



## Clinical trial results: Perindopril and Leucine to improve muscle function in older people Summary

EudraCT number	2014-003455-61
Trial protocol	GB
Global end of trial date	15 January 2020

### Results information

Result version number	v1 (current)
This version publication date	29 May 2021
First version publication date	29 May 2021

### Trial information

#### Trial identification

Sponsor protocol code	2013GR06
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#### Additional study identifiers

ISRCTN number	ISRCTN90094835
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	University of Dundee
Sponsor organisation address	Ninewells Hospital, Dundee, United Kingdom, DD1 9SY
Public contact	Professor Miles Witham 0191 208 1317, Tayside Academic Health Sciences Centre Level 10, Ninewells Hospital, Dundee DD1 9SY 01382 383140, +44 01912081317, Miles.Witham@newcastle.ac.uk
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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	18 February 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 January 2020
Global end of trial reached?	Yes
Global end of trial date	15 January 2020
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

To determine the efficacy of leucine and ACEi in improving physical function in older people with sarcopenia

Protection of trial subjects:

Monitoring of serum potassium, creatinine, and orthostatic blood pressure (safety for perindopril)  
Selection of outcomes and study length to minimise burden on participants

Background therapy:

Usual care. Participants undertaking exercise training were excluded as the trial aimed to test the efficacy of perindopril and leucine in participants who were not already exercising. Previous work had already examined the effect of perindopril and leucine as adjuncts to exercise training.

Evidence for comparator:

Placebo selected as this was an efficacy trial and there are no other pharmacological interventions with proven efficacy for sarcopenia.

Actual start date of recruitment	01 May 2015
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	United Kingdom: 145
Worldwide total number of subjects	145
EEA total number of subjects	0

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	112
85 years and over	33

## Subject disposition

### Recruitment

Recruitment details:

Recruitment in UK (14 centres) from June 2018 to December 2020

### Pre-assignment

Screening details:

320 attended screening visit. Screen fail reasons:

- Not met sarcopenia criteria: 129
- Symptomatic orthostatic hypotension: 13
- High potassium: 6
- Excluded medication: 4
- Excluded medical condition: 10
- Other: 16

### 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, Carer

Blinding implementation details:

Matching placebo for perindopril and for leucine

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Perindopril + Leucine

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Perindopril
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral powder
Routes of administration	Oral use

Dosage and administration details:

2mg once daily, rising to 4mg once daily after 2 weeks if tolerated

Investigational medicinal product name	Leucine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral powder
Routes of administration	Oral use

Dosage and administration details:

2.5g three times a day with meals

<b>Arm title</b>	Perindopril placebo + Leucine
Arm description: -	
Arm type	Mixed placebo/active arm
Investigational medicinal product name	Placebo for perindopril
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral powder
Routes of administration	Oral use

Dosage and administration details:

placebo for 2mg perindopril once daily, changing to placebo for 4mg perindopril once daily after 2 weeks if tolerated

Investigational medicinal product name	Leucine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral powder
Routes of administration	Oral use

Dosage and administration details:

2.5g three times a day with meals

<b>Arm title</b>	Perindopril + Leucine placebo
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Arm description: -

Arm type	Mixed placebo/active arm
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No investigational medicinal product assigned in this arm

<b>Arm title</b>	Placebo/Placebo
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Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo for perindopril and placebo for leucine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral powder
Routes of administration	Oral use

Dosage and administration details:

Placebo for 4mg perindopril once daily and placebo for leucine 2.5g three times a day with food

<b>Number of subjects in period 1</b>	Perindopril + Leucine	Perindopril placebo + Leucine	Perindopril + Leucine placebo
Started	39	33	34
Completed	28	24	24
Not completed	11	9	10
Adverse event, serious fatal	-	-	1
Physician decision	3	1	1
Adverse event, non-fatal	1	1	-
Other	2	1	-
Patient choice	5	6	8

<b>Number of subjects in period 1</b>	Placebo/Placebo
Started	39
Completed	33
Not completed	6
Adverse event, serious fatal	-
Physician decision	-
Adverse event, non-fatal	-
Other	-
Patient choice	6



## Baseline characteristics

<b>Reporting groups</b>	
Reporting group title	Perindopril + Leucine
Reporting group description: -	
Reporting group title	Perindopril placebo + Leucine
Reporting group description: -	
Reporting group title	Perindopril + Leucine placebo
Reporting group description: -	
Reporting group title	Placebo/Placebo
Reporting group description: -	

<b>Reporting group values</b>	Perindopril + Leucine	Perindopril placebo + Leucine	Perindopril + Leucine placebo
Number of subjects	39	33	34
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	32	29	31
85 years and over	7	4	3
Age continuous Units: years			
arithmetic mean	78.1	78.6	79.5
standard deviation	± 5.5	± 6.5	± 6.6
Gender categorical Units: Subjects			
Female	22	16	17
Male	17	17	17
Short Physical Performance Battery Units: Points			
arithmetic mean	7.3	6.7	6.8
standard deviation	± 2.1	± 2.2	± 2.5
Number of medications Units: count			
median	4	5	5
inter-quartile range (Q1-Q3)	2 to 6	2.5 to 7	4 to 7

<b>Reporting group values</b>	Placebo/Placebo	Total	
Number of subjects	39	145	
Age categorical Units: Subjects			
In utero	0	0	

Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	33	125	
85 years and over	6	20	
Age continuous Units: years			
arithmetic mean	79.0		
standard deviation	± 5.7	-	
Gender categorical Units: Subjects			
Female	23	78	
Male	16	67	
Short Physical Performance Battery Units: Points			
arithmetic mean	7.1		
standard deviation	± 2.6	-	
Number of medications Units: count			
median	5		
inter-quartile range (Q1-Q3)	3 to 7	-	

### Subject analysis sets

Subject analysis set title	Perindopril vs placebo
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All randomised participants; comparison of all those receiving perindopril vs all those receiving the placebo for perindopril

Subject analysis set title	Leucine vs placebo
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All randomised participants. Analysis of all those receiving leucine vs all those receiving leucine placebo

Reporting group values	Perindopril vs placebo	Leucine vs placebo	
Number of subjects	145	145	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	125	125	

85 years and over	20	20	
Age continuous Units: years arithmetic mean standard deviation	78.8 ± 6.0	78.8 ± 6.0	
Gender categorical Units: Subjects			
Female	78	78	
Male	67	67	
Short Physical Performance Battery Units: Points arithmetic mean standard deviation	7.0 ± 2.3	7.0 ± 2.3	
Number of medications Units: count median inter-quartile range (Q1-Q3)	5 3 to 7	5 3 to 7	

## End points

### End points reporting groups

Reporting group title	Perindopril + Leucine
Reporting group description: -	
Reporting group title	Perindopril placebo + Leucine
Reporting group description: -	
Reporting group title	Perindopril + Leucine placebo
Reporting group description: -	
Reporting group title	Placebo/Placebo
Reporting group description: -	
Subject analysis set title	Perindopril vs placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description: All randomised participants; comparison of all those receiving perindopril vs all those receiving the placebo for perindopril	
Subject analysis set title	Leucine vs placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description: All randomised participants. Analysis of all those receiving leucine vs all those receiving leucine placebo	

### Primary: Short physical performance battery

End point title	Short physical performance battery
End point description: Repeated measures mixed model adjusted for baseline age, sex, Charlson score, handgrip	
End point type	Primary
End point timeframe: 12 months	

End point values	Perindopril vs placebo	Leucine vs placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	145	145		
Units: points				
arithmetic mean (confidence interval 95%)	-0.1 (-1.2 to 1.0)	0.1 (-1.0 to 1.1)		

### Statistical analyses

Statistical analysis title	Repeated measures mixed model
Comparison groups	Perindopril vs placebo v Leucine vs placebo

Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	superiority <sup>[1]</sup>
P-value	= 0.89
Method	Mixed models analysis
Parameter estimate	Mean difference, repeated measures
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	1

Notes:

[1] - Unable to enter results for both comparisons in this 2x2 trial, and the software has incorrectly added the two analysis sets together. The comparison involving perindopril has been reported here, and the number in the analysis is 145 participants.

### Secondary: Six minute walk distance

End point title	Six minute walk distance
End point description: Repeated measures mixed model adjusted for baseline age, sex, Charlson score, handgrip	
End point type	Secondary
End point timeframe: 12 months	

End point values	Perindopril vs placebo	Leucine vs placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	145	145		
Units: metres				
arithmetic mean (confidence interval 95%)	-32 (-75 to 12)	17 (-25 to 59)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Appendicular muscle mass

End point title	Appendicular muscle mass
End point description: Repeated measures mixed model adjusted for baseline age, sex, Charlson score, handgrip	
End point type	Secondary
End point timeframe: 12 months	

<b>End point values</b>	Perindopril vs placebo	Leucine vs placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	145	145		
Units: kg/m <sup>2</sup>				
arithmetic mean (confidence interval 95%)	-0.4 (-1.1 to 0.3)	-0.25 (-0.95 to 0.44)		

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From consent to 30 days after completion of participation for each individual

Adverse event reporting additional description:

AEs collected at each study visit and by medical records review

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	21
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### Reporting groups

Reporting group title	Perindopril + Leucine
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Reporting group description: -

Reporting group title	Perindopril placebo + Leucine
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Reporting group description: -

Reporting group title	Perindopril + Leucine placebo
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Reporting group description: -

Reporting group title	Placebo/Placebo
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Reporting group description: -

<b>Serious adverse events</b>	Perindopril + Leucine	Perindopril placebo + Leucine	Perindopril + Leucine placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 39 (0.00%)	0 / 33 (0.00%)	1 / 34 (2.94%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	1
Blood and lymphatic system disorders			
leukaemia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 33 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

<b>Serious adverse events</b>	Placebo/Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 39 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Blood and lymphatic system disorders			
leukaemia			

subjects affected / exposed	0 / 39 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

<b>Non-serious adverse events</b>	Perindopril + Leucine	Perindopril placebo + Leucine	Perindopril + Leucine placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 39 (97.44%)	29 / 33 (87.88%)	31 / 34 (91.18%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin cancer			
subjects affected / exposed	0 / 39 (0.00%)	0 / 33 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
Vascular disorders			
Hot flush			
subjects affected / exposed	1 / 39 (2.56%)	2 / 33 (6.06%)	0 / 34 (0.00%)
occurrences (all)	1	2	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 39 (2.56%)	0 / 33 (0.00%)	2 / 34 (5.88%)
occurrences (all)	1	0	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 39 (15.38%)	3 / 33 (9.09%)	3 / 34 (8.82%)
occurrences (all)	6	3	3
Psychiatric disorders			
Anxiety disorder			
subjects affected / exposed	0 / 39 (0.00%)	0 / 33 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
Depression			
subjects affected / exposed	1 / 39 (2.56%)	0 / 33 (0.00%)	2 / 34 (5.88%)
occurrences (all)	1	0	2
Injury, poisoning and procedural complications			
Joint injury			

subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0
Muscle strain subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0
Pelvic fracture subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	0 / 33 (0.00%) 0	2 / 34 (5.88%) 2
Soft tissue injury subjects affected / exposed occurrences (all)	8 / 39 (20.51%) 8	3 / 33 (9.09%) 3	4 / 34 (11.76%) 4
Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2	1 / 33 (3.03%) 1	0 / 34 (0.00%) 0
Palpitations subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	5 / 39 (12.82%) 5	2 / 33 (6.06%) 2	5 / 34 (14.71%) 5
Headache subjects affected / exposed occurrences (all)	5 / 39 (12.82%) 5	0 / 33 (0.00%) 0	1 / 34 (2.94%) 1
Lethargy subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	2 / 33 (6.06%) 2	0 / 34 (0.00%) 0
Loss of consciousness subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	0 / 33 (0.00%) 0	2 / 34 (5.88%) 2
Migraine subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	2 / 33 (6.06%) 2	0 / 34 (0.00%) 0
Eye disorders			

Cataract subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0
Gastrointestinal disorders			
Abdominal pain upper subjects affected / exposed occurrences (all)	3 / 39 (7.69%) 3	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	2 / 33 (6.06%) 2	5 / 34 (14.71%) 5
Diarrhoea subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2	2 / 33 (6.06%) 2	3 / 34 (8.82%) 3
Diverticulitis subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0
Irritable bowel syndrome subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	3 / 39 (7.69%) 3	1 / 33 (3.03%) 1	2 / 34 (5.88%) 2
Rectal haemorrhage subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	0 / 33 (0.00%) 0	2 / 34 (5.88%) 2
Vomiting subjects affected / exposed occurrences (all)	4 / 39 (10.26%) 4	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0
Skin and subcutaneous tissue disorders			
Rash subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2	1 / 33 (3.03%) 1	0 / 34 (0.00%) 0
Skin ulcer subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	0 / 33 (0.00%) 0	2 / 34 (5.88%) 2
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	1 / 39 (2.56%)	2 / 33 (6.06%)	1 / 34 (2.94%)
occurrences (all)	1	2	1
Arthritis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 33 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
Back pain			
subjects affected / exposed	2 / 39 (5.13%)	2 / 33 (6.06%)	1 / 34 (2.94%)
occurrences (all)	2	2	1
Muscle spasms			
subjects affected / exposed	3 / 39 (7.69%)	0 / 33 (0.00%)	1 / 34 (2.94%)
occurrences (all)	3	0	1
Osteoarthritis			
subjects affected / exposed	1 / 39 (2.56%)	1 / 33 (3.03%)	0 / 34 (0.00%)
occurrences (all)	1	1	0
Infections and infestations			
Ear infection			
subjects affected / exposed	3 / 39 (7.69%)	0 / 33 (0.00%)	1 / 34 (2.94%)
occurrences (all)	3	0	1
Gastroenteritis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 33 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
Gastroenteritis viral			
subjects affected / exposed	1 / 39 (2.56%)	0 / 33 (0.00%)	2 / 34 (5.88%)
occurrences (all)	1	0	2
Herpes zoster			
subjects affected / exposed	0 / 39 (0.00%)	0 / 33 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	3 / 39 (7.69%)	0 / 33 (0.00%)	1 / 34 (2.94%)
occurrences (all)	3	0	1
Lower respiratory tract infection			
subjects affected / exposed	4 / 39 (10.26%)	0 / 33 (0.00%)	3 / 34 (8.82%)
occurrences (all)	4	0	3
Pneumonia			

subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	3 / 33 (9.09%) 3	0 / 34 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 39 (7.69%) 3	1 / 33 (3.03%) 1	1 / 34 (2.94%) 1
Urinary tract infection subjects affected / exposed occurrences (all)	3 / 39 (7.69%) 3	7 / 33 (21.21%) 7	4 / 34 (11.76%) 4
Metabolism and nutrition disorders Hyponatraemia subjects affected / exposed occurrences (all)	3 / 39 (7.69%) 3	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0

<b>Non-serious adverse events</b>	Placebo/Placebo		
Total subjects affected by non-serious adverse events subjects affected / exposed	33 / 39 (84.62%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Skin cancer subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0		
Vascular disorders Hot flush subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	4 / 39 (10.26%) 4		
Psychiatric disorders Anxiety disorder subjects affected / exposed occurrences (all)  Depression	0 / 39 (0.00%) 0		

subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0		
Injury, poisoning and procedural complications			
Joint injury			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Muscle strain			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences (all)	0		
Pelvic fracture			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences (all)	0		
Soft tissue injury			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences (all)	1		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Palpitations			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 39 (7.69%)		
occurrences (all)	3		
Headache			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences (all)	1		
Lethargy			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences (all)	0		
Loss of consciousness			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences (all)	0		
Migraine			

subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0		
Eye disorders Cataract subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1		
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all)  Constipation subjects affected / exposed occurrences (all)  Diarrhoea subjects affected / exposed occurrences (all)  Diverticulitis subjects affected / exposed occurrences (all)  Irritable bowel syndrome subjects affected / exposed occurrences (all)  Nausea subjects affected / exposed occurrences (all)  Rectal haemorrhage subjects affected / exposed occurrences (all)  Vomiting subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0  1 / 39 (2.56%) 1  0 / 39 (0.00%) 0  2 / 39 (5.13%) 2  0 / 39 (0.00%) 0  2 / 39 (5.13%) 2  0 / 39 (0.00%) 0  1 / 39 (2.56%) 1		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)  Skin ulcer	1 / 39 (2.56%) 1		

subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0		
<b>Musculoskeletal and connective tissue disorders</b>			
Arthralgia subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2		
Arthritis subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0		
Back pain subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1		
Muscle spasms subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0		
Osteoarthritis subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2		
<b>Infections and infestations</b>			
Ear infection subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0		
Gastroenteritis subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2		
Gastroenteritis viral subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0		
Herpes zoster subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2		
Influenza subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1		
Lower respiratory tract infection			

subjects affected / exposed occurrences (all)	4 / 39 (10.26%) 4		
Pneumonia subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 39 (7.69%) 3		
Urinary tract infection subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2		
Metabolism and nutrition disorders Hyponatraemia subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 March 2019	Changes made over course of trial: <ul style="list-style-type: none"><li>- Recruitment extended from 18 months to 30 months</li><li>- Screening criteria for muscle mass changed (to use Sergi equation and to use cutoffs stratified by BMI)</li><li>- Removal of pedometer step count as a secondary outcome</li><li>- Lowering of SARC-F screening threshold from 4 points to 3 points</li></ul>

Notes:

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### 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.

Number of participants recruited (145) is lower than planned recruitment (440) due to slow recruitment. Confidence intervals around outcomes are therefore wider than anticipated and may not exclude minimum clinically important changes
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Notes:

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/29301558>