



Clinical trial results:

Diet, physical exercise, and metabolic control intervention to reduce the incidence of major neurocognitive disorders among individuals with type 2 diabetes combined with mild neurocognitive impairment – a pilot study

Summary

EudraCT number	2019-003772-39
Trial protocol	SE
Global end of trial date	28 February 2022

Results information

Result version number	v1 (current)
This version publication date	28 October 2022
First version publication date	28 October 2022

Trial information

Trial identification

Sponsor protocol code	DEMAND-pilot
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03877783
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Umeå University
Sponsor organisation address	Department of Public Health and Clinical Medicine, Family Medicine, Umeå University, Umeå, Sweden, 90187
Public contact	Olov Rolandsson, Umeå University, +46 705902052, olov.rolandsson@umu.se
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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	07 October 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 February 2022
Global end of trial reached?	Yes
Global end of trial date	28 February 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine whether the chosen study design is feasible in terms of recruitment, retainment, adherence, and acceptance.

Protection of trial subjects:

The study participants were followed regularly, both by study visits and by phone calls. All study participants were interviewed to minimize stress and discomfort.

Adverse Events were registered from study start (randomisation) until the last study visit. All reported SAEs that had not been resolved by the end of the study was followed up until the event had subsided (or disappeared), the condition was stabilized, the event was otherwise explained or the study subject was lost to follow-up.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 October 2020
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	Sweden: 11
Worldwide total number of subjects	11
EEA total number of subjects	11

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)	0
From 65 to 84 years	11

85 years and over	0
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Subject disposition

Recruitment

Recruitment details:

Subjects were recruited via advertisements posted in national and local newspapers and in social media. Persons identified with diagnosis of diabetes type 2 based on ICD codes also received a letter of invitation to participate in the study.

Pre-assignment

Screening details:

Persons interested in participating in the study were pre-screened by phone. If determined as suitable for the study, a screening visit at site was performed where xxxxx

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Intervention

Arm description:

Intervention consisting of a Mediterranean diet, an individualized physical training program and optimal pharmacological treatment for T2D.

Arm type	Experimental
Investigational medicinal product name	PR1
Investigational medicinal product code	A10BA02
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

3 gram/day

Investigational medicinal product name	PR2
Investigational medicinal product code	A10BK01
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

10 milligram/day

Investigational medicinal product name	PR3
Investigational medicinal product code	A10BK02
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

300 milligram/day

Investigational medicinal product name	PR4
Investigational medicinal product code	A10BK03
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:	
25 milligram/day	
Investigational medicinal product name	PR5
Investigational medicinal product code	A10BJ02
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
1,8 milligram/day	
Investigational medicinal product name	PR6
Investigational medicinal product code	A10BJ06
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
0,14 milligram/day	
Investigational medicinal product name	PR7
Investigational medicinal product code	A10BH01
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
100 milligram/day	
Investigational medicinal product name	PR8
Investigational medicinal product code	A10BH05
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
5 milligram/day	
Investigational medicinal product name	PR9
Investigational medicinal product code	A10BX02
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
16 milligram/day	
Investigational medicinal product name	PR10
Investigational medicinal product code	A10BG03
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
45 milligram/day	
Investigational medicinal product name	PR11
Investigational medicinal product code	A10BF01
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
300 milligram/day	

Investigational medicinal product name	PR12
Investigational medicinal product code	A10BB07
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
20 milligram/day	
Investigational medicinal product name	PR13
Investigational medicinal product code	A10BB12
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
6 milligram/day	
Investigational medicinal product name	PR14
Investigational medicinal product code	C09AA02
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
20 milligram/day	
Investigational medicinal product name	PR15
Investigational medicinal product code	C09AA01
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
150 milligram/day	
Investigational medicinal product name	PR16
Investigational medicinal product code	C09AA03
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
80 milligram/day	
Investigational medicinal product name	PR17
Investigational medicinal product code	C09AA04
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
10 milligram/day	
Investigational medicinal product name	PR18
Investigational medicinal product code	C09AA05
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
10 milligram/day	
Investigational medicinal product name	PR19
Investigational medicinal product code	C09CA06
Other name	

Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
32 milligram/day	
Investigational medicinal product name	PR20
Investigational medicinal product code	C09CA01
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
150 milligram/day	
Investigational medicinal product name	PR21
Investigational medicinal product code	C09CA03
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
320 milligram/day	
Investigational medicinal product name	PR22
Investigational medicinal product code	C09CA04
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
300 milligram/day	
Investigational medicinal product name	PR23
Investigational medicinal product code	C09CA02
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
600 milligram/day	
Investigational medicinal product name	PR24
Investigational medicinal product code	C09CA07
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
80 milligram/day	
Investigational medicinal product name	PR25
Investigational medicinal product code	C07AB02
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
200 milligram/day	
Investigational medicinal product name	PR26
Investigational medicinal product code	C07AB03
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:	
100 milligram/day	
Investigational medicinal product name	PR27
Investigational medicinal product code	C07AB07
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
20 milligram/day	
Investigational medicinal product name	PR28
Investigational medicinal product code	C03AA01
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
5 milligram/day	
Investigational medicinal product name	PR29
Investigational medicinal product code	C03AA03
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
100 milligram/day	
Investigational medicinal product name	PR30
Investigational medicinal product code	C03CC01
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
240 milligram/day	
Investigational medicinal product name	PR31
Investigational medicinal product code	C03DA01
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
200 milligram/day	
Investigational medicinal product name	PR32
Investigational medicinal product code	C03DA04
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
50 milligram/day	
Investigational medicinal product name	PR33
Investigational medicinal product code	C08CA01
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
10 milligram/day	

Investigational medicinal product name	PR34
Investigational medicinal product code	C08CA02
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
10 milligram/day	
Investigational medicinal product name	PR35
Investigational medicinal product code	C08CA05
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
80 milligram/day	
Investigational medicinal product name	PR36
Investigational medicinal product code	C08DA01
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
480 milligram/day	
Investigational medicinal product name	PR37
Investigational medicinal product code	C08DB01
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
360 milligram/day	
Investigational medicinal product name	PR38
Investigational medicinal product code	C10AA01
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
80 milligram/day	
Investigational medicinal product name	PR39
Investigational medicinal product code	C10AA03
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
40 milligram/day	
Investigational medicinal product name	PR40
Investigational medicinal product code	C10AA05
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
80 milligram/day	
Investigational medicinal product name	PR41
Investigational medicinal product code	C10AA07
Other name	

Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
40 milligram/day	
Investigational medicinal product name	PR42
Investigational medicinal product code	C10AX09
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
10 milligram/day	
Investigational medicinal product name	PR43
Investigational medicinal product code	C10AB02
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
600 milligram/day	
Investigational medicinal product name	PR44
Investigational medicinal product code	C10AB04
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
1200 milligram/day	
Investigational medicinal product name	PR45
Investigational medicinal product code	C10AB05
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
200 milligram/day	
Investigational medicinal product name	PR46
Investigational medicinal product code	C10AC01
Other name	
Pharmaceutical forms	Tablet, Powder for oral suspension
Routes of administration	Oral use
Dosage and administration details:	
24 gram/day	
Investigational medicinal product name	PR47
Investigational medicinal product code	C10AC02
Other name	
Pharmaceutical forms	Tablet, Powder for oral suspension
Routes of administration	Oral use
Dosage and administration details:	
30 gram/day	
Arm title	Control
Arm description:	
Usual care	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Intervention	Control
Started	5	6
Completed	5	4
Not completed	0	2
Adverse event, serious fatal	-	1
Consent withdrawn by subject	-	1

Baseline characteristics

Reporting groups

Reporting group title	Intervention
Reporting group description: Intervention consisting of a Mediterranean diet, an individualized physical training program and optimal pharmacological treatment for T2D.	
Reporting group title	Control
Reporting group description: Usual care	

