Clinical trial results:
Effect of colchicine on cardiovascular target organ damage in patients with type 2 diabetes - A randomized placebo-controlled trial

Summary

EudraCT number	2021-003525-30
Trial protocol	DK
Global end of trial date	11 December 2023

Results information

Result version number	v1 (current)
This version publication date	02 October 2024
First version publication date	02 October 2024

Trial information

Trial identification

Sponsor protocol code	COLCAD

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Aarhus University Hospital, Steno Diabetes Center Aarhus
Sponsor organisation address	Palle Juul-Jensens Blvd. 11, Aarhus N, Denmark, 8200
Public contact	Medical/Steno Aarhus Research Lab, Aarhus University Hospital, Steno Diabetes Center Aarhus, baier@clin.au.dk
Scientific contact	Medical/Steno Aarhus Research Lab, Aarhus University Hospital, Steno Diabetes Center Aarhus, baier@clin.au.dk

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	28 August 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 December 2023
Global end of trial reached?	Yes
Global end of trial date	11 December 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to evaluate the effect of colchicine on arterial stiffness assessed as carotid-femoral pulse wave velocity compared to placebo in patients with type 2 diabetes.

Protection of trial subjects:

Ethical Approval:

The trial was conducted in accordance with the Declaration of Helsinki and the International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) guidelines. The study protocol, informed consent forms, and all other study-related documents were reviewed and approved by an independent ethics committee (IEC) or institutional review board (IRB) before the initiation of the trial.

Informed Consent:

Prior to participation, all subjects were provided with comprehensive information regarding the study’s purpose, procedures, potential risks, and benefits. Written informed consent was obtained from each participant before any study-related procedures were conducted. Participants were informed of their right to withdraw from the study at any time without penalty or loss of benefits to which they were otherwise entitled.

Confidentiality:

The confidentiality of participants' data was strictly maintained throughout the study. Personal identifiers were replaced with unique codes to protect participants’ identities. Access to the data was restricted to authorized personnel only, and all data handling complied with applicable data protection regulations, including the General Data Protection Regulation (GDPR).

Monitoring:
The trial was conducted in accordance with Good Clinical practice and was monitored by a local independent GCP-monitoring unit. Any unexpected risks or adverse effects were promptly reported to the IEC/IRB, regulatory authorities, and study participants as necessary.

Risk Minimization:

The study was designed to minimize risks to participants. Measures included regular monitoring of participants' health, provision of rescue medication or interventions as needed, and pre-specified stopping rules for individual participants or the entire trial in case of significant safety concerns.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 100
Worldwide total number of subjects	100
EEA total number of subjects	100

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)	19
From 65 to 84 years	81
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The screening process involved identifying potential participants, obtaining informed consent, and assessing eligibility based on inclusion/exclusion criteria through medical history, physical exams, and necessary tests. Ineligible individuals were excluded, and their data were handled confidentially. Only eligible participants proceeded to randomi

Period 1

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

Blinding implementation details:

Blinding was implemented by assigning participants to study groups using a computer-generated randomization code, kept confidential by an independent third party. Investigators, participants, and outcome assessors were blinded to group assignments. Colchicine/placeboe were identical in appearance, packaging, and labeling, ensuring that neither participants nor staff could distinguish between them, maintaining blinding integrity throughout the trial.

Arms

Are arms mutually exclusive?	Yes
Arm title	Active

Arm description:

Colchicine 0.5 mg once daily

Arm type	Active comparator
Investigational medicinal product name	Colchicine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

1 tablet (0.5 mg) once daily

Arm title	Placebo

Arm description:

Placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo, one tablet once daily

Number of subjects in period 1	Active	Placebo
Started	50	50
Completed	48	47
Not completed	2	3
Consent withdrawn by subject	1	2
Adverse event, non-fatal	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Active
Reporting group description: Colchicine 0.5 mg once daily	
Reporting group title	Placebo
Reporting group description: Placebo	

Reporting group values	Active	Placebo	Total
Number of subjects	50	50	100
Age categorical Units: Subjects			
Adults (18-64 years)	10	9	19
From 65-84 years	40	41	81
Age continuous Units: years			
arithmetic mean	70	72	
standard deviation	± 6	± 7	-
Gender categorical Units: Subjects			
Female	10	7	17
Male	40	43	83
History of cardiovascular disease Units: Subjects			
Yes	28	35	63
No	22	15	37
Current smoking Units: Subjects			
Yes	7	5	12
No	43	45	88
Renal function stage 1 or 2 Units: Subjects			
Yes	45	44	89
No	5	6	11
Renal function stage 3a Units: Subjects			
Yes	5	6	11
No	45	44	89
Metformin use Units: Subjects			
Yes	44	44	88
No	6	6	12
SGLT2i use Units: Subjects			
Yes	23	26	49
No	27	24	51

GLP-1 RA use Units: Subjects			
Yes	22	22	44
No	28	28	56
Insulin use Units: Subjects			
Yes	13	20	33
No	37	30	67
Any lipid lowering agent Units: Subjects			
Yes	46	48	94
No	4	2	6
Antiplatelet therapy Units: Subjects			
Yes	29	33	62
No	21	17	38
Anticoagulant Units: Subjects			
Yes	7	13	20
No	43	37	80
Single antihypertensive agent Units: Subjects			
Yes	12	7	19
No	38	43	81
Two or more antihypertensive agents Units: Subjects			
Yes	38	39	77
No	12	11	23
Body mass index Units: kg/m2			
arithmetic mean	29.7	30.8	
standard deviation	± 4.8	± 4.9	-
Diabetes duration Units: years			
median	15	15	
inter-quartile range (Q1-Q3)	10 to 18	10 to 20	-
24 h systolic blood pressure Units: mmHg			
arithmetic mean	127	126	
standard deviation	± 13	± 12	-
24 h diastolic blood pressure Units: mmHg			
arithmetic mean	76	76	
standard deviation	± 8	± 7	-
Heart rate Units: Beats per minute			
arithmetic mean	73	75	
standard deviation	± 14	± 12	-
HbA1c Units: mmol/mol			
arithmetic mean	56	56	

