



Clinical trial results:

A Phase 4, Interventional, Single-arm, Open-label Study Evaluating the Effect of Guselkumab on Cardiovascular Risk Surrogate Markers in Participants with Moderate to Severe Plaque Psoriasis

Summary

EudraCT number	2020-004061-39
Trial protocol	DE SE GR IT
Global end of trial date	28 July 2023

Results information

Result version number	v1 (current)
This version publication date	07 August 2024
First version publication date	07 August 2024

Trial information

Trial identification

Sponsor protocol code	CNT01959PSO4015
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05125679
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen-Cilag Limited
Sponsor organisation address	Turnhoutseweg 30, Beerse, Belgium, B-2340
Public contact	Clinical Registry Group, Janssen-Cilag Limited, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen-Cilag Limited, ClinicalTrialsEU@its.jnj.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	23 October 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 July 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study was to evaluate the effect of guselkumab on coronary flow reserve (CFR) measured by transthoracic doppler-echocardiography, in subjects with moderate-to-severe psoriasis and intermediate cardiovascular risk (ICR, defined by CFR greater than or equal to $[>=]$ 2 and less than or equal to $[<=]$ 3.5 at second screening visit 2 [2 to 4 weeks prior to Week 0]).

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 November 2021
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	Germany: 4
Country: Number of subjects enrolled	Greece: 7
Country: Number of subjects enrolled	Italy: 4
Worldwide total number of subjects	15
EEA total number of subjects	15

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)	14

From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 15 subjects with moderate-to-severe plaque psoriasis (with or without psoriatic arthritis) for at least 6 months prior to the first dose of guselkumab at Week 0 (baseline) of the study entry were enrolled and treated with at least one dose of guselkumab.

Pre-assignment

Screening details:

One subject of arm "Guselkumab 100 mg: Nicotine Users" who was treated with adenosine during the screening period was considered as screen failure but was counted in the safety analysis set (N=16) alone and not included in Full analysis set (N=15).

Period 1

Period 1 title	Overall (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Guselkumab 100 mg (Nicotine Users)

Arm description:

Subjects who were nicotine users (who had used tobacco products and/or nicotine products) received guselkumab 100 milligrams (mg) subcutaneous (SC) injection at Weeks 0, 4, 12, 20 and 28.

Arm type	Experimental
Investigational medicinal product name	Guselkumab
Investigational medicinal product code	CNT01959
Other name	TREMFYA
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

A single dose of guselkumab 100 mg at weeks 0, 4, 12, 20 and 28.

Arm title	Guselkumab 100 mg (Non-Nicotine Users)
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Arm description:

Subjects who were non-nicotine users (who had refrained from using tobacco/nicotine products for at least 3 months prior to screening visit 1 [4 to 6 weeks prior to Week 0]) received guselkumab 100 mg SC injection at Weeks 0, 4, 12, 20 and 28.

Arm type	Experimental
Investigational medicinal product name	Guselkumab
Investigational medicinal product code	CNT01959
Other name	TREMFYA
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

A single dose of guselkumab 100 mg injection at weeks 0, 4, 12, 20 and 28.

Number of subjects in period 1	Guselkumab 100 mg (Nicotine Users)	Guselkumab 100 mg (Non-Nicotine Users)
Started	7	8
Full Analysis Set (FAS)	7	8
Subjects with ICR	3 ^[1]	5
Completed	5	3
Not completed	2	5
Early termination of study	2	5

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Subjects who had CFR value greater than or equal to (\geq) 2 and less than or equal to (\leq) 3.5 at screening Visit 2 were included.

Baseline characteristics

Reporting groups

Reporting group title	Guselkumab 100 mg (Nicotine Users)
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Reporting group description:

Subjects who were nicotine users (who had used tobacco products and/or nicotine products) received guselkumab 100 milligrams (mg) subcutaneous (SC) injection at Weeks 0, 4, 12, 20 and 28.

Reporting group title	Guselkumab 100 mg (Non-Nicotine Users)
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Reporting group description:

Subjects who were non-nicotine users (who had refrained from using tobacco/nicotine products for at least 3 months prior to screening visit 1 [4 to 6 weeks prior to Week 0]) received guselkumab 100 mg SC injection at Weeks 0, 4, 12, 20 and 28.

