



Clinical trial results:

A Phase IIa, single centre, open label, proof of concept study concerning efficacy of the novel intravenous contrast agent SN132D in patients with suspected endometriosis.

Summary

EudraCT number	2022-000652-11
Trial protocol	SE
Global end of trial date	20 June 2023

Results information

Result version number	v1 (current)
This version publication date	30 June 2024
First version publication date	30 June 2024

Trial information

Trial identification

Sponsor protocol code	SPAGOPIX-02
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05664828
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Spago Nanomedical AB
Sponsor organisation address	Scheelevagen 22, Lund, Sweden,
Public contact	mats.hansen@spagonanomedical.se, Spago Nanomedical AB, +46 46 811 88, mats.hansen@spagonanomedical.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	02 October 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 June 2023
Global end of trial reached?	Yes
Global end of trial date	20 June 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To evaluate the MRI enhancing properties of SN132D in participants with suspected endometriosis

Protection of trial subjects:

GDPR followed. GCP Followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 December 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	Sweden: 8
Worldwide total number of subjects	8
EEA total number of subjects	8

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)	8
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were prescreened with TUS

Pre-assignment

Screening details:

Patients with suspected endometriosis

Period 1

Period 1 title	Active infusion baseline (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

N/A

Arms

Arm title	SN132D
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Arm description:

Dose of 20 µmol Mn/kg

Arm type	Experimental
Investigational medicinal product name	SN132D
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

SN132D was administered as a 1-hour single i.v. infusion using a syringe pump with a saline carrier. Participants received a single i.v. infusion of SN132D at a dose of 20 µmol Mn/kg.

Number of subjects in period 1	SN132D
Started	8
Completed	8

Baseline characteristics

Reporting groups

Reporting group title	Active infusion baseline
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Reporting group description: -

Reporting group values	Active infusion baseline	Total	
Number of subjects	8	8	
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)	8	8	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	37.9		
standard deviation	± 7.0	-	
Gender categorical			
Units: Subjects			
Female	8	8	
Race			
Units: Subjects			
White	7	7	
Asian	1	1	
Ethnicity			
Units: Subjects			
Hispanic or Latino	2	2	
Not Hispanic or Latino	6	6	
Body weight			
Units: kg			
arithmetic mean	72.3		
standard deviation	± 12.2	-	
Body mass index (BMI)			
Units: kg/m ²			
arithmetic mean	27.2		
standard deviation	± 4.5	-	

End points

End points reporting groups

Reporting group title	SN132D
Reporting group description:	
Dose of 20 µmol Mn/kg	
Subject analysis set title	MRI analysis set - baseline values
Subject analysis set type	Full analysis
Subject analysis set description:	
The MRI analysis set consisted of all participants who received the IMP and for whom at least the predose MRI scan and 1 post-dose MRI scan had been performed. Results for individual participants at baseline.	
Subject analysis set title	1h after end of MRI infusion
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants in the magnetic resonance imaging (MRI) analysis set who received the SND132D infusion 1 hour after the end of the SN132D infusion	
Subject analysis set title	4h after end of MRI infusion
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants in the magnetic resonance imaging (MRI) analysis set who received the SND132D infusion 4 hours after the end of the SN132D infusion	
Subject analysis set title	TUS analysis set
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants in the magnetic resonance imaging (MRI) analysis set whose endometriosis lesions were evaluated at baseline by transvaginal ultrasound	

Primary: Contrast-to-noise ratio in endometriosis lesions vs endometrium reference tissue

End point title	Contrast-to-noise ratio in endometriosis lesions vs endometrium reference tissue ^[1]
End point description:	
This primary endpoint covered the primary objective of evaluating the MRI enhancing properties of SN132D in participants with suspected endometriosis. The MRI enhancing effect was assessed by evaluating changes between pre-dose images and post-dose images acquired using longitudinal relaxation time (T1)-weighted imaging sequences. Following the baseline MRI scan, study participants received a single dose of SN132D, administered as an intravenous infusion over 1 hour. Post-dose MRI scans were performed twice, at 1 hour and 4 hours after the end of the infusion. The contrast-to-noise ratio in endometriosis lesions was compared to that of reference tissue in a) endometrium (prespecified reference tissue) and b) skeletal muscle (post hoc reference tissue). Note for lesion 9, no MRI scan was performed 4h after the end of the infusion for this participant.	
End point type	Primary
End point timeframe:	
From baseline (pre-dose) to 4 hours after the end of the infusion. Magnetic resonance imaging (MRI) scans were performed at baseline (0h) and at 1h and 4h post-infusion.	

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: No statistical analysis was performed - imaging endpoints were presented using standard descriptive statistics for baseline and post-dose scans for individual participants.

End point values	MRI analysis set - baseline values	1h after end of MRI infusion	4h after end of MRI infusion	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	8	8	7	
Units: Ratio				
number (not applicable)				
Lesion 1 Endometrioma (right ovary)	85.1	46.5	85.7	
Lesion 2 Endometrioma (left ovary)	89.6	55.1	84.4	
Lesion 3 Endometrioma (right ovary)	87.6	108.0	116.3	
Lesion 4 Endometrioma (left ovary)	153.8	115.4	115.9	
Lesion 5 Superficial endometriosis (uterine)	91.2	63.3	96.7	
Lesion 6 Deep endometriosis (abdominal wall)	43.2	44.0	33.4	
Lesion 7 Deep endometriosis (uterine post)	42.5	16.6	15.7	
Lesion 8 Deep endometriosis (uterine ant)	47.5	23.1	19.0	
Lesion 9 Superficial endometriosis (rectal wall)	22.8	8.1	0	
Lesion 10 Superficial endometriosis (rectal wall)	5.5	-11.5	-11.6	
Lesion 11 deep endometriosis (rectal wall)	-47.4	-6.1	-8.7	
Lesion 12 Endometrioma (left ovary)	32.2	44.2	34.8	
Lesion 13 Endometrioma (left ovary)	56.4	62.7	40.5	

Statistical analyses

No statistical analyses for this end point

Primary: Signal-to-noise ratio in endometriosis lesions

End point title	Signal-to-noise ratio in endometriosis lesions ^[2]
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End point description:

This primary endpoint covered the primary objective of evaluating the MRI enhancing properties of SN132D in participants with suspected endometriosis. The MRI enhancing effect was assessed by evaluating changes between pre-dose images and post-dose images acquired using longitudinal relaxation time (T1)-weighted imaging sequences.

Following the baseline MRI scan, study participants received a single dose of SN132D, administered as an intravenous infusion over 1 hour. Post-dose MRI scans were performed twice, at 1 hour and 4 hours after the end of the infusion. The signal-to-noise ratio in endometriosis lesions was compared to that of reference tissue.

Note for lesion 9, no MRI scan was performed 4h after the end of the infusion for this participant.

End point type	Primary
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End point timeframe:

From baseline (pre-dose) to 4 hours after the end of the infusion. Magnetic resonance imaging (MRI) scans were performed at baseline (0h) and at 1h and 4h post-infusion.

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: No statistical analysis was performed - imaging endpoints were presented using standard descriptive statistics for baseline and post-dose scans for individual participants.

End point values	MRI analysis set - baseline values	1h after end of MRI infusion	4h after end of MRI infusion	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	8	8	7	
Units: Ratio				
number (not applicable)				
Lesion 1 Endometrioma (right ovary)	170.9	113.1	192.8	
Lesion 2 Endometrioma (left ovary)	202.2	127.8	196.5	
Lesion 3 Endometrioma (right ovary)	103.0	135.0	144.4	
Lesion 4 Endometrioma (left ovary)	181.3	159.6	152.0	
Lesion 5 Superficial endometriosis (uterine)	121.5	99.4	149.3	
Lesion 6 Deep endometriosis (abdominal wall)	121.5	115.3	103.1	
Lesion 7 Deep endometriosis (uterine post)	105.6	100.7	92.8	
Lesion 8 Deep endometriosis (uterine ant)	105.1	93.6	91.1	
Lesion 9 Superficial endometriosis (rectal wall)	74.6	99.9	0	
Lesion 10 Superficial endometriosis (rectal wall)	38.8	53.3	89.4	
Lesion 11 Deep endometriosis (rectal wall)	56.7	123.0	92.4	
Lesion 12 Endometrioma (left ovary)	139.5	208.7	156.1	
Lesion 13 Endometrioma (left ovary)	224.4	262.4	217.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Compare the number, size and site of deep pelvic endometriosis lesions/endometriosis lesions obtained by SN132D imaging to TUS and clinically used non-contrast MRI

End point title	Compare the number, size and site of deep pelvic endometriosis lesions/endometriosis lesions obtained by SN132D imaging to TUS and clinically used non-contrast MRI
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End point description:

Addresses the secondary objective of evaluating the diagnostic value of SN132D for detection of deep pelvic endometriosis lesions/endometriosis lesions in participants with suspected endometriosis. Following the baseline MRI scan, study participants received a single dose of SN132D by intravenous infusion over 1 hour. Post-dose MRI scans were performed twice, at 1 and 4 hours after the end of the infusion. Endometriosis lesions were measured and classified using the Enzian 2021 classification, a non-invasive and surgical description system for endometriosis. The diagnostic value of SN132D was evaluated by comparing the number, size and site of lesions obtained by SN132D imaging to transvaginal ultrasound and clinically used non-contrast MRI (observed at baseline, 0 h). P=peritoneum. O=ovary. T=tube. A=vagina/rectovaginal space. B=uterosacral ligaments/cardinal ligaments/pelvic sidewall. C=rectum. F=far location (uterine and other extragenital locations).

End point type	Secondary
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End point timeframe:

From baseline (pre-dose) to 4 hours after the end of the infusion. MRI scans were performed at baseline (0h) and at 1h and 4h post-infusion.

End point values	MRI analysis set - baseline values	1h after end of MRI infusion	4h after end of MRI infusion	TUS analysis set
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	8	7	8
Units: Number of participants				
P0: no lesions	8	8	7	7
P1: sum of all diameters <3 cm	0	0	0	0
P2: sum of all diameters 3-7 cm	0	0	0	1
P3: sum of all diameters >7 cm	0	0	0	0
O0 (left): no lesions	3	2	3	3
O1 (left): sum of all diameters <3 cm	1	3	1	2
O2 (left): sum of all diameters 3-7 cm	3	2	1	2
O3 (left): sum of all diameters >7 cm	1	1	2	1
O0 (right): no lesions	3	2	2	3
O1 (right): sum of all diameters <3 cm	4	5	4	2
O2 (right): sum of all diameters 3-7 cm	1	1	1	2
O3 (right): sum of all diameters >7 cm	0	0	0	0
O (right) missing	0	0	0	1
T0 (left): no lesions	1	3	1	1
T1 (left): mild	3	1	1	0
T2 (left): moderate	3	3	4	5
T3 (left): severe	1	1	1	2
T0 (right): no lesions	2	3	1	1
T1 (right): mild	3	4	2	0
T2 (right): moderate	2	0	4	4
T3 (right): severe	1	1	0	2
T (right) missing	0	0	0	1
A0: no lesions	4	4	4	7
A1: <1 cm	0	0	1	0
A2: 1-3 cm	4	3	2	1
A3: >3 cm	0	1	0	0
B0 (left): no lesions	1	2	2	0
B1 (left): <1 cm	1	0	0	1
B2 (left): 1-3 cm	5	5	4	7
B3 (left): >3 cm	1	1	1	0
B0 (right): no lesions	0	3	2	5
B1 (right): <1 cm	2	0	0	0
B2 (right): 1-3 cm	6	5	5	3
B3 (right): >3 cm	0	0	0	0
C0: no lesions	3	4	4	1
C1: <1 cm	1	0	0	0
C2: 1-3 cm	1	1	1	6
C3: >3 cm	3	3	2	1
FA: Adenomyosis	1	0	0	3
FB: Bladder	0	0	0	0
FI: Intestinum	0	0	0	3
FU: Ureter	0	0	0	0

FO: Other location	4	4	3	1
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Statistical analyses

No statistical analyses for this end point

Post-hoc: Contrast-to-noise ratio in endometriosis lesions vs skeletal muscle reference tissue

End point title	Contrast-to-noise ratio in endometriosis lesions vs skeletal muscle reference tissue
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End point description:

This endpoint covered the primary objective of evaluating the MRI enhancing properties of SN132D in participants with suspected endometriosis. The MRI enhancing effect was assessed by evaluating changes between pre-dose images and post-dose images acquired using longitudinal relaxation time (T1)-weighted imaging sequences.

Following the baseline MRI scan, study participants received a single dose of SN132D, administered as an intravenous infusion over 1 hour. Post-dose MRI scans were performed twice, at 1 hour and 4 hours after the end of the infusion. The contrast-to-noise ratio in endometriosis lesions was compared to that of reference tissue in a) endometrium (prespecified) and b) skeletal muscle (post hoc reference tissue). Note for lesion 9, no MRI scan was performed 4h after the end of the infusion for this participant.

End point type	Post-hoc
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End point timeframe:

From baseline (pre-dose) to 4 hours after the end of the infusion. Magnetic resonance imaging (MRI) scans were performed at baseline (0h) and at 1h and 4h post-infusion.

End point values	MRI analysis set - baseline values	1h after end of MRI infusion	4h after end of MRI infusion	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	8	8	7	
Units: Ratio				
number (not applicable)				
Lesion 1 Endometrioma (right ovary)	112.7	68.5	119.6	
Lesion 2 Endometrioma (left ovary)	115.1	71.4	107.1	
Lesion 3 Endometrioma (right ovary)	64.2	85.5	81.6	
Lesion 4 Endometrioma (left ovary)	110.0	94.7	91.2	
Lesion 5 Superficial endometriosis (uterine)	58.8	20.8	39.9	
Lesion 6 Deep endometriosis (abdominal wall)	8.7	9.2	9.4	
Lesion 7 Deep endometriosis (uterine post)	6.3	19.1	15.4	
Lesion 8 Deep endometriosis (uterine ant)	8.0	-5.7	-5.7	
Lesion 9 Superficial endometriosis (rectal wall)	-4.7	4.3	0	
Lesion 10 Superficial endometriosis (rectal wall)	-0.2	4.1	-2.3	
Lesion 11 Deep endometriosis (rectal wall)	-35.2	12.9	12.0	

Lesion 12 Endometrioma (left ovary)	94.3	140.4	101.9	
Lesion 13 Endometrioma (left ovary)	109.3	98.3	87.0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events (AEs, including serious AEs) were collected from the start of IMP administration on day 1 (visit 2) until the follow-up visit (visit 3) on day 3-14.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.1
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Reporting groups

Reporting group title	Full analysis set (FAS)
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Reporting group description:

The FAS consisted of all participants who received at least 1 dose of IMP. This population was used as the safety analysis set.

Serious adverse events	Full analysis set (FAS)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Full analysis set (FAS)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 8 (87.50%)		
Vascular disorders			
Flushing			
subjects affected / exposed	5 / 8 (62.50%)		
occurrences (all)	5		
Hypertension			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		

General disorders and administration site conditions Injection site pain subjects affected / exposed occurrences (all)	5 / 8 (62.50%) 5		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	6 / 8 (75.00%) 6 2 / 8 (25.00%) 2		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		

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