Reporting group values	Intervention	Control	Total
Number of subjects	5	6	11
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)	0	0	0
From 65-84 years	5	6	11
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	1	3	4
Male	4	3	7

End points

End points reporting groups

Reporting group title	Intervention
Reporting group description: Intervention consisting of a Mediterranean diet, an individualized physical training program and optimal pharmacological treatment for T2D.	
Reporting group title	Control
Reporting group description: Usual care	

Primary: Feasibility: recruitment rate

End point title	Feasibility: recruitment rate ^[1]
End point description: Recruitment rate is assessed as the number of participants recruited during a specific time period.	
End point type	Primary
End point timeframe: After study completion	

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: We have performed a feasibility study with the aim to assess recruitment rate, retention rate, and acceptance. These endpoints are evaluated by numbers, proportions, and interviews, but not by using standard statistical methods.

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	6		
Units: number	5	6		

Statistical analyses

No statistical analyses for this end point

Primary: Feasibility: retention rate

End point title	Feasibility: retention rate ^[2]
End point description: Retention rate is assessed as the number of participants remaining in the study at 12 months	
End point type	Primary
End point timeframe: After study completion	

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: We have performed a feasibility study with the aim to assess recruitment rate, retention rate, and acceptance. These endpoints are evaluated by numbers, proportions, and interviews, but not by using standard statistical methods.

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: number	5	5		

Statistical analyses

No statistical analyses for this end point

Primary: Feasibility: adherence rate

End point title	Feasibility: adherence rate ^[3]
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End point description:

End point type	Primary
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End point timeframe:

At 0, 6 and 12 months

Notes:

[3] - 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: We have performed a feasibility study with the aim to assess recruitment rate, retention rate, and acceptance. These endpoints are evaluated by numbers, proportions, and interviews, but not by using standard statistical methods.

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: number	5	5		

Statistical analyses

No statistical analyses for this end point

Primary: Feasibility: acceptance rate

End point title	Feasibility: acceptance rate ^[4]
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End point description:

Acceptance is assessed by interviews

End point type	Primary
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End point timeframe:

Between 6 weeks after study start and the 6-month visit, and at the end of the study

Notes:

[4] - 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: We have performed a feasibility study with the aim to assess recruitment rate, retention rate, and acceptance. These endpoints are evaluated by numbers, proportions, and interviews, but not by using standard statistical methods.

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: number	5	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Metabolic control: Blood pressure

End point title	Metabolic control: Blood pressure
End point description:	Metabolic control: Blood pressure
End point type	Secondary
End point timeframe:	At 0, 3, 6, 9 and 12 months

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: number	5	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Estimated food intake: Recorded intake of approximately 20 food items over 4 consecutive days.

End point title	Estimated food intake: Recorded intake of approximately 20 food items over 4 consecutive days.
End point description:	Estimated food intake: Recorded intake of approximately 20 food items over 4 consecutive days.
End point type	Secondary
End point timeframe:	At 0, 6 and 12 months

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: number	5	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Cardiovascular fitness: Aerobic capacity (VO2max) estimated with the Ekblom-Bak test.

End point title	Cardiovascular fitness: Aerobic capacity (VO2max) estimated with the Ekblom-Bak test.
End point description:	Cardiovascular fitness: Aerobic capacity (VO2max) estimated with the Ekblom-Bak test.
End point type	Secondary
End point timeframe:	At 0, 6 and 12 months.

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: number	5	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Physical activity and sedentary behavior: The accelerometer activPAL will be used to measure physical activity and sedentary behavior

End point title	Physical activity and sedentary behavior: The accelerometer activPAL will be used to measure physical activity and sedentary behavior
End point description:	Physical activity and sedentary behavior: The accelerometer activPAL will be used to measure physical activity and sedentary behavior
End point type	Secondary
End point timeframe:	At 0, 6 and 12 months

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: number	5	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Grip strength: Grip strength in the left and right hand measured with a hand dynamometer.

End point title	Grip strength: Grip strength in the left and right hand measured with a hand dynamometer.
End point description:	Grip strength: Grip strength in the left and right hand measured with a hand dynamometer.
End point type	Secondary
End point timeframe:	At 0, 6 and 12 months.

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: number	5	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Leg strength: Functional leg strength and endurance measured using the Chair Stand Test

End point title	Leg strength: Functional leg strength and endurance measured using the Chair Stand Test
End point description:	Leg strength: Functional leg strength and endurance measured using the Chair Stand Test
End point type	Secondary
End point timeframe:	At 0, 6 and 12 months.

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: number	5	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Exercise Self-Efficacy Scale (ESES): To investigate participants selfefficacy regarding performing exercise.

End point title	Exercise Self-Efficacy Scale (ESES): To investigate participants selfefficacy regarding performing exercise.
End point description:	Exercise Self-Efficacy Scale (ESES): To investigate participants selfefficacy regarding performing exercise.
End point type	Secondary
End point timeframe:	At 0, 6 and 12 months

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: number	5	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Exercise Regulations Questionnaire (BREQ-2): To investigate participants motivation to exercise.

End point title	Exercise Regulations Questionnaire (BREQ-2): To investigate participants motivation to exercise.
End point description:	Exercise Regulations Questionnaire (BREQ-2): To investigate participants motivation to exercise.
End point type	Secondary
End point timeframe:	At 0, 6 and 12 months

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: number	5	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Cognitive function: Evaluated with standardized neuropsychological tests.

End point title	Cognitive function: Evaluated with standardized neuropsychological tests.
End point description:	Cognitive function: Evaluated with standardized neuropsychological tests.
End point type	Secondary
End point timeframe:	At 0 and 12 months

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: number	5	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Metabolic control: Blood levels of HbA1c and lipids, height, body weight, BMI and waist circumference.

End point title	Metabolic control: Blood levels of HbA1c and lipids, height, body weight, BMI and waist circumference.
End point description:	Metabolic control: Blood levels of HbA1c and lipids, height, body weight, BMI and waist circumference.
End point type	Secondary
End point timeframe:	At 0, 6 and 12 months

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: units	5	4		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From study start (after randomisation) until the last study visit

Assessment type	Non-systematic
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Dictionary used

Dictionary name	CTCAE
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Dictionary version	5.0
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Reporting groups

Reporting group title	Intervention
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Reporting group description:

Intervention consisting of a Mediterranean diet, an individualized physical training program and optimal pharmacological treatment for T2D

Reporting group title	Control
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Reporting group description:

Usual care

Serious adverse events	Intervention	Control	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events		0	
General disorders and administration site conditions			
Sudden death	Additional description: Traffic accident		
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

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

Non-serious adverse events	Intervention	Control	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	5 / 5 (100.00%)	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 5 (40.00%)	0 / 5 (0.00%)	
occurrences (all)	5	0	
Dizziness			

subjects affected / exposed	1 / 5 (20.00%)	2 / 5 (40.00%)	
occurrences (all)	1	3	
Syncope			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Chills			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Pain	Additional description: Pain in trunk, hip, hand or finger		
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Fever			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Toothache			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Oral pain	Additional description: Oral pain after dental surgery		
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			

Postnasal drip subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0	
Cough subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0	
Dyspnea	Additional description: Breathlessness		
subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 5 (20.00%) 1	
Musculoskeletal and connective tissue disorders			
Pain in extremity subjects affected / exposed occurrences (all)	2 / 5 (40.00%) 2	1 / 5 (20.00%) 1	
Other	Additional description: Bursit		
subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 5 (20.00%) 1	
Infections and infestations			
Vaginal infection	Additional description: vaginal yeast infection		
subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0	
Abdominal infection	Additional description: Stomach sickness		
subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0	
Conjunctivitis subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0	
Lung infection subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 5 (20.00%) 1	
Metabolism and nutrition disorders			
Hypoglycaemia subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 3	0 / 5 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported