



Clinical trial results:

Methylphenidate for fatigue in haematological cancer. A randomized, double-blind, placebo-controlled, Crossover trial - the MICRO trial

Summary

EudraCT number	2017-001844-36
Trial protocol	DK
Global end of trial date	16 January 2025

Results information

Result version number	v1 (current)
This version publication date	14 February 2026
First version publication date	14 February 2026

Trial information

Trial identification

Sponsor protocol code	1
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Odense University Hospital
Sponsor organisation address	Kløvervænget 10, Odense , Denmark, 5000
Public contact	Henrik Frederiksen, Odense University Hospital, +45 21849307, henrik.frederiksen@rsyd.dk
Scientific contact	Henrik Frederiksen, Odense University Hospital, +45 21849307, henrik.frederiksen@rsyd.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	02 December 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 January 2025
Global end of trial reached?	Yes
Global end of trial date	16 January 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To study if methylphenidate is superior compared to placebo in relieving fatigue and thereby improving

Primary end-point: Change in fatigue score from baseline to end of treatment in each treatment period

Secondary end-points:

- change in hours awake
- Change in time spend at work, being social, house work / gardening, being outside, participating in exercise
- change in muscle strength and endurance
- change in quality-of-life
- change in number of blood transfusions

Protection of trial subjects:

AEs and SAEs were continuously monitored and managed. Visits were kept to the necessities. Emergency unblinding of study drugs were available 24/7 and performed twice due to SAEs. Safety reports were submitted to Danish authorities who approved all. Safety was discussed among study board members at pre-specified time-points and did not result in any warnings.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 2017
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: 152
Worldwide total number of subjects	152
EEA total number of subjects	152

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	114
From 65 to 84 years	38
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from all Danish Hospitals treating hematological cancer from 2018 to 2024

Pre-assignment

Screening details:

No pre-screening results were recorded. Patients who expressed fatigue during their usual clinical follow-up were screened for eligibility. There were no systematic recording of (pre)screen failures. Main causes for non-inclusion were ongoing cancer treatment, concomitant anti-depressants, cardiovascular disease or glaucoma.

Period 1

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

Blinding implementation details:

Study drug and placebo provided as identical looking tablets. Unblinding was performed after last patient last visit. Emergency unblinding was performed twice due to SAEs

Arms

Are arms mutually exclusive?	No
Arm title	MTP period

Arm description:

Period (first or second) where patients were receiving IMP

Arm type	Experimental
Investigational medicinal product name	Methylphenidate
Investigational medicinal product code	N06BA04
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

week 1: 5 mg twice daily
week 2: 10 mg twice daily
week 3-6: 20 mg twice daily

Arm title	Placebo
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Arm description:

Period (first or second) where participants received placebo

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

Dosage and administration details:

Week 1: half a tablet twice daily
Week 2: one tablet twice daily
From Week 3 2 tablets twice daily

Number of subjects in period 1	MTP period	Placebo
Started	152	152
Completed	139	143
Not completed	13	9
Consent withdrawn by subject	7	1
Physician decision	1	-
Adverse event, non-fatal	5	5
Protocol deviation	-	3

Baseline characteristics

Reporting groups

Reporting group title	RCT crossover design
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Reporting group description: -

Reporting group values	RCT crossover design	Total	
Number of subjects	152	152	
Age categorical			
Age span 21-83. n=114 age 18-64 n=38 age 65-84 n=0 age 85+			
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)	114	114	
From 65-84 years	38	38	
85 years and over	0	0	
Gender categorical			
Males: n= 85 Females: n=67			
Units: Subjects			
Female	67	67	
Male	85	85	

End points

End points reporting groups

Reporting group title	MTP period
Reporting group description:	
Period (first or second) where patients were receiving IMP	
Reporting group title	Placebo
Reporting group description:	
Period (first or second) where participants received placebo	
Subject analysis set title	Main analysis
Subject analysis set type	Per protocol
Subject analysis set description:	
All 130/152 who completed both treatment periods. As per CONSORT guidelines this is the relevant sample for analysis of primary outcome in a cross-over trial	

Primary: Fatigue score

End point title	Fatigue score
End point description:	
Change in FACIT-F score between baseline and end of each treatment period (MTP period vs placebo period)	
End point type	Primary
End point timeframe:	
Change in FACIT-F score between baseline and end of each treatment period (MTP period vs placebo period) - i.e. week 0 to end of week 6 and week 8 to end of week 13	

End point values	MTP period	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130 ^[1]	130 ^[2]		
Units: FACIT-F score				
number (confidence interval 95%)	8.9 (7.3 to 10.4)	3.9 (2.3 to 5.4)		

Notes:

[1] - The 130 patients that completed both periods

[2] - The 130 patients that completed both periods

Statistical analyses

Statistical analysis title	mixed effects linear regression
Statistical analysis description:	
To evaluate whether statistically significant or minimal clinically important differences in FACIT-F scores are observed we formally tested differences in scores across treatment weeks and by treatment using mixed effects linear regression including a week x treatment interaction and a random Gaussian intercept for each patient.	
Comparison groups	Placebo v MTP period

Number of subjects included in analysis	260
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	5
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.8
upper limit	7.2

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Study start to completion (last patient last study visit)

Adverse event reporting additional description:

As recorded by investigators

Assessment type	Systematic
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Dictionary used

Dictionary name	CTCAE
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Dictionary version	4
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Reporting groups

Reporting group title	Both treatment periods
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Reporting group description:

Both periods. The n=130 number reflect subject who had an AE during MTP (n=73) or placebo (n=52). These numbers are not mutually exclusive

Serious adverse events	Both treatment periods		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 152 (3.95%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung cancer	Additional description: One patient was diagnosed with lung cancer during trial and was excluded		
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Dizziness	Additional description: One patient was registered with nausea and dizziness as an SAE but the event was categorized as grade 1.		
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia	Additional description: One patient was registered with a SAE since a blood transfusion required hospital admission.		
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Immune system disorders			
Allergic oedema	Additional description: Angioedema after first IMP. Unblinded to be during MTP		
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Transaminases abnormal	Additional description: Grade 4 transaminitis was unblinded to be during placebo treatment		
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Fracture	Additional description: Metatarsal fracture. Admitted for surgery		
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Both treatment periods		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	125 / 152 (82.24%)		
Cardiac disorders			
Hypertension	Additional description: Heart / circulation: Palpitations, hypertension, atrial fibrillation. across both treatment periods		
subjects affected / exposed	25 / 152 (16.45%)		
occurrences (all)	25		
Nervous system disorders			
Headache	Additional description: Headache, migraine, dizziness, tremor, sleeplessness, impaired concentration.		
subjects affected / exposed	57 / 152 (37.50%)		
occurrences (all)	57		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	11 / 152 (7.24%)		
occurrences (all)	11		
Xerostomia			

subjects affected / exposed occurrences (all)	9 / 152 (5.92%) 9		
Skin and subcutaneous tissue disorders			
Rash	Additional description: Sweating, dryness, oedema, flushing, itching, rash		
subjects affected / exposed occurrences (all)	18 / 152 (11.84%) 18		
Psychiatric disorders			
Anxiety	Additional description: Agitation, restlessness, anxiety		
subjects affected / exposed occurrences (all)	7 / 152 (4.61%) 7		
Musculoskeletal and connective tissue disorders			
Pain	Additional description: Muscle pain, joint pain, back pain, neck pain		
subjects affected / exposed occurrences (all)	17 / 152 (11.18%) 17		
Infections and infestations			
Infection	Additional description: Gastroenteritis, upper respiratory tract infection, lung infection, urinary tract infection, fever, herpes zoster, tooth infection, COVID-19.		
subjects affected / exposed occurrences (all)	19 / 152 (12.50%) 19		

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