Reporting group values	Guselkumab 100 mg (Nicotine Users)	Guselkumab 100 mg (Non-Nicotine Users)	Total
Number of subjects	7	8	15
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	6	8	14
From 65 to 84 years	1	0	1
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	49.9	39.1	
standard deviation	± 14.09	± 12.8	-
Title for Gender Units: subjects			
Female	0	5	5
Male	7	3	10

End points

End points reporting groups

Reporting group title	Guselkumab 100 mg (Nicotine Users)
Reporting group description: Subjects who were nicotine users (who had used tobacco products and/or nicotine products) received guselkumab 100 milligrams (mg) subcutaneous (SC) injection at Weeks 0, 4, 12, 20 and 28.	
Reporting group title	Guselkumab 100 mg (Non-Nicotine Users)
Reporting group description: Subjects who were non-nicotine users (who had refrained from using tobacco/nicotine products for at least 3 months prior to screening visit 1 [4 to 6 weeks prior to Week 0]) received guselkumab 100 mg SC injection at Weeks 0, 4, 12, 20 and 28.	

Primary: Change from Baseline in Coronary Flow Reserve (CFR) at Week 32

End point title	Change from Baseline in Coronary Flow Reserve (CFR) at Week 32 ^[1]
End point description: Change from baseline in CFR at Week 32 were reported. CFR described ability of coronary blood flow to increase substantially when required by metabolic demands, which might be up to 4 to 5 times greater during normal exercise compared to resting, and even greater with administration of pharmacological agents. CFR was measured non-invasively using transthoracic doppler echocardiography with administration of adenosine 140 micrograms per kilogram per minute (mcg/kg/min) as vasodilator. Doppler signals were recorded continuously at baseline (Week 0) and during adenosine infusion (for 5 minutes). CFR is ratio of blood flow at stress during maximal dilation of coronary arteries to blood flow at rest. FAS included all subjects who received at least 1 dose of guselkumab. Here, 'N' (number of subjects analysed) signifies number of treated and evaluable subjects with ICR defined by CFR ≥ 2 and ≤ 3.5 at screening visit 2 (2 to 4 weeks prior to Week 0) and baseline (Week 0).	
End point type	Primary
End point timeframe: Baseline (Week 0) and Week 32	

Notes:

[1] - 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: Due to too small number of enrolled subjects, no meaningful statistical comparisons between groups could be performed.

End point values	Guselkumab 100 mg (Nicotine Users)	Guselkumab 100 mg (Non-Nicotine Users)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Ratio				
arithmetic mean (standard deviation)	-0.080 (\pm 0.2773)	0.173 (\pm 0.6478)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CFR at Week 16

End point title	Change from Baseline in CFR at Week 16
End point description:	
Change from baseline in CFR at Week 16 were reported. CFR described ability of coronary blood flow to increase substantially when required by metabolic demands, which might be up to 4 to 5 times greater during normal exercise compared to resting, and even greater with administration of pharmacological agents. CFR was measured non-invasively using transthoracic doppler echocardiography with administration of adenosine 140 mcg/kg/min as vasodilator. Doppler signals were recorded continuously at baseline (Week 0) and during adenosine infusion (for 5 minutes). CFR is the ratio of blood flow at stress during maximal dilation of coronary arteries to blood flow at rest. FAS included all subjects who received at least 1 dose of guselkumab. Here, 'N' (number of subjects analysed) signifies number of treated and evaluable subjects with ICR defined by CFR ≥ 2 and ≤ 3.5 at screening visit 2 (2 to 4 weeks prior to Week 0) and baseline (Week 0).	
End point type	Secondary
End point timeframe:	
Baseline (Week 0) and Week 16	

End point values	Guselkumab 100 mg (Nicotine Users)	Guselkumab 100 mg (Non-Nicotine Users)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	2		
Units: Ratio				
arithmetic mean (standard deviation)	0.113 (\pm 0.3099)	0.435 (\pm 0.2899)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Absolute Global Longitudinal Strain (GLS) at Week 16

End point title	Change from Baseline in Absolute Global Longitudinal Strain (GLS) at Week 16
End point description:	
Change from baseline in absolute GLS at Week 16 were reported. GLS is a myocardial deformation analysis that predominantly reflects the function of sub-endocardial longitudinally oriented fibers, which are most prone to ischemic damage and wall stress. The GLS is calculated at systole and diastole. Speckle tracking echocardiography (STE) were employed for the detection of left-ventricular (LV) myocardial strain. GLS is a measure of longitudinal shortening of the myocardium as a percentage (change in length as a proportion to baseline length), thus explaining the negative values. FAS included all subjects who received at least 1 dose of guselkumab. Here, 'N' (number of subjects analysed) signifies number of treated subjects evaluable for this endpoint with ICR defined by CFR ≥ 2 and ≤ 3.5 at screening visit 2 (2 to 4 weeks prior to Week 0) and baseline (Week 0).	
End point type	Secondary
End point timeframe:	
Baseline (Week 0) and Week 16	

End point values	Guselkumab 100 mg (Nicotine Users)	Guselkumab 100 mg (Non- Nicotine Users)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	2		
Units: percentage of myocardial shortening				
arithmetic mean (standard deviation)	-1.377 (± 0.9660)	-2.625 (± 0.9829)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Absolute GLS at Week 32

End point title	Change from Baseline in Absolute GLS at Week 32
End point description:	
Change from baseline in absolute GLS at Week 32 were reported. GLS is a myocardial deformation analysis that predominantly reflects the function of sub-endocardial longitudinally oriented fibers, which are most prone to ischemic damage and wall stress. The GLS is calculated at systole and diastole. Speckle tracking echocardiography (STE) were employed for the detection of left-ventricular (LV) myocardial strain. GLS is a measure of longitudinal shortening of the myocardium as a percentage (change in length as a proportion to baseline length), thus explaining the negative values. FAS included all subjects who received at least 1 dose of guselkumab. Here, 'N' (number of subjects analysed) signifies number of treated subjects evaluable for this endpoint with ICR defined by CFR ≥ 2 and ≤ 3.5 at screening visit 2 (2 to 4 weeks prior to Week 0) and baseline (Week 0).	
End point type	Secondary
End point timeframe:	
Baseline (Week 0) and Week 32	

End point values	Guselkumab 100 mg (Nicotine Users)	Guselkumab 100 mg (Non- Nicotine Users)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: percentage of myocardial shortening				
arithmetic mean (standard deviation)	0.850 (± 0.6065)	-3.063 (± 3.0593)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Carotid-femoral Pulse Wave Velocity (cfPWV) at Week 16

End point title	Change from Baseline in Carotid-femoral Pulse Wave Velocity
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End point description:

Change from baseline in cfPWV at Week 16 were reported. cfPWV is a direct measurement, and the most simple, non-invasive, robust, and reproducible method to determine arterial stiffness. cfPWV was determined from the time taken for the arterial pulse to propagate from the carotid to the femoral artery. cfPWV was calculated as $\text{cfPWV} = \text{distance (meters)} / \text{transit time (seconds)}$. FAS included all subjects who received at least 1 dose of guselkumab. Here, 'N' (number of subjects analysed) signifies number of treated subjects evaluable for this endpoint with ICR defined by CFR ≥ 2 and ≤ 3.5 at screening visit 2 (2 to 4 weeks prior to Week 0) and baseline (Week 0).

End point type	Secondary
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End point timeframe:

Baseline (Week 0) and Week 16

End point values	Guselkumab 100 mg (Nicotine Users)	Guselkumab 100 mg (Non- Nicotine Users)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	2		
Units: meters per seconds (m/s)				
arithmetic mean (standard deviation)	0.77 (\pm 0.503)	-0.35 (\pm 0.495)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in cfPWV at Week 32

End point title	Change from Baseline in cfPWV at Week 32
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End point description:

Change from baseline in cfPWV at Week 32 were reported. cfPWV is a direct measurement, and the most simple, non-invasive, robust, and reproducible method to determine arterial stiffness. cfPWV was determined from the time taken for the arterial pulse to propagate from the carotid to the femoral artery. cfPWV was calculated as $\text{cfPWV} = \text{distance (meters)} / \text{transit time (seconds)}$. FAS included all subjects who received at least 1 dose of guselkumab. Here, 'N' (number of subjects analysed) signifies number of treated subjects evaluable for this endpoint with ICR defined by CFR ≥ 2 and ≤ 3.5 at screening visit 2 (2 to 4 weeks prior to Week 0) and baseline (Week 0).

End point type	Secondary
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End point timeframe:

Baseline (Week 0) and Week 32

End point values	Guselkumab 100 mg (Nicotine Users)	Guselkumab 100 mg (Non- Nicotine Users)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	2		
Units: meter per second (m/s)				
arithmetic mean (standard deviation)	1.37 (\pm 1.332)	-1.00 (\pm		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CFR at Week 16 Among Subjects with CFR ≥ 2 to Less than ($<$)2.75 at Baseline

End point title	Change from Baseline in CFR at Week 16 Among Subjects with CFR ≥ 2 to Less than ($<$)2.75 at Baseline
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End point description:

Change from baseline in CFR at Week 16 among subjects with CFR ≥ 2 to <2.75 at baseline were reported. CFR: ability of coronary blood flow to increase substantially when required by metabolic demands, which might be 4 to 5 times greater during normal exercise than resting, and even more with pharmacological agents. CFR was measured using transthoracic doppler echocardiography with adenosine 140 mcg/kg/min as vasodilator. Doppler signals were recorded continuously at baseline (Week 0) and during adenosine infusion (for 5 minutes). CFR: ratio of blood flow at stress during maximal dilation of coronary arteries to blood flow at rest. FAS included all subjects who received at least 1 dose of guselkumab. Here, 'N' (number of subjects analysed) signifies number of treated subjects evaluable for this endpoint with ICR defined by CFR ≥ 2 to <2.75 at baseline (Week 0).

End point type	Secondary
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End point timeframe:

Baseline (Week 0) and Week 16

End point values	Guselkumab 100 mg (Nicotine Users)	Guselkumab 100 mg (Non- Nicotine Users)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[2]	2		
Units: ratio				
arithmetic mean (standard deviation)	()	0.435 (\pm 0.2899)		

Notes:

[2] - Here, N=0, indicates that no subjects had baseline CFR measurement of ≥ 2 to <2.75 .

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CFR at Week 32 Among Subjects with CFR ≥ 2 to <2.75 at Baseline

End point title	Change from Baseline in CFR at Week 32 Among Subjects with CFR ≥ 2 to <2.75 at Baseline
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End point description:

Change from baseline in CFR at Week 32 among subjects with CFR ≥ 2 to <2.75 at baseline were reported. CFR: ability of coronary blood flow to increase substantially when required by metabolic demands, which might be 4 to 5 times greater during normal exercise than resting, and even more with pharmacological agents. CFR was measured using transthoracic doppler echocardiography with

adenosine 140 mcg/kg/min as vasodilator. Doppler signals were recorded continuously at baseline (Week 0) and during administration of adenosine infusion (for 5 minutes). CFR: ratio of blood flow at stress during maximal dilation of coronary arteries to blood flow at rest. FAS included all subjects who received at least 1 dose of guselkumab. Here, 'N' (number of subjects analysed) signifies number of treated subjects evaluable for this endpoint with ICR defined by CFR ≥ 2 to < 2.75 at baseline (Week 0).

End point type	Secondary
End point timeframe:	
Baseline (Week 0) and Week 32	

End point values	Guselkumab 100 mg (Nicotine Users)	Guselkumab 100 mg (Non-Nicotine Users)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[3]	3		
Units: ratio				
arithmetic mean (standard deviation)	()	0.173 (\pm 0.6478)		

Notes:

[3] - Here, N=0, indicates that no subjects had baseline CFR measurement of ≥ 2 to < 2.75 .

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CFR at Week 16 Among Subjects with CFR ≥ 2.75 to ≤ 3.5 at Baseline

End point title	Change from Baseline in CFR at Week 16 Among Subjects with CFR ≥ 2.75 to ≤ 3.5 at Baseline
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End point description:

Change from baseline in CFR at Week 16 among subjects with CFR ≥ 2.75 to ≤ 3.5 at baseline were reported. CFR: ability of coronary blood flow to increase substantially when required by metabolic demands, which might be 4 to 5 times greater during normal exercise than resting, and even more with pharmacological agents. CFR was measured using transthoracic doppler echocardiography with adenosine 140 mcg/kg/min as vasodilator. Doppler signals were recorded continuously at baseline (Week 0) and during administration of adenosine infusion (for 5 minutes). CFR: ratio of blood flow at stress during maximal dilation of coronary arteries to blood flow at rest. FAS included all subjects who received at least 1 dose of guselkumab. Here, 'N' (number of subjects analysed) signifies number of treated subjects evaluable for this endpoint with ICR defined by CFR ≥ 2.75 to ≤ 3.5 at baseline (Week 0).

End point type	Secondary
End point timeframe:	
Baseline (Week 0) and Week 16	

End point values	Guselkumab 100 mg (Nicotine Users)	Guselkumab 100 mg (Non- Nicotine Users)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	0 ^[4]		
Units: ratio				
arithmetic mean (standard deviation)	0.113 (± 0.3099)	()		

Notes:

[4] - Here, N=0 indicates that no subjects had baseline CFR measurement of ≥ 2.75 to ≤ 3.5 .

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Absolute GLS Among Nicotine Users and Non-users at Week 16

End point title	Change from Baseline in Absolute GLS Among Nicotine Users and Non-users at Week 16
End point description:	
Change from baseline in absolute GLS at Week 16 among nicotine users and non-nicotine users were reported. GLS is a myocardial deformation analysis that predominantly reflects the function of sub-endocardial longitudinally oriented fibers, which are most prone to ischemic damage and wall stress. The GLS is calculated at systole and diastole. Speckle tracking echocardiography (STE) were employed for the detection of left-ventricular (LV) myocardial strain. GLS is a measure of longitudinal shortening of the myocardium as a percentage (change in length as a proportion to baseline length), thus explaining the negative values. FAS included all subjects who received at least 1 dose of guselkumab. Here, 'N' (number of subjects analysed) signifies number of subjects evaluable for this endpoint.	
End point type	Secondary
End point timeframe:	
Baseline (Week 0) and Week 16	

End point values	Guselkumab 100 mg (Nicotine Users)	Guselkumab 100 mg (Non- Nicotine Users)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: percentage of myocardial shortening				
arithmetic mean (standard deviation)	-1.496 (± 0.8452)	-0.780 (± 2.3553)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CFR Among Nicotine Users and Non-nicotine Users at Weeks 32

End point title	Change from Baseline in CFR Among Nicotine Users and Non-
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End point description:

Change from baseline in CFR at Week 32 among nicotine users and non-users were reported. CFR described ability of coronary blood flow to increase substantially when required by metabolic demands, which might be up to 4 to 5 times greater during normal exercise compared to resting, and even greater with administration of pharmacological agents. CFR was measured non-invasively using transthoracic doppler echocardiography with administration of adenosine 140 mcg/kg/min as vasodilator. Doppler signals were recorded continuously at baseline (Week 0) and during administration of adenosine infusion (for 5 minutes). CFR is the ratio of blood flow at stress during maximal dilation of coronary arteries to blood flow at rest. FAS included all subjects who received at least 1 dose of guselkumab. Here, 'N' (number of subjects analysed) signifies number of subjects evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Baseline (Week 0) and Week 32

End point values	Guselkumab 100 mg (Nicotine Users)	Guselkumab 100 mg (Non-Nicotine Users)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: ratio				
arithmetic mean (standard deviation)	0.487 (\pm 1.1418)	-0.253 (\pm 0.7173)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CFR Among Nicotine Users and Non-nicotine Users at Weeks 16

End point title	Change from Baseline in CFR Among Nicotine Users and Non-nicotine Users at Weeks 16
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End point description:

Change from baseline in CFR among nicotine users and non-users at Week 16 were reported. CFR described ability of coronary blood flow to increase substantially when required by metabolic demands, which might be up to 4 to 5 times greater during normal exercise compared to resting, and even greater with administration of pharmacological agents. CFR was measured non-invasively using transthoracic doppler echocardiography with administration of adenosine 140 mcg/kg/min as vasodilator. Doppler signals were recorded continuously at baseline (Week 0) and during administration of adenosine infusion (for 5 minutes). CFR is ratio of blood flow at stress during maximal dilation of coronary arteries to blood flow at rest. FAS included all subjects who received at least 1 dose of guselkumab. Here, 'N' (number of subjects analysed) signifies number of subjects evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Baseline (Week 0) and Week 16

End point values	Guselkumab 100 mg (Nicotine Users)	Guselkumab 100 mg (Non- Nicotine Users)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: ratio				
arithmetic mean (standard deviation)	0.024 (\pm 0.6124)	0.132 (\pm 0.7874)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CFR at Week 32 Among Subjects with CFR ≥ 2.75 to ≤ 3.5 at Baseline

End point title	Change from Baseline in CFR at Week 32 Among Subjects with CFR ≥ 2.75 to ≤ 3.5 at Baseline
End point description: Change from baseline in CFR at Week 32 among subjects with CFR ≥ 2.75 to ≤ 3.5 at baseline were reported. CFR: ability of coronary blood flow to increase substantially when required by metabolic demands, which might be 4 to 5 times greater during normal exercise than resting, and even more with pharmacological agents. CFR was measured using transthoracic doppler echocardiography with adenosine 140 mcg/kg/min as vasodilator. Doppler signals were recorded continuously at baseline (Week 0) and during administration of adenosine infusion (for 5 minutes). CFR: ratio of blood flow at stress during maximal dilation of coronary arteries to blood flow at rest. FAS included all subjects who received at least 1 dose of guselkumab. Here, 'N' (number of subjects analysed) signifies number of treated subjects evaluable for this endpoint with ICR defined by CFR ≥ 2.75 to ≤ 3.5 at baseline (Week 0).	
End point type	Secondary
End point timeframe: Baseline (Week 0) and Week 32	

End point values	Guselkumab 100 mg (Nicotine Users)	Guselkumab 100 mg (Non- Nicotine Users)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	0 ^[5]		
Units: ratio				
arithmetic mean (standard deviation)	-0.080 (\pm 0.2773)	()		

Notes:

[5] - Here, N=0 indicates that no subjects had baseline CFR measurement of ≥ 2.75 to ≤ 3.5 .

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in cfPWV Among Nicotine Users and Non-users at Week 16

End point title	Change from Baseline in cfPWV Among Nicotine Users and Non-users at Week 16
End point description: Change from baseline in cfPWV among nicotine users and non-nicotine users at Week 16 were reported. cfPWV is a direct measurement, and the most simple, non-invasive, robust, and reproducible method to determine arterial stiffness. cfPWV was determined from the time taken for the arterial pulse to propagate from the carotid to the femoral artery. cfPWV was calculated as cfPWV= distance (meters)/ transit time (seconds). FAS included all subjects who received at least 1 dose of guselkumab. Here, 'N' (number of subjects analysed) signifies number of subjects evaluable for this endpoint.	
End point type	Secondary
End point timeframe: Baseline (Week 0) and Week 16	

End point values	Guselkumab 100 mg (Nicotine Users)	Guselkumab 100 mg (Non-Nicotine Users)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: meter per second (m/s)				
arithmetic mean (standard deviation)	0.34 (± 0.716)	-0.38 (± 0.330)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Absolute GLS Among Nicotine Users and Non-users at Week 32

End point title	Change from Baseline in Absolute GLS Among Nicotine Users and Non-users at Week 32
End point description: Change from baseline in absolute GLS at Week 32 among nicotine users and non-nicotine users were reported. GLS is a myocardial deformation analysis that predominantly reflects the function of sub-endocardial longitudinally oriented fibers, which are most prone to ischemic damage and wall stress. The GLS is calculated at systole and diastole. Speckle tracking echocardiography (STE) were employed for the detection of left-ventricular (LV) myocardial strain. GLS is a measure of longitudinal shortening of the myocardium as a percentage (change in length as a proportion to baseline length), thus explaining the negative values. FAS included all subjects who received at least 1 dose of guselkumab. Here, 'N' (number of subjects analysed) signifies number of subjects evaluable for this endpoint.	
End point type	Secondary
End point timeframe: Baseline (Week 0) and Week 32	

End point values	Guselkumab 100 mg (Nicotine Users)	Guselkumab 100 mg (Non-Nicotine Users)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: percentage of myocardial shortening				
arithmetic mean (standard deviation)	-0.060 (± 2.2065)	-2.490 (± 2.3020)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in cfPWV Among Nicotine Users and Non-users at Week 32

End point title	Change from Baseline in cfPWV Among Nicotine Users and Non-users at Week 32
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End point description:

Change from baseline in cfPWV among nicotine users and non-nicotine users at Week 32 were reported. cfPWV is a direct measurement, and the most simple, non-invasive, robust, and reproducible method to determine arterial stiffness. cfPWV was determined from the time taken for the arterial pulse to propagate from the carotid to the femoral artery. cfPWV was calculated as cfPWV= distance (meters)/transit time (seconds). FAS included all subjects who received at least 1 dose of guselkumab. Here, 'N' (number of subjects analysed) signifies number of subjects evaluable for this endpoint.

End point type	Secondary
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End point timeframe:

Baseline (Week 0) and Week 32

End point values	Guselkumab 100 mg (Nicotine Users)	Guselkumab 100 mg (Non-Nicotine Users)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: meter per second (m/s)				
arithmetic mean (standard deviation)	0.84 (± 1.191)	-0.80 (± 0.791)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Subjects with Treatment-emergent Adverse Events (TEAEs)
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End point description:

Number of subjects with TEAEs among subjects treated with guselkumab were reported. An adverse

event (AE) was any untoward medical occurrence in a subject participating in a clinical study that does not necessarily have a causal relationship with the pharmaceutical/biological agent under study. Any AE occurring at or after administration of adenosine or the initial administration of study intervention (guselkumab) through the day of last dose within the study phase plus 12 weeks or the date of the Final Safety visit, whichever was the latest, was considered to be TEAE. The safety analysis set included all subjects who received at least 1 dose of study treatment (either guselkumab or and adenosine) during study period.

End point type	Secondary
End point timeframe:	
Week 0 up to 12 weeks post last dose of study drug (up to Week 40)	

End point values	Guselkumab 100 mg (Nicotine Users)	Guselkumab 100 mg (Non- Nicotine Users)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7 ^[6]	8		
Units: subjects	2	2		

Notes:

[6] - 1 subject treated with adenosine (screen failure) was also counted in safety analysis set, thus N=8.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Week 0 Up to 12 weeks post last dose of study drug (up to Week 40)

Adverse event reporting additional description:

The safety analysis set included all subjects who received at least 1 dose of study treatment (either guselkumab or and adenosine) during study period. One subject of arm "Guselkumab 100 mg: Nicotine Users" who was treated with adenosine during screening period was considered as screen failure but was counted in safety analysis set (N=16) alone.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.0
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Reporting groups

Reporting group title	Guselkumab 100 mg (Nicotine Users)
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Reporting group description:

Subjects who were nicotine users (who had used tobacco products and/or nicotine products) received guselkumab 100 milligrams (mg) subcutaneous (SC) injection at Weeks 0, 4, 12, 20 and 28.

Reporting group title	Guselkumab 100 mg (Non-nicotine Users)
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Reporting group description:

Subjects who were non-nicotine users (who had refrained from using tobacco/nicotine products for at least 3 months prior to screening visit 1 [4 to 6 weeks prior to Week 0]) received guselkumab 100 mg SC injection at Weeks 0, 4, 12, 20 and 28.

Serious adverse events	Guselkumab 100 mg (Nicotine Users)	Guselkumab 100 mg (Non-nicotine Users)	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Ligament Rupture			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Panic attack			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Guselkumab 100 mg (Nicotine Users)	Guselkumab 100 mg (Non-nicotine Users)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 8 (12.50%)	2 / 8 (25.00%)	
Injury, poisoning and procedural complications			
Ligament Rupture			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Cardiac disorders			
Atrial Fibrillation			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 May 2021	The purpose of this amendment was to include tests and measurements to screen study subjects for metabolic syndrome. In addition, the method used for calculation of body surface area (BSA) affected by psoriasis was updated, and the latest versions of the patient reported outcomes (PRO) questionnaires were added to the protocol.
13 May 2022	The purpose of this amendment was to ensure exclusion criterion regarding low density lipoprotein (LDL) cutoff value (above which statin therapy should be initiated) was in line with the guidelines for management of dyslipidemia by the European Society of Cardiology.

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.

Sponsor terminated the study solely due to lack of enrolment. Due to small number of enrolled subjects, it was not possible to evaluate the primary or secondary objectives for this study as planned.

Notes: