Clinical trial results:
A randomized, double-blind, placebo-controlled, phase III study evaluating the efficacy and safety of canakinumab in combination with docetaxel versus placebo in combination with docetaxel in subjects with non-small cell lung cancer (NSCLC) previously treated with PD-(L)1 inhibitors and platinum-based chemotherapy (CANOPY-2)

Summary

EudraCT number	2018-002480-26
Trial protocol	GR DE FR ES BE CZ PL NL HU DK IT
Global end of trial date	20 December 2021

Results information

Result version number	v1
This version publication date	20 September 2022
First version publication date	20 September 2022

Trial information

Trial identification

Sponsor protocol code	CACZ885V2301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03626545
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 December 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 December 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial is to evaluate the efficacy and safety of canakinumab in combination with docetaxel versus placebo in combination with docetaxel, as second or third-line treatment.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 January 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 8
Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	Belgium: 21
Country: Number of subjects enrolled	Brazil: 4
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	Chile: 4
Country: Number of subjects enrolled	China: 12
Country: Number of subjects enrolled	Czechia: 4
Country: Number of subjects enrolled	Germany: 20
Country: Number of subjects enrolled	Denmark: 2
Country: Number of subjects enrolled	Spain: 48
Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	Greece: 9
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Israel: 2
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	Jordan: 2
Country: Number of subjects enrolled	Japan: 14
Country: Number of subjects enrolled	Korea, Republic of: 17

Country: Number of subjects enrolled	Lebanon: 3
Country: Number of subjects enrolled	Netherlands: 8
Country: Number of subjects enrolled	Poland: 8
Country: Number of subjects enrolled	Russian Federation: 10
Country: Number of subjects enrolled	Singapore: 2
Country: Number of subjects enrolled	Taiwan: 3
Country: Number of subjects enrolled	United States: 11
Worldwide total number of subjects	245
EEA total number of subjects	146

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	135
From 65 to 84 years	110
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The Safety run-in (Part 1) was conducted in 6 centers across 4 countries and the Randomized part (Part 2) was conducted in 85 centers across 26 countries.

Pre-assignment

Screening details:

In the randomized part, a total of 352 subjects were screened. 237 subjects completed the screening phase and were randomized in a 1:1 ratio to treatment with either canakinumab plus docetaxel or placebo plus docetaxel. Three randomized subjects in the placebo plus docetaxel group were not treated

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Carer, Data analyst, Subject, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Safety run-in part: Canakinumab+docetaxel

Arm description:

Participants were treated with full doses of docetaxel 75mg/m^2 intravenous and canakinumab 200 mg subcutaneous on Day 1 of each 21-Day cycle (dose level 1).

Arm type	Experimental
Investigational medicinal product name	Canakinumab
Investigational medicinal product code	ACZ885
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Canakinumab, 200 mg, subcutaneous. The initial dose regimen was once every 3 weeks (on Day 1 of each 21-day cycle)

Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Docetaxel 75mg/m^2, intravenous, administered on Day 1 of each 21-day cycle

Arm title	Randomized part: Canakinumab + docetaxel

Arm description:

Participants were randomized to receive canakinumab subcutaneous at RP3R and docetaxel at 75 mg/m^2 on Day 1 of each 21-Day cycle

Arm type	Experimental
Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details: Docetaxel 75mg/m^2, intravenous, administered on Day 1 of each 21-day cycle	
Investigational medicinal product name	Canakinumab
Investigational medicinal product code	ACZ885
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use
Dosage and administration details: Canakinumab, 200 mg, subcutaneous, administered on Day 1 of each 21-day cycle	
Arm title	Randomized part: Placebo + docetaxel
Arm description: Participants were randomized to receive placebo subcutaneous at RP3R and docetaxel at 75 mg/m^2 on Day 1 of each 21-Day cycle	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use
Dosage and administration details: Placebo, sub-cutaneous, every 3 weeks, administered on Day 1 of each 21-day cycle	
Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Docetaxel 75mg/m^2, intravenous, administered on Day 1 of each 21-day cycle	

Number of subjects in period 1	Safety run-in part: Canakinumab+docetaxel	Randomized part: Canakinumab + docetaxel	Randomized part: Placebo + docetaxel
Started	8	120	117
Completed	0	0	0
Not completed	8	120	117
Adverse event, serious fatal	1	1	1
Physician decision	1	18	14
Subject Decision	-	5	5
Adverse event, non-fatal	3	13	10
Protocol Deviation	-	1	1
Guardian Decision	-	-	1
Progressive disease	3	82	85

Baseline characteristics

Reporting groups	
Reporting group title	Safety run-in part: Canakinumab+docetaxel
Reporting group description:	
Participants were treated with full doses of docetaxel 75mg/m^2 intravenous and canakinumab 200 mg subcutaneous on Day 1 of each 21-Day cycle (dose level 1).	
Reporting group title	Randomized part: Canakinumab + docetaxel
Reporting group description:	
Participants were randomized to receive canakinumab subcutaneous at RP3R and docetaxel at 75 mg/m^2 on Day 1 of each 21-Day cycle	
Reporting group title	Randomized part: Placebo + docetaxel
Reporting group description:	
Participants were randomized to receive placebo subcutaneous at RP3R and docetaxel at 75 mg/m^2 on Day 1 of each 21-Day cycle	

Reporting group values	Safety run-in part: Canakinumab+docetaxel	Randomized part: Canakinumab + docetaxel	Randomized part: Placebo + docetaxel
Number of subjects	8	120	117
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	8	61	66
From 65-84 years	0	59	51
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	55.9	63.4	62.2
standard deviation	± 4.19	± 9.13	± 10.05
Sex: Female, Male Units: Participants			
Female	2	38	32
Male	6	82	85
Race/Ethnicity, Customized Units: Subjects			
White	8	91	83
Asian	0	22	27
Unknown	0	4	7
Black or African American	0	3	0

Reporting group values	Total		
Number of subjects	245		

Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	135		
From 65-84 years	110		
85 years and over	0		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Participants			
Female	72		
Male	173		
Race/Ethnicity, Customized Units: Subjects			
White	182		
Asian	49		
Unknown	11		
Black or African American	3		

End points

End points reporting groups

Reporting group title	Safety run-in part: Canakinumab+docetaxel
Reporting group description:	
Participants were treated with full doses of docetaxel 75mg/m^2 intravenous and canakinumab 200 mg subcutaneous on Day 1 of each 21-Day cycle (dose level 1).	
Reporting group title	Randomized part: Canakinumab + docetaxel
Reporting group description:	
Participants were randomized to receive canakinumab subcutaneous at RP3R and docetaxel at 75 mg/m^2 on Day 1 of each 21-Day cycle	
Reporting group title	Randomized part: Placebo + docetaxel
Reporting group description:	
Participants were randomized to receive placebo subcutaneous at RP3R and docetaxel at 75 mg/m^2 on Day 1 of each 21-Day cycle	

Primary: Randomized part: Overall Survival (OS)

End point title	Randomized part: Overall Survival (OS)[1]
End point description:	
OS is defined as the time from randomization to date of death due to any cause. The OS distribution was estimated using the Kaplan-Meier method and associated 95% confidence intervals were calculated for each treatment group. If a subject was not known to have died, then OS was censored at the latest date the subject was known to be alive (on or before the cut-off date).	
End point type	Primary
End point timeframe:	
From randomization until death or final analysis data cutoff date (08-Jan-2021) whichever comes first (up to approximately 18 months)	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint refers to the randomized part only. The arm of the safety run-in part is not included in this analysis

End point values	Randomized part: Canakinumab + docetaxel	Randomized part: Placebo + docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	120	117		
Units: Months				
median (confidence interval 95%)	10.55 (8.15 to 12.39)	11.30 (8.54 to 13.80)		

Statistical analyses

Statistical analysis title	Cox regression model for overall survival
Comparison groups	Randomized part: Canakinumab + docetaxel v Randomized part: Placebo + docetaxel

Number of subjects included in analysis	237
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.633
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.48

Primary: Safety run-in part: Percentage of participants with dose limiting toxicities (DLTs)

End point title	Safety run-in part: Percentage of participants with dose limiting toxicities (DLTs)[2][3]

End point description:

Percentage of participants with DLTs. A dose-limiting toxicity (DLT) is defined as an adverse event or abnormal laboratory value assessed as unrelated to disease, disease progression, inter-current illness, or concomitant medications that occurs within the first 42 days of docetaxel and canakinumab treatment.

End point type	Primary

End point timeframe:

During the first 42 days of dosing

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this primary endpoint

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint refers to the safety run-in part only. Arms of the randomized part are not included in this analysis

End point values	Safety run-in part: Canakinumab+ docetaxel			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Participants	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall response rate (ORR)

End point title	Overall response rate (ORR)

End point description:

ORR is defined as the percentage of participants with confirmed best overall response of complete

response (CR) or partial response (PR), as per investigator's assessment by RECIST 1.1
CR: Disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm
PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.

End point type	Secondary

End point timeframe:

Through final analysis data cutoff date of 08-Jan-2021 (assessed up to approximately 10 months for the safety run-in part and 18 months for the randomized part)

End point values	Safety run-in part: Canakinumab+ docetaxel	Randomized part: Canakinumab + docetaxel	Randomized part: Placebo + docetaxel	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	120	117	
Units: Percentage of participants				
number (confidence interval 95%)	0.0 (-9999 to 9999)	15.0 (9.1 to 22.7)	13.7 (8.0 to 21.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (DOR)

End point title	Duration of response (DOR)

End point description:

DOR is defined as the time from first documented response of CR or PR to date of first documented progression or death, by investigator's assessment according to RECIST 1.1 criteria. The DOR distribution was estimated using the Kaplan-Meier method and associated 95% confidence intervals were calculated for each treatment group.
CR: Disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm
PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.

End point type	Secondary

End point timeframe:

From first documented response of CR or PR to date of first documented progression, death or final analysis data cutoff date (08-Jan-2021) whichever comes first (up to approximately 10 months for the safety run-in and 18 months for the randomized)

End point values	Safety run-in part: Canakinumab+ docetaxel	Randomized part: Canakinumab + docetaxel	Randomized part: Placebo + docetaxel	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[4]	18	16	
Units: Months				
median (confidence interval 95%)	(to)	4.14 (2.89 to 11.17)	5.42 (4.17 to 9999)	

Notes:
[4] - No participants had CR or PR

Statistical analyses

No statistical analyses for this end point

Secondary: Disease control rate (DCR)

End point title	Disease control rate (DCR)

End point description:

DCR is defined as the percentage of participants with CR or PR or with stable disease (SD) as per investigator assessment according to RECIST 1.1 criteria.
CR: Disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm
PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.
SD: Neither sufficient shrinkage to qualify for PR or CR nor an increase in lesions which would qualify for progressive disease.

End point type	Secondary

End point timeframe:

Through final analysis data cutoff date of 08-Jan-2021 (assessed up to approximately 10 months for the safety run-in part and 18 months for the randomized part)

End point values	Safety run-in part: Canakinumab+ docetaxel	Randomized part: Canakinumab + docetaxel	Randomized part: Placebo + docetaxel	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	120	117	
Units: Percentage of participants				
number (confidence interval 95%)	62.5 (24.5 to 91.5)	65.8 (56.6 to 74.2)	61.5 (52.1 to 70.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Progression-Free Survival (PFS)

End point title	Randomized part: Progression-Free Survival (PFS)[5]

End point description:

PFS is defined as the time from randomization to the date of the first documented radiological progression by investigator assessment according to RECIST 1.1 response criteria or death due to any cause.
The PFS distribution was estimated using the Kaplan-Meier method and associated 95% confidence intervals were calculated for each treatment group. If a participant did not have disease progression or die at the analysis cut-off date, PFS was censored at the date of last adequate tumor assessment.

End point type	Secondary

End point timeframe:

From randomization until disease progression, death or final analysis data cutoff date (08-Jan-2021) whichever comes first (assessed up to approximately 18 months)

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint refers to the randomized part only. The arm of the safety run-in part is not included in this analysis

End point values	Randomized part: Canakinumab + docetaxel	Randomized part: Placebo + docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	120	117		
Units: Months				
median (confidence interval 95%)	4.17 (2.96 to 5.42)	4.21 (3.06 to 5.13)		

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Time to Response (TTR)

End point title	Randomized part: Time to Response (TTR)[6]

End point description:

TTR is defined as the time from the date of randomization to the date of first documented response of either CR or PR, by investigator's assessment according to RECIST 1.1 criteria. The TTR distribution was estimated using the Kaplan-Meier method and associated 95% confidence intervals were calculated for each treatment group. Subjects without a confirmed CR or PR at the time of the analysis cut-off date were censored at the study-maximum follow-up time for subjects with a PFS event (i.e., disease progression or death due to any cause), or at the date of the last adequate tumor assessment for subjects without a PFS event.
CR: Disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm
PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.

End point type	Secondary

End point timeframe:

From randomization until first documented response or final analysis data cutoff date (08-Jan-2021) whichever comes first (up to approximately 18 months)

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint refers to the randomized part only. The arm of the safety run-in part is not included in this analysis

End point values	Randomized part: Canakinumab + docetaxel	Randomized part: Placebo + docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	120	117		
Units: Months				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Time to definitive 10-point deterioration (TTD) symptom scores of chest pain, cough and dyspnea per European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ) Lung Cancer (LC13) questionnaire

End point title	Randomized part: Time to definitive 10-point deterioration (TTD) symptom scores of chest pain, cough and dyspnea per European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ) Lung Cancer (LC13) questionnaire[7]

End point description:

The EORTC QLQ-LC13 comprises both multi-item and single-item measures of lung cancer-associated symptoms (ie, coughing, dyspnea, and chest pain) and treatment-related symptoms from conventional chemotherapy and radiotherapy (ie. hair loss, neuropathy, sore mouth, and dysphagia). Scores for each scale and single-item range from 0 to 100, with higher scores indicating higher level of symptoms. TTD for chest pain, cough and dyspnea is defined as the time from randomization to the date of event, which is defined as at least 10 points absolute worsening from baseline of the corresponding scale score, with no later change below this threshold ie.<10 points was observed or if this worsening was observed at the last assessment for the subject, or death due to any cause (whichever occurs earlier). If a subject did not have an event, TTD was censored at the last adequate assessment.

End point type	Secondary

End point timeframe:

From baseline through final analysis data cutoff date of 08-Jan-2021 (assessed up to approximately 18 months)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint refers to the randomized part only. The arm of the safety run-in part is not included in this analysis

End point values	Randomized part: Canakinumab + docetaxel	Randomized part: Placebo + docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	120	117		
Units: Months				
median (confidence interval 95%)				
Chest Pain	7.23 (4.96 to 9999)	13.14 (7.06 to 9999)		
Cough	7.23 (5.09 to 9999)	13.14 (7.85 to 9999)		
Dyspnea	3.45 (2.14 to 4.83)	4.27 (2.63 to 5.65)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Randomized part: Time to definitive 10-point deterioration in global health status (GHS)/quality of life (QoL), shortness of breath and pain per EORTC QLQ-C30 questionnaire[8]

End point description:

The EORTC QLQ-C30 includes 5 functional scales (physical,role,cognitive,emotional and social), 3 symptom scales (fatigue,pain and nausea/vomiting), a GHS/QoL scale, and 6 single items (constipation,diarrhea,insomnia,shortness of breath,appetite loss and financial difficulties). For each scale and single-item, scores range between 0 and 100. A high score for functional scales/ GHS/QoL represents better functioning or QoL, a high score for symptom scales/single items represents significant symptomatology. TTD in GHS/QoL, shortness of breath and pain is defined as the time from randomization to the date of event, defined as at least 10 points absolute worsening from baseline of the corresponding scale score, with no later change below this threshold i.e.<10 points was observed or if this worsening was observed at the last assessment for the subject, or death due to any cause (whichever occurs earlier). If a subject did not have an event, TTD was censored at the last adequate

End point type	Secondary

End point timeframe:

From baseline through final analysis data cutoff date of 08-Jan-2021 (assessed up to approximately 18 months)

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint refers to the randomized part only. The arm of the safety run-in part is not included in this analysis

End point values	Randomized part: Canakinumab + docetaxel	Randomized part: Placebo + docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	120	117		
Units: Months				
median (confidence interval 95%)				
GHS/QOL	4.83 (3.48 to 6.97)	7.16 (4.80 to 13.14)		
Shortness of breath	6.57 (4.60 to 7.89)	5.78 (4.27 to 9999)		
Pain	6.05 (4.47 to 7.72)	8.54 (4.27 to 10.38)		

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Change from baseline in GHS/QoL, shortness of breath and pain scores as per the EORTC QLQ C30 questionnaire

End point title	Randomized part: Change from baseline in GHS/QoL, shortness of breath and pain scores as per the EORTC QLQ C30 questionnaire[9]

End point description:

The EORTC QLQ-C30 includes 5 functional scales (physical, role, cognitive, emotional and social functioning), 3 symptom scales (fatigue, pain and nausea/vomiting), a GHS/QoL scale, and six single

items (constipation, diarrhea, insomnia, shortness of breath, appetite loss and financial difficulties). For each scale and single-item, scores range between 0 and 100. A high score for functional scales/ GHS/QoL represents better functioning ability or QoL; a high score for symptom scales/single items represents significant symptomatology. Changes from baseline in GHS/QoL, shortness of breath and pain scores are presented. For QoL, a negative change from baseline indicates improvement; for shortness of breath and pain a positive change from baseline indicates improvement. Post-treatment efficacy follow up visits were conducted every 6 weeks (for the first 12 months since start of treatment) or every 12 weeks (after 12 months since start of treatment)

End point type	Secondary

End point timeframe:

Baseline, every 3 weeks from Week 3 until end of treatment, every 6 or 12 weeks post-treatment and 7 and 28 days post disease progression through final analysis data cutoff date of 08-Jan-2021 (assessed up to approximately 18 months)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint refers to the randomized part only. The arm of the safety run-in part is not included in this analysis

End point values	Randomized part: Canakinumab + docetaxel	Randomized part: Placebo + docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	120	117		
Units: Score on a scale				
arithmetic mean (standard deviation)				
GHS/QoL: Week 3	-0.5 (± 18.34)	1.8 (± 21.51)		
GHS/QoL: Week 6	-3.3 (± 17.48)	1.4 (± 22.19)		
GHS/QoL: Week 9	-2.7 (± 20.04)	-0.4 (± 23.50)		
GHS/QoL: Week 12	-7.4 (± 19.75)	2.5 (± 22.14)		
GHS/QoL: Week 15	-2.9 (± 19.85)	-4.2 (± 22.60)		
GHS/QoL: Week 18	-3.9 (± 22.75)	2.8 (± 24.69)		
GHS/QoL: Week 21	-3.5 (± 25.31)	-4.2 (± 27.25)		
GHS/QoL: Week 24	-3.6 (± 16.08)	-0.7 (± 24.90)		
GHS/QoL: Week 27	-4.7 (± 16.25)	-2.2 (± 26.51)		
GHS/QoL: Week 30	-3.7 (± 19.43)	-5.7 (± 30.31)		
GHS/QoL: Week 33	-3.2 (± 15.79)	0.4 (± 31.82)		
GHS/QoL: Week 36	-4.5 (± 15.97)	3.3 (± 27.06)		
GHS/QoL: Week 39	-5.8 (± 18.02)	1.2 (± 28.28)		
GHS/QoL: Week 42	-9.2 (± 16.41)	2.8 (± 29.15)		
GHS/QoL: Week 45	-3.6 (± 16.57)	-3.5 (± 22.32)		
GHS/QoL: Week 48	-8.3 (± 19.72)	-13.9 (± 13.82)		
GHS/QoL: Week 51	-8.3 (± 16.67)	-6.7 (± 21.80)		
GHS/QoL: Week 54	-6.9 (± 17.01)	-4.8 (± 31.86)		
GHS/QoL: Week 57	-12.5 (± 14.43)	-8.3 (± 36.32)		
GHS/QoL: Week 60	-8.3 (± 22.05)	2.1 (± 38.71)		
GHS/QoL: Week 63	-5.6 (± 17.35)	2.8 (± 4.81)		
GHS/QoL: Week 66	8.3 (± 11.79)	-8.3 (± 11.79)		
GHS/QoL: Week 69	16.7 (± 9999)	0.0 (± 23.57)		
GHS/QoL: Week 72	9999 (± 9999)	-8.3 (± 11.79)		
GHS/QoL: Week 75	9999 (± 9999)	-16.7 (± 9999)		
GHS/QoL: Week 78	9999 (± 9999)	-16.7 (± 9999)		
GHS/QoL: post treatment efficacy 1	-16.7 (± 11.79)	5.6 (± 9.62)		

GHS/QoL: post treatment efficacy 2	-16.7 (± 16.67)	16.7 (± 9999)		
GHS/QoL: post treatment efficacy 3	9999 (± 9999)	-8.3 (± 23.57)		
GHS/QoL: post treatment efficacy 5	9999 (± 9999)	25.0 (± 9999)		
GHS/QoL: 7 days post disease progression	-7.5 (± 26.65)	-4.6 (± 22.11)		
GHS/QoL: 28 days post disease progression	-3.7 (± 29.60)	-7.8 (± 20.08)		
Shortness of breath: Week 3	31.2 (± 28.30)	31.7 (± 30.02)		
Shortness of breath: Week 6	7.3 (± 24.99)	4.0 (± 28.06)		
Shortness of breath: Week 9	6.7 (± 27.13)	5.7 (± 28.36)		
Shortness of breath: Week 12	12.2 (± 25.61)	4.4 (± 29.73)		
Shortness of breath: Week 15	7.8 (± 21.69)	7.3 (± 29.58)		
Shortness of breath: Week 18	8.5 (± 26.54)	3.5 (± 30.93)		
Shortness of breath: Week 21	34.2 (± 29.71)	29.8 (± 27.72)		
Shortness of breath: Week 24	4.8 (± 21.61)	6.9 (± 32.60)		
Shortness of breath: Week 27	13.0 (± 24.08)	-1.2 (± 36.38)		
Shortness of breath: Week 30	16.7 (± 20.61)	5.3 (± 38.10)		
Shortness of breath: Week 33	17.9 (± 22.01)	-1.7 (± 39.70)		
Shortness of breath: Week 36	9.1 (± 21.56)	-2.2 (± 32.04)		
Shortness of breath: Week 39	33.3 (± 27.22)	40.5 (± 26.73)		
Shortness of breath: Week 42	23.3 (± 27.44)	-6.7 (± 31.37)		
Shortness of breath: Week 45	9.5 (± 31.71)	8.3 (± 40.51)		
Shortness of breath: Week 48	22.2 (± 34.43)	3.7 (± 26.06)		
Shortness of breath: Week 51	16.7 (± 18.26)	0.0 (± 22.22)		
Shortness of breath: Week 54	11.1 (± 17.21)	9.5 (± 37.09)		
Shortness of breath: Week 57	8.3 (± 31.91)	20.0 (± 38.01)		
Shortness of breath: Week 60	0.0 (± 33.33)	16.7 (± 43.03)		
Shortness of breath: Week 63	0.0 (± 33.33)	0.0 (± 33.33)		
Shortness of breath: Week 66	-16.7 (± 23.57)	0.0 (± 47.14)		
Shortness of breath: Week 69	0.0 (± 9999)	-16.7 (± 70.71)		
Shortness of breath: Week 72	9999 (± 9999)	-16.7 (± 70.71)		
Shortness of breath: Week 75	9999 (± 9999)	33.3 (± 9999)		
Shortness of breath: Week 78	9999 (± 9999)	33.3 (± 9999)		
Shortness of breath: post treatment efficacy 1	33.3 (± 47.14)	33.3 (± 33.33)		
Shortness of breath: post treatment efficacy 2	0.0 (± 33.33)	0.0 (± 9999)		
Shortness of breath: post treatment efficacy 3	9999 (± 9999)	16.7 (± 23.57)		
Shortness of breath: post treatment efficacy 5	9999 (± 9999)	0.00 (± 9999)		
Shortness of breath 7days postdisease progression	8.6 (± 21.03)	8.0 (± 29.08)		
Shortness of breath 28days postdisease progression	3.7 (± 27.75)	15.7 (± 29.15)		
Pain: Week 3	-5.1 (± 21.07)	-2.0 (± 22.53)		
Pain: Week 6	-5.1 (± 20.33)	-1.6 (± 24.07)		
Pain: Week 9	-4.1 (± 19.33)	-3.1 (± 21.85)		
Pain: Week 12	2.2 (± 24.61)	-1.4 (± 27.32)		
Pain: Week 15	-0.7 (± 20.81)	0.7 (± 22.07)		
Pain: Week 18	2.3 (± 23.34)	0.7 (± 25.25)		
Pain: Week 21	3.3 (± 24.52)	0.0 (± 25.70)		

Pain: Week 24	25.2 (± 25.36)	19.1 (± 21.76)		
Pain: Week 27	1.4 (± 22.42)	1.2 (± 19.57)		
Pain: Week 30	2.8 (± 19.17)	4.0 (± 26.03)		
Pain: Week 33	-8.3 (± 19.46)	6.7 (± 21.22)		
Pain: Week 36	22.7 (± 17.12)	26.7 (± 23.40)		
Pain: Week 39	-10.0 (± 21.08)	10.7 (± 31.08)		
Pain: Week 42	-3.3 (± 10.54)	11.1 (± 30.65)		
Pain: Week 45	-11.9 (± 23.00)	15.3 (± 30.53)		
Pain: Week 48	-5.6 (± 22.77)	5.6 (± 20.41)		
Pain: Week 51	2.8 (± 24.53)	8.3 (± 18.00)		
Pain: Week 54	8.3 (± 20.41)	-2.4 (± 32.53)		
Pain: Week 57	0.0 (± 13.61)	6.7 (± 19.00)		
Pain: Week 60	16.7 (± 16.67)	0.0 (± 36.00)		
Pain: Week 63	5.6 (± 25.46)	-16.7 (± 16.7)		
Pain: Week 66	0.0 (± 0.00)	0.0 (± 0.00)		
Pain: Week 69	33.3 (± 9999)	8.3 (± 11.79)		
Pain: Week 72	9999 (± 9999)	0.0 (± 0.00)		
Pain: Week 75	9999 (± 9999)	0.0 (± 9999)		
Pain: Week 78	9999 (± 9999)	0.0 (± 9999)		
Pain: post treatment efficacy 1	-33.3 (± 23.57)	-11.1 (± 19.25)		
Pain: post treatment efficacy 2	0.0 (± 16.67)	0.0 (± 9999)		
Pain: post treatment efficacy 3	9999 (± 9999)	33.3 (± 0.00)		
Pain: post treatment efficacy 5	9999 (± 9999)	0.0 (± 9999)		
Pain: 7 days post disease progression	1.6 (± 18.44)	2.3 (± 31.41)		
Pain: 28 days post disease progression	9.3 (± 23.02)	13.7 (± 20.61)		

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Change from baseline in chest pain, cough and dyspnea scores as per the EORTC-QLQ LC13 questionnaire

End point title	Randomized part: Change from baseline in chest pain, cough and dyspnea scores as per the EORTC-QLQ LC13 questionnaire[10]

End point description:

The EORTC QLQ-LC13 is a 13-item questionnaire. It comprises both multi-item and single-item measures of lung cancer-associated symptoms (ie, coughing, dyspnea, and chest pain) and treatment-related symptoms from conventional chemotherapy and radiotherapy (ie, hair loss, neuropathy, sore mouth, and dysphagia). Scores for each scale and single-item range from 0 to 100, with higher scores indicating higher ("worse") level of symptoms. Changes from baseline in chest pain, cough and dyspnea scores are presented. A positive change from baseline indicates improvement.
Post-treatment efficacy follow up visits were conducted every 6 weeks (for the first 12 months since start of treatment) or every 12 weeks (after 12 months since start of treatment)

End point type	Secondary

End point timeframe:

Baseline, every 3 weeks from Week 3 until end of treatment, every 6 or 12 weeks post-treatment and 7 and 28 days post disease progression through final analysis data cutoff date of 08-Jan-2021 (assessed up to approximately 18 months)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint refers to the randomized part only. The arm of the safety run-in part is not included in this analysis

End point values	Randomized part: Canakinumab + docetaxel	Randomized part: Placebo + docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	120	117		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Chest pain: Week 3	-2.2 (± 16.24)	-3.2 (± 24.48)		
Chest pain: Week 6	0.4 (± 19.73)	-3.9 (± 24.89)		
Chest pain: Week 9	0.5 (± 19.09)	-3.8 (± 22.37)		
Chest pain: Week 12	1.1 (± 23.16)	-3.3 (± 24.32)		
Chest pain: Week 15	0.7 (± 25.38)	-0.7 (± 24.05)		
Chest pain: Week 18	0.7 (± 21.59)	-4.1 (± 26.90)		
Chest pain: Week 21	2.5 (± 26.57)	0.9 (± 18.15)		
Chest pain: Week 24	1.9 (± 21.30)	-1.0 (± 17.38)		
Chest pain: Week 27	2.9 (± 19.88)	6.2 (± 27.79)		
Chest pain: Week 30	3.7 (± 19.43)	6.7 (± 23.57)		
Chest pain: Week 33	-5.1 (± 18.49)	0.0 (± 15.71)		
Chest pain: Week 36	-9.1 (± 15.57)	0.0 (± 21.82)		
Chest pain: Week 39	0.0 (± 22.22)	9.5 (± 30.46)		
Chest pain: Week 42	0.0 (± 15.71)	0.0 (± 17.82)		
Chest pain: Week 45	0.0 (± 19.25)	8.3 (± 15.08)		
Chest pain: Week 48	0.0 (± 21.08)	11.1 (± 16.67)		
Chest pain: Week 51	0.0 (± 21.08)	10.0 (± 22.50)		
Chest pain: Week 54	0.0 (± 21.08)	9.5 (± 31.71)		
Chest pain: Week 57	0.0 (± 0.00)	20.0 (± 18.26)		
Chest pain: Week 60	-11.1 (± 19.25)	25.0 (± 16.67)		
Chest pain: Week 63	0.0 (± 33.33)	0.0 (± 0.00)		
Chest pain: Week 66	0.0 (± 47.14)	0.0 (± 0.00)		
Chest pain: Week 69	0.0 (± 9999)	0.0 (± 0.00)		
Chest pain: Week 72	9999 (± 9999)	0.0 (± 0.00)		
Chest pain: Week 75	9999 (± 9999)	0.0 (± 9999)		
Chest pain: Week 78	9999 (± 9999)	33.3 (± 9999)		
Chest pain: Efficacy follow-up visit 1	0.0 (± 0.00)	-22.2 (± 19.25)		
Chest pain: Efficacy follow-up visit 2	11.1 (± 19.25)	0.0 (± 9999)		
Chest pain: Efficacy follow-up visit 3	9999 (± 9999)	16.7 (± 23.57)		
Chest pain: Efficacy follow-up visit 5	9999 (± 9999)	0.0 (± 9999)		
Chest pain: 7 days post disease progression	5.4 (± 17.42)	-5.7 (± 21.95)		
Chest pain: 28 days post disease progression	14.8 (± 26.13)	-2.1 (± 25.73)		
Coughing: Week 3	0.0 (± 21.54)	-3.2 (± 24.03)		
Coughing: Week 6	3.0 (± 26.42)	-4.7 (± 27.77)		
Coughing: Week 9	2.6 (± 32.44)	0.5 (± 25.69)		
Coughing: Week 12	4.8 (± 33.79)	0.0 (± 26.75)		

Coughing: Week 15	2.0 (± 27.82)	-0.7 (± 24.05)		
Coughing: Week 18	-1.3 (± 26.63)	0.0 (± 31.18)		
Coughing: Week 21	-4.2 (± 30.37)	-4.4 (± 28.13)		
Coughing: Week 24	-1.0 (± 31.81)	-3.9 (± 24.29)		
Coughing: Week 27	-4.3 (± 25.23)	-1.2 (± 28.47)		
Coughing: Week 30	-5.6 (± 36.60)	-4.0 (± 26.03)		
Coughing: Week 33	2.6 (± 16.45)	-3.5 (± 26.98)		
Coughing: Week 36	12.1 (± 16.82)	-6.7 (± 28.73)		
Coughing: Week 39	3.3 (± 18.92)	-4.8 (± 25.68)		
Coughing: Week 42	6.7 (± 26.29)	-8.9 (± 29.46)		
Coughing: Week 45	0.0 (± 19.25)	2.8 (± 17.16)		
Coughing: Week 48	11.1 (± 17.21)	3.7 (± 20.03)		
Coughing: Week 51	16.7 (± 18.26)	-3.3 (± 18.92)		
Coughing: Week 54	16.7 (± 18.26)	-4.8 (± 23.00)		
Coughing: Week 57	-8.3 (± 16.67)	6.7 (± 27.89)		
Coughing: Week 60	0.0 (± 0.00)	-8.3 (± 31.91)		
Coughing: Week 63	0.0 (± 0.00)	-11.1 (± 19.25)		
Coughing: Week 66	-16.7 (± 23.57)	-16.7 (± 23.57)		
Coughing: Week 69	0.0 (± 9999)	-33.3 (± 47.14)		
Coughing: Week 72	9999 (± 9999)	-33.3 (± 47.14)		
Coughing: Week 75	9999 (± 9999)	0.0 (± 9999)		
Coughing: Week 78	9999 (± 9999)	0.0 (± 9999)		
Coughing: Efficacy follow-up visit 1	0.0 (± 0.00)	0.0 (± 0.00)		
Coughing: Efficacy follow-up visit 2	-22.2 (± 19.25)	33.3 (± 9999)		
Coughing: Efficacy follow-up visit 3	9999 (± 9999)	-16.7 (± 23.57)		
Coughing: Efficacy follow-up visit 5	9999 (± 9999)	0.0 (± 9999)		
Coughing: 7 days post disease progression	-1.1 (± 25.07)	3.4 (± 31.30)		
Coughing: 28 days post disease progression	-3.7 (± 27.75)	-4.2 (± 31.91)		
Dyspnea: Week 3	4.8 (± 17.84)	2.9 (± 18.47)		
Dyspnea: Week 6	4.4 (± 16.83)	5.0 (± 19.59)		
Dyspnea: Week 9	4.8 (± 19.44)	5.2 (± 20.17)		
Dyspnea: Week 12	7.4 (± 19.25)	6.9 (± 20.57)		
Dyspnea: Week 15	6.5 (± 16.66)	10.9 (± 21.69)		
Dyspnea: Week 18	10.2 (± 19.98)	4.3 (± 22.43)		
Dyspnea: Week 21	8.9 (± 19.36)	6.7 (± 21.07)		
Dyspnea: Week 24	7.9 (± 23.89)	9.2 (± 20.19)		
Dyspnea: Week 27	10.1 (± 21.43)	8.6 (± 20.52)		
Dyspnea: Week 30	8.0 (± 14.66)	8.0 (± 21.40)		
Dyspnea: Week 33	13.7 (± 17.66)	7.0 (± 22.89)		
Dyspnea: Week 36	12.1 (± 22.47)	7.4 (± 21.28)		
Dyspnea: Week 39	14.4 (± 16.60)	10.3 (± 25.21)		
Dyspnea: Week 42	20.0 (± 27.62)	3.0 (± 23.18)		
Dyspnea: Week 45	20.6 (± 26.00)	13.0 (± 20.56)		
Dyspnea: Week 48	20.4 (± 30.97)	14.8 (± 13.61)		
Dyspnea: Week 51	22.2 (± 29.81)	7.8 (± 15.76)		
Dyspnea: Week 54	22.2 (± 26.29)	12.7 (± 13.50)		

Dyspnea: Week 57	19.4 (± 31.91)	11.1 (± 11.11)		
Dyspnea: Week 60	25.9 (± 44.91)	-2.8 (± 24.64)		
Dyspnea: Week 63	18.5 (± 44.91)	-3.7 (± 12.83)		
Dyspnea: Week 66	-11.1 (± 15.71)	0.0 (± 15.71)		
Dyspnea: Week 69	-22.2 (± 9999)	-11.1 (± 47.14)		
Dyspnea: Week 72	9999 (± 9999)	-11.1 (± 47.14)		
Dyspnea: Week 75	9999 (± 9999)	22.2 (± 9999)		
Dyspnea: Week 78	9999 (± 9999)	22.2 (± 9999)		
Dyspnea: Efficacy follow-up visit 1	16.7 (± 23.57)	3.7 (± 16.97)		
Dyspnea: Efficacy follow-up visit 2	-3.7 (± 44.91)	22.2 (± 9999)		
Dyspnea: Efficacy follow-up visit 3	9999 (± 9999)	16.7 (± 7.86)		
Dyspnea: Efficacy follow-up visit 5	9999 (± 9999)	-11.1 (± 9999)		
Dyspnea: 7 days post disease progression	5.0 (± 17.88)	2.3 (± 20.22)		
Dyspnea: 28 days post disease progression	3.7 (± 16.61)	10.4 (± 19.23)		

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Change from baseline in European Quality of Life-5 Dimensions-5 Level (EQ-5D-5L) Health State Scores

End point title	Randomized part: Change from baseline in European Quality of Life-5 Dimensions-5 Level (EQ-5D-5L) Health State Scores[11]

End point description:

The EQ-5D-5L descriptive system provides a profile of the participant's health state in 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression). For each of these dimensions, the participant self-assigned a score: from 1 (no problems) to 5 (extreme problems). The 5 digit health states obtained for each dimension was converted into a single mean index value based on the EQ-5D crosswalk value set for the UK using the time trade-off method. This index ranges from -0.594 (worst health) to 1.0 (best health). A positive change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline, every 3 weeks from Week 3 until end of treatment, every 6 or 12 weeks post-treatment and 7 and 28 days post disease progression through final analysis data cutoff date of 08-Jan-2021 (assessed up to approximately 18 months)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint refers to the randomized part only. The arm of the safety run-in part is not included in this analysis

End point values	Randomized part: Canakinumab + docetaxel	Randomized part: Placebo + docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	120	117		
Units: Score on a scale				
arithmetic mean (standard deviation)				

Week 3	-0.017 (± 0.1960)	-0.007 (± 0.1731)		
Week 6	-0.016 (± 0.1972)	0.001 (± 0.2283)		
Week 9	-0.006 (± 0.1759)	0.011 (± 0.1865)		
Week 12	-0.028 (± 0.1849)	0.014 (± 0.2315)		
Week 15	-0.057 (± 0.2229)	-0.042 (± 0.1827)		
Week 18	-0.062 (± 0.1835)	0.009 (± 0.2810)		
Week 21	-0.097 (± 0.2234)	0.005 (± 0.1952)		
Week 24	-0.070 (± 0.2075)	0.027 (± 0.1900)		
Week 27	-0.043 (± 0.1820)	0.008 (± 0.2272)		
Week 30	-0.023 (± 0.2378)	-0.014 (± 0.2068)		
Week 33	-0.031 (± 0.2148)	0.029 (± 0.2361)		
Week 36	0.017 (± 0.1942)	0.050 (± 0.2743)		
Week 39	-0.007 (± 0.1898)	-0.012 (± 0.2842)		
Week 42	-0.010 (± 0.2286)	0.116 (± 0.2180)		
Week 45	0.017 (± 0.1866)	-0.036 (± 0.1801)		
Week 48	-0.087 (± 0.3178)	0.003 (± 0.2424)		
Week 51	-0.151 (± 0.2663)	0.071 (± 0.2197)		
Week 54	-0.102 (± 0.3527)	0.056 (± 0.2011)		
Week 57	0.476 (± 0.2190)	0.652 (± 0.1308)		
Week 60	-0.193 (± 0.3653)	0.149 (± 0.1616)		
Week 63	-0.140 (± 0.3435)	0.165 (± 0.1717)		
Week 66	0.034 (± 0.0481)	0.124 (± 0.0085)		
Week 69	0.000 (± 9999)	0.340 (± 0.1230)		
Week 72	9999 (± 9999)	0.168 (± 0.0530)		
Week 75	9999 (± 9999)	0.130 (± 9999)		
Week 78	9999 (± 9999)	0.130 (± 9999)		
Efficacy follow-up visit 1	0.100 (± 0.0955)	-0.026 (± 0.0368)		
Efficacy follow-up visit 2	0.644 (± 0.1749)	0.704 (± 9999)		
Efficacy follow-up visit 3	9999 (± 9999)	0.601 (± 0.0990)		
Efficacy follow-up visit 5	9999 (± 9999)	1.000 (± 9999)		
7 days post disease progression	0.639 (± 0.2558)	0.657 (± 0.2654)		
28 days post disease progression	0.692 (± 0.1633)	0.692 (± 0.2149)		

Statistical analyses

No statistical analyses for this end point

Secondary: Safety run-in part: Maximum plasma concentration (Cmax) of canakinumab

End point title	Safety run-in part: Maximum plasma concentration (Cmax) of canakinumab[12]

End point description:

Venous whole blood samples were collected for pharmacokinetics characterization. Cmax of canakinumab was calculated from canakinumab plasma concentration-time data using non-compartmental methods and summarized using descriptive statistics.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 at pre-dose and end of infusion and 24, 48, 168 and 336 hours (h) post-infusion. Each cycle is 21 days

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint refers to the safety run-in part only. Arms of the randomized part are not included in this analysis

End point values	Safety run-in part: Canakinumab+ docetaxel			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: microgram/milliliter (ug/mL)				
geometric mean (geometric coefficient of variation)	13.4 (± 29.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Safety run-in part: Time of maximum plasma concentration (Tmax) of canakinumab

End point title	Safety run-in part: Time of maximum plasma concentration (Tmax) of canakinumab[13]

End point description:

Venous whole blood samples were collected for pharmacokinetics characterization. Tmax of canakinumab was calculated from canakinumab plasma concentration-time data using non-compartmental methods and summarized using descriptive statistics.
Actual recorded sampling times were considered for the calculations.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 at pre-dose and end of infusion and 24, 48, 168 and 336 hours (h) post-infusion. Each cycle is 21 days

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint refers to the safety run-in part only. Arms of the randomized part are not included in this analysis

End point values	Safety run-in part: Canakinumab+ docetaxel			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Hours (h)				
median (full range (min-max))	169 (48.2 to 336)			

Statistical analyses

No statistical analyses for this end point

Secondary: Safety run-in part: Area Under the plasma Concentration-time Curve From Time Zero to the Last Quantifiable Concentration (AUClast) of canakinumab

End point title	Safety run-in part: Area Under the plasma Concentration-time Curve From Time Zero to the Last Quantifiable Concentration (AUClast) of canakinumab[14]

End point description:

Venous whole blood samples were collected for pharmacokinetics characterization. AUClast of canakinumab was calculated from canakinumab plasma concentration-time data using non-compartmental methods and summarized using descriptive statistics.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 at pre-dose and end of infusion and 24, 48, 168 and 336 hours (h) post-infusion. Each cycle is 21 days

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint refers to the safety run-in part only. Arms of the randomized part are not included in this analysis

End point values	Safety run-in part: Canakinumab+ docetaxel			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: hour*microgram/mililiter (hr*ug/mL)				
geometric mean (geometric coefficient of variation)	5470 (± 30.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Safety run-in part: Cmax of docetaxel

End point title	Safety run-in part: Cmax of docetaxel[15]

End point description:

Venous whole blood samples were collected for pharmacokinetics characterization. Cmax of docetaxel was calculated from docetaxel plasma concentration-time data using non-compartmental methods and summarized using descriptive statistics.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 and Cycle 2 Day 1 at pre-infusion, end of infusion, and 2, 4, 6 and 8 hours post-dose. Each cycle is 21 days

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint refers to the safety run-in part only. Arms of the randomized part are not included in this analysis

End point values	Safety run-in part: Canakinumab+ docetaxel			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: nanogram/miliLiter (ng/mL)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	476 (± 182.5)			
Cycle 2 Day 1	1630 (± 117.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Safety run-in part: Tmax of docetaxel

End point title	Safety run-in part: Tmax of docetaxel[16]

End point description:

Venous whole blood samples were collected for pharmacokinetics characterization. Tmax of docetaxel was calculated from docetaxel plasma concentration-time data using non-compartmental methods and summarized using descriptive statistics.
Actual recorded sampling times were considered for the calculations.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 and Cycle 2 Day 1 at pre-infusion, end of infusion, and 2, 4, 6 and 8 hours post-dose.

Each cycle is 21 days

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint refers to the safety run-in part only. Arms of the randomized part are not included in this analysis

End point values	Safety run-in part: Canakinumab+ docetaxel			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Hour (hr)				
median (full range (min-max))				
Cycle 1 Day 1	1.08 (0.917 to 6.12)			
Cycle 2 Day 1	1.00 (0.917 to 1.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: Safety run-in part: AUClast of docetaxel

End point title	Safety run-in part: AUClast of docetaxel[17]

End point description:

Venous whole blood samples were collected for pharmacokinetics characterization. AUClast of docetaxel was calculated from docetaxel plasma concentration-time data using non-compartmental methods and summarized using descriptive statistics.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 and Cycle 2 Day 1 at pre-infusion, end of infusion, and 2, 4, 6 and 8 hours post-dose. Each cycle is 21 days

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint refers to the safety run-in part only. Arms of the randomized part are not included in this analysis

End point values	Safety run-in part: Canakinumab+ docetaxel			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Hour *nanogram/miliLiter (hr*ng/mL)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	884 (± 70.8)			
Cycle 2 Day 1	2120 (± 86.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Pre-dose plasma trough concentration (CTrough) of canakinumab

End point title	Randomized part: Pre-dose plasma trough concentration (CTrough) of canakinumab[18]

End point description:

Venous whole blood samples were collected for pharmacokinetics characterization. CTrough of canakinumab was calculated from canakinumab plasma concentration-time data using non-compartmental methods and summarized using descriptive statistics.

End point type	Secondary

End point timeframe:

Pre-dose on Cycle 4 Day 1, Cycle 6 Day 1, Cycle 12 Day 1 and Cycle 18 Day 1 through final analysis data cutoff date of 08-Jan-2021. Each cycle is 21 days.

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint refers to the randomized part only. The arm of the safety run-in part is not included in this analysis

End point values	Randomized part: Canakinumab + docetaxel			
Subject group type	Reporting group			
Number of subjects analysed	112			
Units: microgram/miliLiter (ug/mL)				
geometric mean (geometric coefficient of variation)				
Cycle 4 Day 1	20.5 (± 36.6)			
Cycle 6 Day 1	23.7 (± 32.3)			
Cycle 12 Day 1	25.6 (± 56.7)			
Cycle 18 Day 1	28.3 (± 118.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Cmax of docetaxel

End point title	Randomized part: Cmax of docetaxel[19]

End point description:

Venous whole blood samples were collected for pharmacokinetics characterization. Cmax of docetaxel was calculated from docetaxel plasma concentration-time data using non-compartmental methods and summarized using descriptive statistics.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 and Cycle 4 Day 1 at pre-infusion, end of infusion, and 2, 4 and 6 hours post-dose. Each cycle is 21 days

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint refers to the randomized part only. The arm of the safety run-in part is not included in this analysis

End point values	Randomized part: Canakinumab + docetaxel	Randomized part: Placebo + docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	29		
Units: nanogram/miliLiter (ng/mL)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	1570 (± 116.3)	1190 (± 265.3)		
Cycle 4 Day 1	1530 (± 118.7)	940 (± 215.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Tmax of docetaxel

End point title	Randomized part: Tmax of docetaxel[20]

End point description:

Venous whole blood samples were collected for pharmacokinetics characterization. Tmax of docetaxel was calculated from docetaxel plasma concentration-time data using non-compartmental methods and summarized using descriptive statistics.
Actual recorded sampling times were considered for the calculations.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 and Cycle 4 Day 1 at pre-infusion, end of infusion, and 2, 4 and 6 hours post-dose. Each cycle is 21 days

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint refers to the randomized part only. The arm of the safety run-in part is not included in this analysis

End point values	Randomized part: Canakinumab + docetaxel	Randomized part: Placebo + docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	29		
Units: Hour				
median (full range (min-max))				
Cycle 1 Day 1	1.09 (0.517 to 5.83)	1.10 (0.933 to 6.08)		

Cycle 4 Day 1	1.15 (0.0833 to 3.83)	1.08 (1.00 to 1.42)		

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: AUClast of docetaxel

End point title	Randomized part: AUClast of docetaxel[21]

End point description:

Venous whole blood samples were collected for pharmacokinetics characterization. AUClast of docetaxel was calculated from docetaxel plasma concentration-time data using non-compartmental methods and summarized using descriptive statistics.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 and Cycle 4 Day 1 at pre-infusion, end of infusion, and 2, 4 and 6 hours post-dose. Each cycle is 21 days

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint refers to the randomized part only. The arm of the safety run-in part is not included in this analysis

End point values	Randomized part: Canakinumab + docetaxel	Randomized part: Placebo + docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	29		
Units: hour*nanogram/miliLiter (h*ng/mL)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	2530 (± 79.3)	1790 (± 157.4)		
Cycle 4 Day 1	2210 (± 66.4)	1530 (± 130.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Canakinumab Antidrug antibodies (ADA) at baseline

End point title	Randomized part: Canakinumab Antidrug antibodies (ADA) at baseline[22]

End point description:

ADA prevalence at baseline was calculated as the percentage of participants who had an ADA positive result at baseline

End point type	Secondary

End point timeframe:

Baseline

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint refers to the randomized part only. The arm of the safety run-in part is not included in this analysis

End point values	Randomized part: Canakinumab + docetaxel			
Subject group type	Reporting group			
Number of subjects analysed	120			
Units: Participants	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized part: Canakinumab ADA incidence on-treatment

End point title	Randomized part: Canakinumab ADA incidence on-treatment[23]

End point description:

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 is at least the fold titer change greater than the ADA-positive baseline titer)

End point type	Secondary

End point timeframe:

Pre-dose at Cycle 1 Day 1, Cycle 4 Day 1, Cycle 6 Day 1, Cycle 12 Day 1 , end of treatment, and 130 days after end of treatment through final analysis data cutoff date of 08-Jan-2021 (assessed up to 18 months). Each cycle is 21 days

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint refers to the randomized part only. The arm of the safety run-in part is not included in this analysis

End point values	Randomized part: Canakinumab + docetaxel			
Subject group type	Reporting group			
Number of subjects analysed	120			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Post-hoc: All collected deaths

End point title	All collected deaths

End point description:

Pre-treatment deaths were collected from screening to the first day of treatment, for a maximum duration of 28 days.
On-treatment deaths due to any cause were collected from first dose of study treatment to 130 days after the last dose of study treatment.
Post-treatment deaths were collected from day 131 after last dose of study treatment to end of study.
All deaths refer to the sum of pre-treatment, on-treatment and post-treatment deaths.

End point type	Post-hoc

End point timeframe:

Pre-treatment: up to 28 days before Day 1;On-treatment: up to approximately 10 months (safety run-in) or 25 months (randomized); All deaths: Up to approximately 16 months (safety run in) or 25 months (randomized)

End point values	Safety run-in part: Canakinumab+ docetaxel	Randomized part: Canakinumab + docetaxel	Randomized part: Placebo + docetaxel	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	120	117	
Units: Participants				
Pre-treatment deaths	0	0	1	
On-treatment deaths	6	45	37	
Post-treatment deaths	2	40	38	
All deaths	8	85	76	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From date of first administration of study treatment to 130 days after date of last administration, up to approximately 10 months (safety run-in part) or 25 months (randomized part)

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Safety run-in part: Canakinumab+docetaxel

Reporting group description:

Participants were treated with full doses of docetaxel 75mg/m^2 intravenous and canakinumab 200 mg subcutaneous on Day 1 of each 21-Day cycle (dose level 1).

Reporting group title	Randomized part: Canakinumab+Docetaxel

Reporting group description:

Participants were randomized to receive canakinumab subcutaneous at RP3R and docetaxel at 75 mg/m^2 on Day 1 of each 21-Day cycle

Reporting group title	Randomized part: Placebo+Docetaxel

Reporting group description:

Participants were randomized to receive placebo subcutaneous at RP3R and docetaxel at 75 mg/m^2 on Day 1 of each 21-Day cycle

Serious adverse events	Safety run-in part: Canakinumab+docetaxel	Randomized part: Canakinumab+Docetaxel	Randomized part: Placebo+Docetaxel
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 8 (75.00%)	55 / 120 (45.83%)	50 / 114 (43.86%)
number of deaths (all causes)	6	45	37
number of deaths resulting from adverse events	1	3	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aneurysm			

subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superior vena cava syndrome			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 8 (0.00%)	2 / 120 (1.67%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disease progression			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Fatigue			

subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised oedema			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal inflammation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 8 (0.00%)	6 / 120 (5.00%)	2 / 114 (1.75%)
occurrences causally related to treatment / all	0 / 0	2 / 6	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Dyspnoea			
subjects affected / exposed	0 / 8 (0.00%)	4 / 120 (3.33%)	5 / 114 (4.39%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	1 / 8 (12.50%)	3 / 120 (2.50%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hypoxia			
subjects affected / exposed	0 / 8 (0.00%)	2 / 120 (1.67%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 8 (0.00%)	2 / 120 (1.67%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 8 (12.50%)	0 / 120 (0.00%)	3 / 114 (2.63%)
occurrences causally related to treatment / all	0 / 1	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory failure			

subjects affected / exposed	0 / 8 (0.00%)	3 / 120 (2.50%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	1 / 8 (12.50%)	0 / 120 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			

subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural pneumothorax			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 8 (0.00%)	2 / 120 (1.67%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac tamponade			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pericardial effusion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			

subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Monoplegia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 8 (0.00%)	6 / 120 (5.00%)	8 / 114 (7.02%)
occurrences causally related to treatment / all	0 / 0	8 / 8	11 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	1 / 8 (12.50%)	4 / 120 (3.33%)	5 / 114 (4.39%)
occurrences causally related to treatment / all	1 / 1	4 / 4	3 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ulcerative			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 8 (0.00%)	2 / 120 (1.67%)	2 / 114 (1.75%)
occurrences causally related to treatment / all	0 / 0	1 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Ileus			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			

subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestine ulcer			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	2 / 114 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 8 (0.00%)	2 / 120 (1.67%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hypopituitarism			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	3 / 114 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	2 / 114 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Fistula			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal sepsis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 120 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			

subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			

subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious pleural effusion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 8 (12.50%)	0 / 120 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic sepsis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 8 (25.00%)	13 / 120 (10.83%)	8 / 114 (7.02%)
occurrences causally related to treatment / all	0 / 2	6 / 13	2 / 9
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 1
Pneumonia pneumococcal			

subjects affected / exposed	1 / 8 (12.50%)	0 / 120 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Pneumonia pseudomonal			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural sepsis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary sepsis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	3 / 120 (2.50%)	4 / 114 (3.51%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 8 (0.00%)	2 / 120 (1.67%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Septic shock			
subjects affected / exposed	0 / 8 (0.00%)	3 / 120 (2.50%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	1 / 4	1 / 1
deaths causally related to treatment / all	0 / 0	1 / 2	1 / 1
Spinal cord infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			

subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	4 / 114 (3.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vulvovaginitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Safety run-in part: Canakinumab+docetaxel	Randomized part: Canakinumab+Docetaxel	Randomized part: Placebo+Docetaxel
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 8 (87.50%)	111 / 120 (92.50%)	109 / 114 (95.61%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 120 (0.00%)	2 / 114 (1.75%)
occurrences (all)	1	0	2
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 8 (12.50%)	6 / 120 (5.00%)	5 / 114 (4.39%)
occurrences (all)	1	8	6
Phlebitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 120 (0.00%)	0 / 114 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 8 (25.00%)	28 / 120 (23.33%)	37 / 114 (32.46%)
occurrences (all)	4	36	54
Chest pain			
subjects affected / exposed	0 / 8 (0.00%)	5 / 120 (4.17%)	10 / 114 (8.77%)
occurrences (all)	0	5	13
Fatigue			
subjects affected / exposed	1 / 8 (12.50%)	33 / 120 (27.50%)	19 / 114 (16.67%)
occurrences (all)	1	44	23
Influenza like illness			
subjects affected / exposed	1 / 8 (12.50%)	1 / 120 (0.83%)	3 / 114 (2.63%)
occurrences (all)	2	1	3
Malaise			
subjects affected / exposed	0 / 8 (0.00%)	7 / 120 (5.83%)	7 / 114 (6.14%)
occurrences (all)	0	8	10
Mucosal inflammation			
subjects affected / exposed	0 / 8 (0.00%)	4 / 120 (3.33%)	12 / 114 (10.53%)
occurrences (all)	0	4	13

Oedema			
subjects affected / exposed	1 / 8 (12.50%)	5 / 120 (4.17%)	2 / 114 (1.75%)
occurrences (all)	1	5	2
Oedema peripheral			
subjects affected / exposed	3 / 8 (37.50%)	22 / 120 (18.33%)	25 / 114 (21.93%)
occurrences (all)	3	26	33
Pyrexia			
subjects affected / exposed	1 / 8 (12.50%)	14 / 120 (11.67%)	18 / 114 (15.79%)
occurrences (all)	1	20	27
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 8 (25.00%)	16 / 120 (13.33%)	19 / 114 (16.67%)
occurrences (all)	2	17	23
Dyspnoea			
subjects affected / exposed	2 / 8 (25.00%)	27 / 120 (22.50%)	26 / 114 (22.81%)
occurrences (all)	2	28	28
Dyspnoea exertional			
subjects affected / exposed	1 / 8 (12.50%)	3 / 120 (2.50%)	5 / 114 (4.39%)
occurrences (all)	1	3	5
Epistaxis			
subjects affected / exposed	0 / 8 (0.00%)	5 / 120 (4.17%)	6 / 114 (5.26%)
occurrences (all)	0	6	6
Haemoptysis			
subjects affected / exposed	1 / 8 (12.50%)	10 / 120 (8.33%)	10 / 114 (8.77%)
occurrences (all)	2	12	18
Pleural effusion			
subjects affected / exposed	1 / 8 (12.50%)	4 / 120 (3.33%)	6 / 114 (5.26%)
occurrences (all)	1	5	6
Productive cough			
subjects affected / exposed	1 / 8 (12.50%)	6 / 120 (5.00%)	3 / 114 (2.63%)
occurrences (all)	1	6	4
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 8 (12.50%)	5 / 120 (4.17%)	2 / 114 (1.75%)
occurrences (all)	1	6	2
Insomnia			

subjects affected / exposed	1 / 8 (12.50%)	7 / 120 (5.83%)	8 / 114 (7.02%)
occurrences (all)	1	7	8
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	7 / 120 (5.83%)	3 / 114 (2.63%)
occurrences (all)	0	8	3
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	7 / 120 (5.83%)	0 / 114 (0.00%)
occurrences (all)	0	7	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 8 (25.00%)	5 / 120 (4.17%)	6 / 114 (5.26%)
occurrences (all)	2	5	9
Haemoglobin decreased			
subjects affected / exposed	1 / 8 (12.50%)	1 / 120 (0.83%)	2 / 114 (1.75%)
occurrences (all)	1	1	2
Neutrophil count decreased			
subjects affected / exposed	0 / 8 (0.00%)	17 / 120 (14.17%)	11 / 114 (9.65%)
occurrences (all)	0	27	34
SARS-CoV-2 test negative			
subjects affected / exposed	0 / 8 (0.00%)	10 / 120 (8.33%)	13 / 114 (11.40%)
occurrences (all)	0	10	14
White blood cell count decreased			
subjects affected / exposed	2 / 8 (25.00%)	12 / 120 (10.00%)	8 / 114 (7.02%)
occurrences (all)	3	24	15
Weight decreased			
subjects affected / exposed	1 / 8 (12.50%)	9 / 120 (7.50%)	8 / 114 (7.02%)
occurrences (all)	1	9	9
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 8 (12.50%)	0 / 120 (0.00%)	0 / 114 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	1 / 8 (12.50%)	1 / 120 (0.83%)	2 / 114 (1.75%)
occurrences (all)	1	1	2
Nervous system disorders			

Dysgeusia			
subjects affected / exposed	0 / 8 (0.00%)	8 / 120 (6.67%)	3 / 114 (2.63%)
occurrences (all)	0	8	5
Headache			
subjects affected / exposed	0 / 8 (0.00%)	8 / 120 (6.67%)	6 / 114 (5.26%)
occurrences (all)	0	11	7
Neuropathy peripheral			
subjects affected / exposed	1 / 8 (12.50%)	9 / 120 (7.50%)	15 / 114 (13.16%)
occurrences (all)	1	9	23
Paraesthesia			
subjects affected / exposed	0 / 8 (0.00%)	12 / 120 (10.00%)	8 / 114 (7.02%)
occurrences (all)	0	12	11
Taste disorder			
subjects affected / exposed	1 / 8 (12.50%)	1 / 120 (0.83%)	0 / 114 (0.00%)
occurrences (all)	1	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 8 (12.50%)	32 / 120 (26.67%)	33 / 114 (28.95%)
occurrences (all)	1	47	41
Leukopenia			
subjects affected / exposed	1 / 8 (12.50%)	6 / 120 (5.00%)	15 / 114 (13.16%)
occurrences (all)	2	7	39
Neutropenia			
subjects affected / exposed	2 / 8 (25.00%)	22 / 120 (18.33%)	25 / 114 (21.93%)
occurrences (all)	2	28	42
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 8 (12.50%)	7 / 120 (5.83%)	4 / 114 (3.51%)
occurrences (all)	1	8	4
Constipation			
subjects affected / exposed	0 / 8 (0.00%)	22 / 120 (18.33%)	24 / 114 (21.05%)
occurrences (all)	0	23	33
Diarrhoea			
subjects affected / exposed	3 / 8 (37.50%)	41 / 120 (34.17%)	31 / 114 (27.19%)
occurrences (all)	3	68	45
Dyspepsia			

subjects affected / exposed	0 / 8 (0.00%)	7 / 120 (5.83%)	0 / 114 (0.00%)
occurrences (all)	0	7	0
Nausea			
subjects affected / exposed	1 / 8 (12.50%)	28 / 120 (23.33%)	29 / 114 (25.44%)
occurrences (all)	1	40	36
Odynophagia			
subjects affected / exposed	1 / 8 (12.50%)	1 / 120 (0.83%)	1 / 114 (0.88%)
occurrences (all)	1	1	1
Stomatitis			
subjects affected / exposed	0 / 8 (0.00%)	9 / 120 (7.50%)	6 / 114 (5.26%)
occurrences (all)	0	9	12
Vomiting			
subjects affected / exposed	2 / 8 (25.00%)	15 / 120 (12.50%)	14 / 114 (12.28%)
occurrences (all)	2	23	15
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 8 (12.50%)	31 / 120 (25.83%)	44 / 114 (38.60%)
occurrences (all)	1	31	45
Dry skin			
subjects affected / exposed	0 / 8 (0.00%)	4 / 120 (3.33%)	7 / 114 (6.14%)
occurrences (all)	0	4	7
Nail disorder			
subjects affected / exposed	0 / 8 (0.00%)	7 / 120 (5.83%)	8 / 114 (7.02%)
occurrences (all)	0	7	11
Night sweats			
subjects affected / exposed	1 / 8 (12.50%)	0 / 120 (0.00%)	0 / 114 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	0 / 8 (0.00%)	10 / 120 (8.33%)	9 / 114 (7.89%)
occurrences (all)	0	10	9
Psoriasis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences (all)	1	0	1
Rash			
subjects affected / exposed	0 / 8 (0.00%)	12 / 120 (10.00%)	10 / 114 (8.77%)
occurrences (all)	0	15	11

Endocrine disorders			
Cushingoid			
subjects affected / exposed	1 / 8 (12.50%)	0 / 120 (0.00%)	0 / 114 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 8 (0.00%)	11 / 120 (9.17%)	10 / 114 (8.77%)
occurrences (all)	0	12	11
Back pain			
subjects affected / exposed	1 / 8 (12.50%)	8 / 120 (6.67%)	6 / 114 (5.26%)
occurrences (all)	1	10	7
Muscular weakness			
subjects affected / exposed	1 / 8 (12.50%)	0 / 120 (0.00%)	0 / 114 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 120 (0.83%)	6 / 114 (5.26%)
occurrences (all)	0	1	6
Myalgia			
subjects affected / exposed	0 / 8 (0.00%)	9 / 120 (7.50%)	9 / 114 (7.89%)
occurrences (all)	0	10	11
Pain in extremity			
subjects affected / exposed	0 / 8 (0.00%)	6 / 120 (5.00%)	7 / 114 (6.14%)
occurrences (all)	0	6	10
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 8 (12.50%)	4 / 120 (3.33%)	3 / 114 (2.63%)
occurrences (all)	2	4	3
Folliculitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 120 (0.00%)	1 / 114 (0.88%)
occurrences (all)	1	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 8 (12.50%)	5 / 120 (4.17%)	2 / 114 (1.75%)
occurrences (all)	1	7	2
Pneumonia			
subjects affected / exposed	0 / 8 (0.00%)	7 / 120 (5.83%)	4 / 114 (3.51%)
occurrences (all)	0	7	4

Respiratory tract infection			
subjects affected / exposed	1 / 8 (12.50%)	7 / 120 (5.83%)	3 / 114 (2.63%)
occurrences (all)	1	11	8
Upper respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	5 / 120 (4.17%)	6 / 114 (5.26%)
occurrences (all)	0	7	6
Urinary tract infection			
subjects affected / exposed	0 / 8 (0.00%)	8 / 120 (6.67%)	7 / 114 (6.14%)
occurrences (all)	0	9	12
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 8 (0.00%)	32 / 120 (26.67%)	31 / 114 (27.19%)
occurrences (all)	0	41	37
Hyperglycaemia			
subjects affected / exposed	0 / 8 (0.00%)	7 / 120 (5.83%)	5 / 114 (4.39%)
occurrences (all)	0	9	12
Hypoalbuminaemia			
subjects affected / exposed	0 / 8 (0.00%)	8 / 120 (6.67%)	7 / 114 (6.14%)
occurrences (all)	0	9	8
Hyponatraemia			
subjects affected / exposed	0 / 8 (0.00%)	7 / 120 (5.83%)	7 / 114 (6.14%)
occurrences (all)	0	7	9
Steroid diabetes			
subjects affected / exposed	1 / 8 (12.50%)	0 / 120 (0.00%)	0 / 114 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 January 2019	The primary purpose of this amendment was to revise some eligibility criteria either for clarification purpose or in order to allow more flexibility for the enrollment/randomization. In addition, guidelines for dose modifications for canakinumab and follow up on potential DILI were updated based on the new Novartis Hepatotoxicity Clinical safety Guidelines (2018)
10 June 2020	The primary purpose of this amendment was that if OS meets statistical significance at either the interim analysis or the final analysis and the study was unblinded, all subjects on study treatment were allowed to enter into an OLE, irrespective of the treatment arm assignment, and receive open label drug canakinumab

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to EudraCT system limitations, which EMA is aware of, data using 9999 as data points in this record are not an accurate representation of the clinical trial results

Notes: