon local clinical practice and/or guidelines. Typically, chemotherapy was initiated within 60 days of surgery.
- Radiation therapy was allowed if indicated as per local guidelines or practice.
- Had recovered from all toxicities related to prior systemic therapy to grade ≤ 1 (CTCAE v 5.0). Exception to this criterion: subjects with any grade of alopecia and grade 2 or less neuropathy were allowed to enter the study
- Had ECOG performance status (PS) of 0 or 1

Key Exclusion Criteria:

- Had unresectable or metastatic disease, positive microscopic margins on the pathology report, and/or gross disease remaining at the time of surgery
- Had received any neoadjuvant therapy
- Had presence or history of a malignant disease, other than the resected NSCLC, that had been diagnosed and/or required therapy within the past 3 years Exceptions to this exclusion included the following: completely resected basal cell and squamous cell skin cancers, completely resected carcinoma in situ of any type and hormonal maintenance for breast and prostate cancer > 3 years.
- Had a history of current diagnosis of cardiac disease
- Had uncontrolled diabetes
- Had known active or recurrent hepatic disorder including cirrhosis, hepatitis B and C (positive or indeterminate central laboratory results)
- Subjects had to be evaluated for tuberculosis as per local treatment guidelines or clinical practice. Subjects with active tuberculosis were not eligible.
- Had suspected or proven immunocompromised state as described in the protocol
- Had live and attenuated vaccination within 3 months prior to first dose of study drug (e.g. MMR, Yellow Fever, Rotavirus, Smallpox, etc.).

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Participant Flow Table

Overall Study

	Canakinumab	Placebo	Total
Arm/Group Description	Participants receive 200mg of canakinumab subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)	Participants receive canakinumab placebo subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)	
Started	693	689	1382
Treated	692	689	1381
Completed	414	420	834
Not Completed	279	269	548
Progressive disease	138	148	286
Study terminated by Sponsor	60	44	104
Adverse Event	34	31	65
Patient decision	27	27	54
Protocol deviation	4	6	10
Death	2	7	9
Technical problems	1	0	1
Lost to Follow-up	0	1	1
Physician Decision	13	5	18

Baseline Characteristics

	Canakinumab	Placebo	Total

Arm/Group Description	Participants receive 200mg of canakinumab subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)	Participants receive canakinumab placebo subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)	
Number of Participants [units: participants]	693	689	1382
Baseline Analysis Population Description			
Age Continuous (units: Years) Analysis Population Type: Participants Mean ± Standard Deviation			
	61.5±8.90	61.6±9.00	61.6±8.95
Sex: Female, Male (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)			
Female	263	257	520
Male	430	432	862
Race/Ethnicity, Customized (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)			
White	393	391	784
Asian	248	236	484
Black or African American	3	4	7
American Indian or Alaska Native	0	5	5
Multiple	0	1	1
Missing	49	52	101

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Primary Outcome Result(s)

Disease free survival (DFS) by local investigator

Description	DFS is the time from the date of randomization to the date of the first documented NSCLC disease recurrence as assessed by local investigator radiologically or death due to any cause. Disease recurrence included diagnoses of new primary lung malignancies. Clinical deterioration was not considered as a recurrence of disease. In case of non-conclusive radiological evidence, a biopsy assessment was performed to confirm NSCLC recurrence. The median DFS was estimated using the Kaplan-Meier method. DFS was censored if no DFS event was observed prior to the analysis cut-off date or subjects who received any subsequent anti-neoplastic therapy for NSCLC. The censoring date was the date of last assessment before the cut-off date or NSCLC related anti-neoplastic therapy date.
Time Frame	Up to approximately 4 years
Analysis Population Description	Full Analysis Set (FAS) including all participants to whom study treatment was assigned by randomization

	Canakinumab	**Placebo**
Arm/Group Description	Participants receive 200mg of canakinumab subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)	Participants receive canakinumab placebo subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)
Number of Participants Analyzed [units: participants]	693	689
Disease free survival (DFS) by local investigator (units: Months)	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**
	35.02 (28.55 to NA)[1]	29.73 (23.72 to NA)[1]

[1] NA: Not estimable due to the insufficient number of participants with events

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Secondary Outcome Result(s)

Overall Survival (OS)

Description	Overall Survival (OS) is the time from the date of randomization to the date of death due to any cause. The OS was censored at the latest date the subject was known to be alive. The OS distribution was estimated using the Kaplan-Meier method, and Kaplan-Meier medians and 95% confidence intervals of the medians were presented for each treatment group.
Time Frame	Up to approximately 4.3 years
Analysis Population Description	FAS including all participants to whom study treatment was assigned by randomization

	Canakinumab	**Placebo**
Arm/Group Description	Participants receive 200mg of canakinumab subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)	Participants receive canakinumab placebo subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)
Number of Participants Analyzed [units: participants]	693	689
Overall Survival (OS) (units: Months)	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**
	51.12 (46.95 to NA)[1]	NA (NA to NA)[1]

[1] NA = Not estimable due to the insufficient number of participants with events

Overall Survival (OS) in PD-L1 subgroups

Description	Overall Survival (OS) is the time from the date of randomization to the date of death due to any cause. The OS was censored at the latest date the subject was known to be alive. The OS distribution was estimated using the Kaplan-Meier method, and Kaplan-Meier curves, medians and 95% confidence intervals of the medians were presented for each treatment group. OS analysis was performed by programmed cell death-ligand 1 (PD-L1) expression status: PD-L1 <1%, PD-L1 ≥1% and <49%, and PD-L1 ≥50%.
Time Frame	Up to approximately 4.3 years

Analysis Population Description	Participants to whom study treatment was assigned by randomization with a valid baseline measurement of PD-L1 expression.

	Canakinumab	Placebo
Arm/Group Description	Participants receive 200mg of canakinumab subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)	Participants receive canakinumab placebo subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)
Number of Participants Analyzed [units: participants]	396	418
Overall Survival (OS) in PD-L1 subgroups (units: Months)	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**
PD-L1 <1%	NA (NA to NA)[1]	NA (NA to NA)[1]
PD-L1 ≥1% and <49%	46.95 (22.11 to NA)[1]	NA (NA to NA)[1]
PD-L1 ≥50%	51.12 (NA to NA)[1]	NA (NA to NA)[1]

[1] NA: Not estimable due to the insufficient number of participants with events

Overall Survival (OS) in CD8 subgroups

Description	Overall Survival (OS) is the time from the date of randomization to the date of death due to any cause. The OS was censored at the latest date the subject was known to be alive. The OS distribution was estimated using the Kaplan-Meier method, and Kaplan-Meier medians and 95% confidence intervals of the medians were presented for each treatment group. OS analysis was performed by CD8 subgroups with the median of baseline CD8 expression as cut-off.
Time Frame	up to approximately 4.3 years
Analysis Population Description	Participants to whom study treatment was assigned by randomization with a valid baseline measurement of CD8 expression

	Canakinumab	Placebo
Arm/Group Description	Participants receive 200mg of canakinumab subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)	Participants receive canakinumab placebo subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)
Number of Participants Analyzed [units: participants]	429	449
Overall Survival (OS) in CD8 subgroups (units: Months)	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**
CD8 < median	46.95 (32.23 to NA)[1]	NA (NA to NA)[1]
CD8 ≥ median	51.12 (NA to NA)[1]	NA (NA to NA)[1]

[1] NA: Not estimable due to the insufficient number of participants with events

Lung Cancer Specific Survival (LCSS)

Description	LCSS is defined as the time from date of randomization to the date of death due to lung cancer. The LCSS distribution was estimated using the Kaplan-Meier method, and Kaplan-Meier medians and 95% confidence intervals of the medians were presented for each treatment group.
Time Frame	Up to approximately 4.3 years
Analysis Population Description	FAS including all participants to whom study treatment was assigned by randomization

	Canakinumab	Placebo
Arm/Group Description	Participants receive 200mg of canakinumab subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)	Participants receive canakinumab placebo subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)
Number of Participants Analyzed [units: participants]	693	689
Lung Cancer Specific Survival (LCSS) (units: Months)	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**

	51.12 (44.71 to NA)[1]	NA (NA to NA)[1]

[1] NA: Not estimable due to the insufficient number of participants with events

Disease free survival (DFS) by local investigator in PD-L1 subgroups

Description	DFS is the time from the date of randomization to the date of the first documented NSCLC disease recurrence as assessed by local investigator radiologically or death due to any cause. Disease recurrence included diagnoses of new primary lung malignancies. Clinical deterioration was not considered as a recurrence of disease. In case of non-conclusive radiological evidence, a biopsy assessment was performed to confirm NSCLC recurrence. The median DFS was estimated using the Kaplan-Meier method. DFS was censored if no DFS event was observed prior to the analysis cut-off date or subjects who received any subsequent anti-neoplastic therapy for NSCLC. The censoring date was the date of last assessment before the cut-off date or NSCLC related anti-neoplastic therapy date. DFS analysis was performed by baseline programmed cell death-ligand 1 (PD-L1) expression status: PD-L1 <1%, PD-L1 ≥1% and <49%, and PD-L1 ≥50%.
Time Frame	Up to approximately 4 years
Analysis Population Description	Participants to whom study treatment was assigned by randomization with a valid baseline measurement of PD-L1 expression.

	Canakinumab	**Placebo**
Arm/Group Description	Participants receive 200mg of canakinumab subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)	Participants receive canakinumab placebo subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)
Number of Participants Analyzed [units: participants]	396	418
Disease free survival (DFS) by local investigator in PD-L1 subgroups (units: Months)	**Median** **(95% Confidence Interval)**	**Median** **(95% Confidence Interval)**
PD-L1 <1%	30.72 (23.52 to NA)[1]	NA (23.03 to NA)[1]
PD-L1 ≥1% and <49%	30.42 (21.42 to NA)[1]	NA (17.05 to NA)[1]
PD-L1 ≥50%	46.95 (19.45 to NA)[1]	NA (22.31 to NA)[1]

[1] NA: Not estimable due to the insufficient number of participants with events

Disease free survival (DFS) by local investigator in CD8 subgroups

Description	DFS is the time from the date of randomization to the date of the first documented NSCLC disease recurrence as assessed by local investigator radiologically or death due to any cause. Disease recurrence included diagnoses of new primary lung malignancies. Clinical deterioration was not considered as a recurrence of disease. In case of non-conclusive radiological evidence, a biopsy assessment was performed to confirm NSCLC recurrence. The median DFS was estimated using the Kaplan-Meier method. DFS was censored if no DFS event was observed prior to the analysis cut-off date or subjects who received any subsequent anti-neoplastic therapy for NSCLC. The censoring date was the date of last assessment before the cut-off date or NSCLC related anti-neoplastic therapy date. DFS analysis was performed by CD8 subgroups with the median of baseline CD8 expression as cut-off.
Time Frame	Up to approximately 4 years
Analysis Population Description	Participants to whom study treatment was assigned by randomization with a valid baseline measurement of CD8 expression

	Canakinumab	**Placebo**
Arm/Group Description	Participants receive 200mg of canakinumab subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)	Participants receive canakinumab placebo subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)
Number of Participants Analyzed [units: participants]	429	449
Disease free survival (DFS) by local investigator in CD8 subgroups (units: Months)	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**
CD8 < median	26.58 (20.67 to NA)[1]	NA (25.03 to NA)[1]
CD8 ≥ median	46.95 (28.81 to NA)[1]	NA (23.89 to NA)[1]

[1] NA: Not estimable due to the insufficient number of participants with events

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Canakinumab serum concentrations

Description	Serum concentrations of canakinumab were determined using an ELISA method.
Time Frame	Cycle 1 on day 1 (pre-dose), day 8 and 15; Cycle 2, 4, 6, 9 and 12 on day 1 (pre-dose). Cycle=21 days
Analysis Population Description	The Pharmacokinetic analysis set (PAS) including all subjects who received at least one dose of canakinumab and provided at least one evaluable PK sample.

	Canakinumab
Arm/Group Description	Participants receive 200mg of canakinumab subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)
Number of Participants Analyzed [units: participants]	664
Canakinumab serum concentrations (units: ug/ml)	**Mean ± Standard Deviation**
Cycle 1 Day 1	0 ± 0
Cycle 1 Day 8	18.1 ± 6.53
Cycle 1 Day 15	16.9 ± 5.43
Cycle 2 Day 1	15.0 ± 4.91
Cycle 4 Day 1	29.7 ± 10.3
Cycle 6 Day 1	34.7 ± 13.0
Cycle 9 Day 1	37.1 ± 14.5
Cycle 12 Day 1	38.6 ± 15.5

Canakinumab Anti-drug Antibody (ADA) prevalence at baseline

Description	Canakinumab ADA prevalence at baseline was calculated as the percentage of participants who had an ADA positive result at baseline
Time Frame	Baseline

Analysis Population Description	All subjects who received at least one dose of canakinumab

	Canakinumab
Arm/Group Description	Participants receive 200mg of canakinumab subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)
Number of Participants Analyzed [units: participants]	692
Canakinumab Anti-drug Antibody (ADA) prevalence at baseline (units: Participants)	**Count of Participants (Not Applicable)**
	8 (1.16%)

Canakinumab ADA incidence

Description	Canakinumab ADA incidence on-treatment was calculated as the percentage of participants who were treatment-induced ADA positive (post-baseline ADA positive with ADA-negative sample at baseline) and treatment-boosted ADA positive (post-baseline ADA positive with titer that was at least the fold titer change greater than the ADA-positive baseline titer)
Time Frame	From baseline up to 130 days after end of treatment, assessed up to approx. 1.5 years
Analysis Population Description	All subjects who received at least one dose of canakinumab

	Canakinumab
Arm/Group Description	Participants receive 200mg of canakinumab subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)
Number of Participants Analyzed [units: participants]	692

Canakinumab ADA incidence (units: Participants)	Count of Participants (Not Applicable)
	7 (1.01%)

Time to definitive 10 point deterioration symptom scores of pain,cough and dyspnea per European Organization for Research and Treatment of Cancer Quality of Life (EORTC QLQ)- Lung cancer (LC) 13 questionnaire

Description	The Lung Cancer module of the EORTC's quality of life questionnaire (EORTC QLQ-LC13) was used in conjunction with the EORTC QLQ-C30 and provided information on an additional 13 items specifically related to lung cancer. The lung cancer module incorporated one multi-item scale to assess dyspnea, and 9 single items assessing pain, coughing, sore mouth, dysphagia, peripheral neuropathy, alopecia, and hemoptysis. All of the domain scores ranged from 0 to 100. A high score indicated a high level of symptoms. The time to definitive 10 point deterioration symptom scores of pain, cough and dyspnea was defined as the time from the date of randomization to the date of event, which was defined as at least 10 points relative to baseline worsening of the EORTC QLQ-LC13 symptom score with no later change below this threshold or death due to any cause, whichever occurred earlier.
Time Frame	From baseline up to approximately 4 years
Analysis Population Description	FAS including all participants to whom study treatment was assigned by randomization

	Canakinumab	Placebo
Arm/Group Description	Participants receive 200mg of canakinumab subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)	Participants receive canakinumab placebo subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)
Number of Participants Analyzed [units: participants]	693	689
Time to definitive 10 point deterioration symptom scores of pain,cough and dyspnea per European Organization for Research and Treatment of Cancer Quality of Life (EORTC QLQ)-Lung cancer (LC) 13 questionnaire (units: Months)	**Median** **(95% Confidence Interval)**	**Median** **(95% Confidence Interval)**

Pain	NA (35.45 to NA)[1]	NA (NA to NA)[1]
Cough	NA (35.06 to NA)[1]	NA (34.99 to NA)[1]
Dyspnea	28.88 (23.10 to 34.96)	34.99 (23.13 to NA)[1]

[1] NA: Not estimable due to the insufficient number of participants with events

Time to definitive 10 point deterioration of global health status/quality of life (QoL), shortness of breath and pain per EORTC QLQ-C30 questionnaire

Description	The EORTC QLQ-C30 was a questionnaire developed to assess the health-related quality of life of cancer participants. It assessed 15 domains consisting of 5 functional domains (physical, role, emotional, cognitive, social) and 9 symptom domains (fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, financial difficulties) and a global health status/QoL scale. All domain scores ranged from 0 to 100. A high score for the functional or global health status scales indicated a high level of functioning or QoL; a high score for a symptom scale indicated a high level of symptoms. The time to definitive 10 point deterioration of global health status/QoL, shortness of breath and pain was defined as the time from the date of randomization to the date of event, which was defined as at least 10 points relative to baseline worsening of the EORTC QLQ-C30 score with no later change below this threshold or death due to any cause, whichever occured earlier.
Time Frame	From baseline up to approximately 4 years
Analysis Population Description	FAS including all participants to whom study treatment was assigned by randomization

	Canakinumab	**Placebo**
Arm/Group Description	Participants receive 200mg of canakinumab subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)	Participants receive canakinumab placebo subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)
Number of Participants Analyzed [units: participants]	693	689
Time to definitive 10 point deterioration of global health status/quality of life (QoL), shortness of breath and pain per	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**

EORTC QLQ-C30 questionnaire (units: Months)		
Global health status/QoL	34.99 (29.93 to NA)[1]	35.15 (35.15 to NA)[1]
Shortness of breath	NA (NA to NA)[1]	35.15 (34.99 to NA)[1]
Pain	29.93 (28.29 to 35.22)	36.44 (34.99 to NA)[1]

[1] NA: Not estimable due to the insufficient number of participants with events

Time to first 10 point deterioration for symptom scores of pain, cough and dyspnea per EORTC QLQ-LC13 questionnaire

Description	The Lung Cancer module of the EORTC's quality of life questionnaire (EORTC QLQ-LC13) was used in conjunction with the EORTC QLQ-C30 and provided information on an additional 13 items specifically related to lung cancer. The lung cancer module incorporated one multi-item scale to assess dyspnea, and 9 single items assessing pain, coughing, sore mouth, dysphagia, peripheral neuropathy, alopecia, and hemoptysis. All of the domain scores ranged from 0 to 100. A high score indicated a high level of symptoms. The time to first 10 point deterioration symptom scores of pain, cough and dyspnea was defined as the time from the date of randomization to the first onset of at least 10 points absolute increase from baseline (worsening) in symptoms scores or death due to any cause, whichever occurred earlier.
Time Frame	From baseline up to approximately 4 years
Analysis Population Description	FAS including all participants to whom study treatment was assigned by randomization

	Canakinumab	**Placebo**
Arm/Group Description	Participants receive 200mg of canakinumab subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)	Participants receive canakinumab placebo subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)
Number of Participants Analyzed [units: participants]	693	689
Time to first 10 point deterioration for symptom scores of pain, cough and dyspnea per EORTC QLQ-LC13 questionnaire (units: Months)	**Median** **(95% Confidence Interval)**	**Median** **(95% Confidence Interval)**

Pain	35.15 (26.58 to NA)[1]	NA (23.06 to NA)[1]
Cough	15.44 (10.38 to 23.06)	15.01 (9.69 to NA)[1]
Dyspnea	4.17 (3.42 to 5.55)	4.86 (3.48 to 6.97)

[1] NA: Not estimable due to the insufficient number of participants with events

Time to first 10 point deterioration of global health status/QoL, shortness of breath and pain per EORTC QLQ-C30 questionnaire

Description	The EORTC QLQ-C30 was a questionnaire developed to assess the health-related quality of life of cancer participants. It assessed 15 domains consisting of 5 functional domains (physical, role, emotional, cognitive, social) and 9 symptom domains (fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, financial difficulties) and a global health status/QoL scale. All domain scores ranged from 0 to 100. A high score for the functional or global health status scales indicated a high level of functioning or QoL; a high score for a symptom scale indicated a high level of symptoms. The time to first 10 point deterioration of global health status/QoL, shortness of breath and pain scores was defined as the time from the date of randomization to the first onset of at least 10 points absolute increase from baseline (worsening) in symptoms scores or death due to any cause, whichever occurred earlier.
Time Frame	From baseline up to approximately 4 years
Analysis Population Description	FAS including all participants to whom study treatment was assigned by randomization

	Canakinumab	**Placebo**
Arm/Group Description	Participants receive 200mg of canakinumab subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)	Participants receive canakinumab placebo subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)
Number of Participants Analyzed [units: participants]	693	689
Time to first 10 point deterioration of global health status/QoL, shortness of breath and pain per EORTC QLQ-C30 questionnaire (units: Months)	**Median** **(95% Confidence Interval)**	**Median** **(95% Confidence Interval)**

Global health status/QoL	9.23 (7.10 to 11.76)	9.07 (7.62 to 11.76)
Shortness of breath	29.14 (23.03 to NA)[1]	NA (23.13 to NA)[1]
Pain	5.49 (4.21 to 6.90)	5.62 (4.17 to 7.62)

[1] NA: Not estimable due to the insufficient number of participants with events

Change from baseline in the utility score of the EuroQoL- 5 dimension- 5 level (EQ-5D-5L)

Description	EQ-5D-5L was a standardized questionnaire that measured health-related QoL. EQ-5D-5L consisted of 2 components: a health state profile and a visual analogue scale. The health state profile included five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, each with five levels ranging from 1 (no problems) to 5 (extreme problems). The EQ-5D-5L health state profile responses were converted into single index utility score, ranging from -1 to 1, where lower scores representing a higher level of dysfunction. Published weights are available enabling the calculation of the utility score. A positive change from baseline indicated improvement. This endpoint was assessed throughout the study, including safety and efficacy follow-up (FU) visits. Safety FU visits: every 4 weeks after end of treatment up to 130 days post-last dose. Efficacy FU visits: at 18, 24, 30, 36 and 48 months post-randomization (if no recurrence observed during treatment or safety FU)
Time Frame	Baseline, every 3 weeks for 14 months; end of treatment; every 4 weeks up to 130 days post-treatment; at 18,24,30,36 and 48 months post-randomization (if no recurrence); 7 and 28 days post-disease progression, up to approx. 4 years.
Analysis Population Description	All participants to whom study treatment was assigned by randomization with data available at the specified time points. Number analyzed refers to the number of participants with an evaluable value at the specified time point.

	Canakinumab	**Placebo**
Arm/Group Description	Participants receive 200mg of canakinumab subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)	Participants receive canakinumab placebo subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)
Number of Participants Analyzed [units: participants]	643	629
Change from baseline in the utility score of the EuroQoL- 5 dimension- 5 level (EQ-5D-5L) (units: Score on a scale)	**Mean** **± Standard Deviation**	**Mean** **± Standard Deviation**

Week 3	0.0 ± 0.11	0.0 ± 0.12
Week 6	0.0 ± 0.13	0.0 ± 0.12
Week 9	0.0 ± 0.13	0.0 ± 0.13
Week 12	0.0 ± 0.12	0.0 ± 0.12
Week 15	0.0 ± 0.13	0.0 ± 0.12
Week 18	0.0 ± 0.13	0.0 ± 0.13
Week 21	0.0 ± 0.13	0.0 ± 0.15
Week 24	0.0 ± 0.14	0.0 ± 0.14
Week 27	0.0 ± 0.13	0.0 ± 0.14
Week 30	0.0 ± 0.13	0.0 ± 0.14
Week 33	0.0 ± 0.13	0.0 ± 0.14
Week 36	0.0 ± 0.14	0.0 ± 0.15
Week 39	0.0 ± 0.15	0.0 ± 0.13
Week 42	0.0 ± 0.15	0.0 ± 0.14
Week 45	0.0 ± 0.14	0.0 ± 0.14
Week 48	0.0 ± 0.14	0.0 ± 0.15
Week 51	0.0 ± 0.13	0.0 ± 0.14
Week 54	0.0 ± 0.18	0.1 ± 0.12
Week 57	0.0	-0.1
Week 60	-0.2	-0.1
Week 63	0.0	
Week 69	0.0	
Safety FU 1	0.0 ± 0.15	0.0 ± 0.14
Safety FU 2	0.0 ± 0.14	0.0 ± 0.14
Safety FU 3	0.0 ± 0.14	0.0 ± 0.15

Safety FU 4	0.0 ± 0.15	0.0 ± 0.16
Safety FU 5	0.0 ± 0.15	0.0 ± 0.14
Efficacy FU 1	0.0 ± 0.16	0.0 ± 0.14
Efficacy FU 2	0.0 ± 0.15	0.0 ± 0.16
Efficacy FU 3	0.0 ± 0.14	0.0 ± 0.15
Efficacy FU 4	0.0 ± 0.13	0.0 ± 0.15
Efficacy FU 5	0.0 ± 0.10	-0.1 ± 0.17
7 days post disease progression	-0.1 ± 0.16	-0.1 ± 0.22
28 days post disease progression	-0.1 ± 0.18	-0.1 ± 0.18

Other Pre-Specified Outcome Result(s)

No data identified.

Post-Hoc Outcome Result(s)

All collected deaths

Description	Pre-treatment deaths were collected from day of participant's informed consent to the day before first dose of study medication. On-treatment deaths were collected from start of treatment to 130 days after last dose. Post-treatment follow-up deaths were collected from day 131 after last dose of study treatment to end of study.
Time Frame	Pre-treatment: Up to 28 days prior to treatment. On-treatment: Up to approx. 1.5 years. Post-treatment follow-up: Up to approx. 4.3 years
Analysis Population Description	FAS including all participants to whom study treatment was assigned by randomization

	Canakinumab	**Placebo**

Arm/Group Description	Participants receive 200mg of canakinumab subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)	Participants receive canakinumab placebo subcutaneously every 3 weeks for up to 18 cycles (approximately 54 weeks)
Number of Participants Analyzed [units: participants]	693	689
All collected deaths (units: Participants)		
Pre-treatment deaths	0	0
On-treatment deaths	9	17
Post-treatment follow-up deaths	53	51
All deaths	62	68

Safety Results

Time Frame	Pre-treatment: from study consent to the day before first dose, up to 28 days. On-treatment: from first dose of study treatment to 130 days after last dose of study medication, up to approx. 1.5 years. Post-treatment follow-up: from 131 days after last dose of study medication until the end of the study, up to approx. 4.3 years.
Additional Description	Treatment-emergent AEs refer to any signs or symptoms observed during the study treatment and up to 130 days after treatment, considering the Safety Set (including participants who received at least one dose of study treatment). All-Cause Mortality analysis encompasses the Full Analysis Set, including all participants to whom study treatment was assigned by randomization
Source Vocabulary for Table Default	MedDRA (25.1)
Collection Approach for Table Default	Systematic Assessment

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All-Cause Mortality

	All participants - Pre-treatment N = 1382	Canakinumab - On-treatment N = 692	Canakinumab - Post-treatment follow-up N = 671	Placebo - On-treatment N = 689	Placebo - Post-treatment follow-up N = 662
Arm/Group Description	Deaths collected in the pre-treatment period (from day of patient's informed consent to the day before first administration of study treatment)	AEs collected during on-treatment period (up to 130 days post-treatment)	Deaths collected in the post-treatment follow-up period (starting from day 131 post- treatment). No AEs were collected during this period	AEs collected during on-treatment period (up to 130 days post-treatment)	Deaths collected in the post-treatment follow-up period (starting from day 131 post-treatment). No AEs were collected during this period
Total Number Affected	0	9	53	17	51
Total Number At Risk	1382	692	671	689	662

Serious Adverse Events

	All participants - Pre-treatment N = 0	Canakinumab - On-treatment N = 692	Canakinumab - Post-treatment follow-up N = 0	Placebo - On-treatment N = 689	Placebo - Post-treatment follow-up N = 0
Arm/Group Description	Deaths collected in the pre-treatment period (from day of patient's informed consent to the day before first administration of study treatment)	AEs collected during on-treatment period (up to 130 days post-treatment)	Deaths collected in the post-treatment follow-up period (starting from day 131 post- treatment). No AEs were collected during this period	AEs collected during on-treatment period (up to 130 days post-treatment)	Deaths collected in the post-treatment follow-up period (starting from day 131 post-treatment). No AEs were collected during this period
Total # Affected by any Serious Adverse Event	0	141	0	146	0
Total # at Risk by any Serious Adverse Event	0	692	0	689	0

Blood and lymphatic system disorders		
Anaemia	0 (0.00%)	1 (0.15%)
Thrombocytosis	0 (0.00%)	1 (0.15%)
Cardiac disorders		
Acute coronary syndrome	0 (0.00%)	1 (0.15%)
Acute myocardial infarction	0 (0.00%)	1 (0.15%)
Angina pectoris	3 (0.43%)	2 (0.29%)
Atrial fibrillation	2 (0.29%)	0 (0.00%)
Atrial flutter	0 (0.00%)	1 (0.15%)
Cardiac arrest	1 (0.14%)	0 (0.00%)
Cardiac failure	0 (0.00%)	1 (0.15%)
Cardiac failure congestive	1 (0.14%)	0 (0.00%)
Cardiac ventricular thrombosis	0 (0.00%)	1 (0.15%)
Cardiovascular insufficiency	0 (0.00%)	1 (0.15%)
Coronary artery disease	1 (0.14%)	1 (0.15%)
Myocardial infarction	1 (0.14%)	4 (0.58%)
Myocardial ischaemia	0 (0.00%)	2 (0.29%)
Pericarditis constrictive	0 (0.00%)	1 (0.15%)
Supraventricular tachycardia	1 (0.14%)	0 (0.00%)
Ear and labyrinth disorders		
Vertigo	0 (0.00%)	1 (0.15%)

Eye disorders		
Retinal detachment	0 (0.00%)	1 (0.15%)
Retinal tear	0 (0.00%)	1 (0.15%)
Rhegmatogenous retinal detachment	1 (0.14%)	0 (0.00%)
Gastrointestinal disorders		
Abdominal hernia	1 (0.14%)	0 (0.00%)
Abdominal pain	3 (0.43%)	2 (0.29%)
Colitis	1 (0.14%)	0 (0.00%)
Constipation	0 (0.00%)	1 (0.15%)
Diarrhoea	1 (0.14%)	1 (0.15%)
Enterocolitis	1 (0.14%)	0 (0.00%)
Gastrointestinal haemorrhage	1 (0.14%)	2 (0.29%)
Gastrointestinal pain	0 (0.00%)	1 (0.15%)
Haemorrhoids	0 (0.00%)	1 (0.15%)
Large intestine polyp	0 (0.00%)	1 (0.15%)
Lumbar hernia	1 (0.14%)	0 (0.00%)
Pancreatic cyst	1 (0.14%)	0 (0.00%)
Pancreatitis acute	1 (0.14%)	1 (0.15%)
Rectal haemorrhage	0 (0.00%)	1 (0.15%)
Vomiting	1 (0.14%)	1 (0.15%)
General disorders and administration site conditions		

Asthenia	1 (0.14%)	1 (0.15%)
Chest pain	0 (0.00%)	2 (0.29%)
Fatigue	0 (0.00%)	1 (0.15%)
Non-cardiac chest pain	2 (0.29%)	2 (0.29%)
Pain	0 (0.00%)	1 (0.15%)
Pyrexia	2 (0.29%)	1 (0.15%)
Hepatobiliary disorders		
Biliary colic	0 (0.00%)	1 (0.15%)
Cholecystitis	1 (0.14%)	3 (0.44%)
Cholelithiasis	0 (0.00%)	1 (0.15%)
Gallbladder obstruction	1 (0.14%)	0 (0.00%)
Hepatitis acute	1 (0.14%)	0 (0.00%)
Infections and infestations		
Appendicitis	0 (0.00%)	1 (0.15%)
Asymptomatic COVID-19	1 (0.14%)	0 (0.00%)
Bronchitis	2 (0.29%)	1 (0.15%)
Cellulitis	1 (0.14%)	0 (0.00%)
Coronavirus infection	1 (0.14%)	1 (0.15%)
COVID-19	48 (6.94%)	48 (6.97%)
COVID-19 pneumonia	1 (0.14%)	4 (0.58%)
Diverticulitis	0 (0.00%)	1 (0.15%)
Empyema	1 (0.14%)	0 (0.00%)

Endocarditis	0 (0.00%)	1 (0.15%)
Herpes zoster	0 (0.00%)	1 (0.15%)
Infection parasitic	1 (0.14%)	0 (0.00%)
Kidney infection	0 (0.00%)	1 (0.15%)
Localised infection	0 (0.00%)	1 (0.15%)
Lung abscess	1 (0.14%)	0 (0.00%)
Neutropenic sepsis	0 (0.00%)	2 (0.29%)
Pneumonia	13 (1.88%)	9 (1.31%)
Pneumonia pseudomonal	1 (0.14%)	0 (0.00%)
Rectal abscess	0 (0.00%)	1 (0.15%)
Respiratory tract infection	0 (0.00%)	2 (0.29%)
Sepsis	1 (0.14%)	1 (0.15%)
Septic shock	1 (0.14%)	0 (0.00%)
Tuberculosis	1 (0.14%)	0 (0.00%)
Urinary tract infection	1 (0.14%)	1 (0.15%)
Injury, poisoning and procedural complications		
Alcohol poisoning	0 (0.00%)	1 (0.15%)
Head injury	1 (0.14%)	1 (0.15%)
Hip fracture	0 (0.00%)	1 (0.15%)
Ligament rupture	0 (0.00%)	1 (0.15%)
Procedural pneumothorax	0 (0.00%)	1 (0.15%)
Radius fracture	1 (0.14%)	0 (0.00%)

Spinal compression fracture	0 (0.00%)	1 (0.15%)
Toxicity to various agents	0 (0.00%)	2 (0.29%)
Investigations		
Alanine aminotransferase increased	0 (0.00%)	1 (0.15%)
Aspartate aminotransferase increased	0 (0.00%)	1 (0.15%)
C-reactive protein increased	0 (0.00%)	3 (0.44%)
Electrocardiogram T wave amplitude decreased	0 (0.00%)	1 (0.15%)
Hepatic enzyme increased	1 (0.14%)	0 (0.00%)
Influenza A virus test positive	1 (0.14%)	0 (0.00%)
SARS-CoV-2 test positive	3 (0.43%)	2 (0.29%)
Metabolism and nutrition disorders		
Hypokalaemia	1 (0.14%)	1 (0.15%)
Hyponatraemia	1 (0.14%)	1 (0.15%)
Type 2 diabetes mellitus	0 (0.00%)	1 (0.15%)
Musculoskeletal and connective tissue disorders		
Back pain	2 (0.29%)	0 (0.00%)
Intervertebral disc protrusion	0 (0.00%)	3 (0.44%)
Lumbar spinal stenosis	0 (0.00%)	1 (0.15%)
Pain in extremity	1 (0.14%)	1 (0.15%)
Tenosynovitis	1 (0.14%)	0 (0.00%)

Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Basal cell carcinoma	3 (0.43%)	1 (0.15%)
B-cell lymphoma	0 (0.00%)	1 (0.15%)
Colon cancer	1 (0.14%)	0 (0.00%)
Gastric cancer	1 (0.14%)	0 (0.00%)
Lung adenocarcinoma	0 (0.00%)	2 (0.29%)
Myelodysplastic syndrome	0 (0.00%)	1 (0.15%)
Neoplasm swelling	1 (0.14%)	0 (0.00%)
Non-small cell lung cancer	2 (0.29%)	0 (0.00%)
Pancreatic carcinoma	0 (0.00%)	1 (0.15%)
Papillary thyroid cancer	0 (0.00%)	1 (0.15%)
Prostate cancer	1 (0.14%)	1 (0.15%)
Rectal cancer stage 0	1 (0.14%)	0 (0.00%)
Renal cancer	0 (0.00%)	1 (0.15%)
Renal neoplasm	1 (0.14%)	1 (0.15%)
Small cell lung cancer	0 (0.00%)	1 (0.15%)
Transitional cell carcinoma	2 (0.29%)	0 (0.00%)
Nervous system disorders		
Altered state of consciousness	0 (0.00%)	1 (0.15%)
Aphasia	0 (0.00%)	1 (0.15%)
Carotid artery occlusion	0 (0.00%)	1 (0.15%)
Cerebral infarction	0 (0.00%)	1 (0.15%)

Cerebrovascular accident	4 (0.58%)	4 (0.58%)
Epilepsy	1 (0.14%)	0 (0.00%)
Generalised tonic-clonic seizure	1 (0.14%)	1 (0.15%)
Ischaemic stroke	0 (0.00%)	1 (0.15%)
Partial seizures	0 (0.00%)	1 (0.15%)
Peripheral nerve palsy	1 (0.14%)	0 (0.00%)
Syncope	1 (0.14%)	1 (0.15%)
Thrombotic cerebral infarction	1 (0.14%)	0 (0.00%)
Ulnar nerve palsy	1 (0.14%)	0 (0.00%)
Psychiatric disorders		
Schizophrenia	1 (0.14%)	0 (0.00%)
Renal and urinary disorders		
Calculus urinary	1 (0.14%)	0 (0.00%)
Haematuria	1 (0.14%)	0 (0.00%)
Hydronephrosis	0 (0.00%)	1 (0.15%)
Renal colic	0 (0.00%)	2 (0.29%)
Renal haemorrhage	0 (0.00%)	1 (0.15%)
Urinary retention	1 (0.14%)	0 (0.00%)
Reproductive system and breast disorders		
Benign prostatic hyperplasia	1 (0.14%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders		

Acute respiratory failure	1 (0.14%)	0 (0.00%)
Bronchial obstruction	0 (0.00%)	1 (0.15%)
Chronic obstructive pulmonary disease	1 (0.14%)	3 (0.44%)
Cough	0 (0.00%)	1 (0.15%)
Dyspnoea	7 (1.01%)	2 (0.29%)
Dyspnoea exertional	0 (0.00%)	1 (0.15%)
Epistaxis	1 (0.14%)	1 (0.15%)
Haemoptysis	1 (0.14%)	0 (0.00%)
Hypoxia	2 (0.29%)	0 (0.00%)
Interstitial lung disease	1 (0.14%)	0 (0.00%)
Pleural effusion	3 (0.43%)	2 (0.29%)
Pneumonitis	3 (0.43%)	0 (0.00%)
Pneumothorax	3 (0.43%)	0 (0.00%)
Pulmonary embolism	2 (0.29%)	2 (0.29%)
Pulmonary thrombosis	1 (0.14%)	0 (0.00%)
Respiratory failure	2 (0.29%)	1 (0.15%)
Sleep apnoea syndrome	0 (0.00%)	1 (0.15%)
Vocal cord polyp	1 (0.14%)	0 (0.00%)
Skin and subcutaneous tissue disorders		
Dermatitis acneiform	0 (0.00%)	1 (0.15%)
Skin ulcer	0 (0.00%)	1 (0.15%)

Vascular disorders		
Embolism	1 (0.14%)	0 (0.00%)
Hypertension	0 (0.00%)	1 (0.15%)
Peripheral ischaemia	0 (0.00%)	1 (0.15%)

Other (Not Including Serious) Adverse Events

Frequent Event Reporting Threshold 5%

	All participants - Pre-treatment N = 0	**Canakinumab - On-treatment N = 692**	**Canakinumab - Post-treatment follow-up N = 0**	**Placebo - On-treatment N = 689**	**Placebo - Post-treatment follow-up N = 0**
Arm/Group Description	Deaths collected in the pre-treatment period (from day of patient's informed consent to the day before first administration of study treatment)	AEs collected during on-treatment period (up to 130 days post-treatment)	Deaths collected in the post-treatment follow-up period (starting from day 131 post- treatment). No AEs were collected during this period	AEs collected during on-treatment period (up to 130 days post-treatment)	Deaths collected in the post-treatment follow-up period (starting from day 131 post-treatment). No AEs were collected during this period
Total # Affected by any Other Adverse Event	0	465	0	455	0
Total # at Risk by any Other Adverse Event	0	692	0	689	0
Blood and lymphatic system disorders					
Anaemia		46 (6.65%)		50 (7.26%)	

Gastrointestinal disorders		
Constipation	34 (4.91%)	42 (6.10%)
Diarrhoea	57 (8.24%)	48 (6.97%)
Nausea	46 (6.65%)	51 (7.40%)
General disorders and administration site conditions		
Asthenia	47 (6.79%)	33 (4.79%)
Fatigue	70 (10.12%)	60 (8.71%)
Pyrexia	28 (4.05%)	43 (6.24%)
Infections and infestations		
Nasopharyngitis	44 (6.36%)	33 (4.79%)
Upper respiratory tract infection	37 (5.35%)	31 (4.50%)
Investigations		
Alanine aminotransferase increased	65 (9.39%)	49 (7.11%)
Amylase increased	52 (7.51%)	51 (7.40%)
Aspartate aminotransferase increased	53 (7.66%)	37 (5.37%)
Lipase increased	47 (6.79%)	47 (6.82%)
Neutrophil count decreased	45 (6.50%)	13 (1.89%)
Weight increased	63 (9.10%)	48 (6.97%)
White blood cell count decreased	35 (5.06%)	18 (2.61%)
Musculoskeletal and connective tissue disorders		

Arthralgia	74 (10.69%)	88 (12.77%)
Back pain	61 (8.82%)	56 (8.13%)
Nervous system disorders		
Headache	31 (4.48%)	60 (8.71%)
Paraesthesia	29 (4.19%)	44 (6.39%)
Respiratory, thoracic and mediastinal disorders		
Cough	89 (12.86%)	108 (15.67%)
Dyspnoea	67 (9.68%)	50 (7.26%)
Skin and subcutaneous tissue disorders		
Pruritus	35 (5.06%)	34 (4.93%)
Vascular disorders		
Hypertension	35 (5.06%)	24 (3.48%)

Other Relevant Findings

None

Conclusion

Canakinumab did not prolong disease-free survival (DFS) compared to placebo in the patient population. No clinically relevant differences were observed between canakinumab and placebo with regard to overall survival (OS) or lung cancer specific survival (LCSS) results.

No new safety signals or unexpected safety findings were observed in the patients treated with canakinumab. The overall safety and tolerability profile of canakinumab observed in this study was as expected and consistent with the known safety profile, in line with the current prescribing information of canakinumab.

Date of Clinical Trial Report

Primary CSR: 15-Dec-2022

Final CSR: 03-Nov-2023