standard deviation	± 7	± 8	-
LDL Cholesterol			
Units: mmol/l			
median	1.5	1.6	
inter-quartile range (Q1-Q3)	1.2 to 1.8	1.2 to 1.9	-
UACR			
Units: mg/g			
median	12	16	
inter-quartile range (Q1-Q3)	3 to 90	5 to 93	-
hsCRP			
Units: mg/l			
median	1.0	0.9	
inter-quartile range (Q1-Q3)	0.4 to 2.3	0.5 to 2.1	-

End points

End points reporting groups	
Reporting group title	Active
Reporting group description: Colchicine 0.5 mg once daily	
Reporting group title	Placebo
Reporting group description: Placebo	

Primary: Change in MAP-adjusted cfPWV	
End point title	Change in MAP-adjusted cfPWV
End point description:	
End point type	Primary
End point timeframe: 26 weeks	

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	47		
Units: m/s				
arithmetic mean (confidence interval 95%)	-0.2 (-0.7 to 0.2)	0.5 (0.0 to 0.9)		

Statistical analyses

Statistical analysis title	Change in MAP-adjusted cfPWV
Comparison groups	Active v Placebo
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.03
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.1

Secondary: Change in 24h systolic blood pressure

End point title	Change in 24h systolic blood pressure
End point description:	

End point type	Secondary
End point timeframe:	
26 weeks	

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	45		
Units: mmHg				
arithmetic mean (confidence interval 95%)	-1 (-3 to 2)	-4 (-6 to -1)		

Statistical analyses

Statistical analysis title	Change in 24 h systolic blood pressure
Comparison groups	Active v Placebo
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.1
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	6

Secondary: Change in 24 h diastolic blood pressure

End point title	Change in 24 h diastolic blood pressure
End point description:	

End point type	Secondary
End point timeframe:	
26 weeks	

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	45		
Units: mmHg				
arithmetic mean (confidence interval 95%)	-1 (-2 to 1)	-2 (-4 to -1)		

Statistical analyses

Statistical analysis title	Change in 24h diastolic blood pressure
Comparison groups	Active v Placebo
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.17
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	3

Secondary: Change in office systolic BP

End point title	Change in office systolic BP
End point description:	
End point type	Secondary
End point timeframe:	
26 weeks	

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	47		
Units: mmHg				
arithmetic mean (confidence interval 95%)	-1 (-5 to 2)	-9 (-12 to -5)		

Statistical analyses

Statistical analysis title	Change in systolic office BP
Comparison groups	Placebo v Active
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.005
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	7
Confidence interval	
level	95 %
sides	2-sided
lower limit	2
upper limit	12

Secondary: Change in office diastolic BP	
End point title	Change in office diastolic BP
End point description:	
End point type	Secondary
End point timeframe:	
26 weeks	

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	47		
Units: mmHg				
arithmetic mean (confidence interval 95%)	-1 (-3 to 1)	-4 (-6 to -2)		

Statistical analyses

Statistical analysis title	change in office diastolic BP
Comparison groups	Active v Placebo

Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	5

Secondary: Percent change in UACR

End point title	Percent change in UACR

End point description:

End point type	Secondary

End point timeframe:

26 weeks

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	46		
Units: mg/g				
median (inter-quartile range (Q1-Q3))	17 (10 to 28)	19 (11 to 31)		

Statistical analyses

Statistical analysis title	Percent change in UACR
Comparison groups	Active v Placebo
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.98
Method	Mixed models analysis
Parameter estimate	Median difference (final values)
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.5
upper limit	40.4

Adverse events

Adverse events information

Timeframe for reporting adverse events:

May 12 2022 - Jan 29 2024

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25

Reporting groups

Reporting group title	Active
Reporting group description: -	
Reporting group title	Placebo

Reporting group description: -

Serious adverse events	Active	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 50 (6.00%)	2 / 50 (4.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Chest pain	Additional description: Admitted with chest pain - spontaneously resolved		
subjects affected / exposed	1 / 50 (2.00%)	2 / 50 (4.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Headache	Additional description: Admitted with headache and vomiting		
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Septic arthritis staphylococcalis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Active	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 50 (20.00%)	11 / 50 (22.00%)	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 50 (2.00%)	1 / 50 (2.00%)	
occurrences (all)	2	2	
Nausea			
subjects affected / exposed	4 / 50 (8.00%)	3 / 50 (6.00%)	
occurrences (all)	7	7	
Vomiting			
subjects affected / exposed	1 / 50 (2.00%)	1 / 50 (2.00%)	
occurrences (all)	2	2	
Diarrhoea			
subjects affected / exposed	1 / 50 (2.00%)	3 / 50 (6.00%)	
occurrences (all)	4	4	
Flatulence			
subjects affected / exposed	1 / 50 (2.00%)	1 / 50 (2.00%)	
occurrences (all)	2	2	
Constipation			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			
Myopathy			
subjects affected / exposed	1 / 50 (2.00%)	1 / 50 (2.00%)	
occurrences (all)	2	2	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	
occurrences (all)	1	1	
Metabolism and nutrition disorders			
Hyperkalaemia			

subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	1	1	
Hypokalaemia			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 May 2022	A high-sensitivity C-reactive protein > 2 mg/l was removed as inclusion criterion as of May 2022 due to delayed recruitment. Only one participant had been included prior to this change.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported