Clinical trial results:
Pilot study:
Anti-inflammatory effect of preoperative stimulation of the enteric nervous system: a potential new therapeutic intervention to shorten gastroparesis

Summary

EudraCT number	2014-000361-52
Trial protocol	BE
Global end of trial date	27 February 2016

Results information

Result version number	v1 (current)
This version publication date	10 September 2025
First version publication date	10 September 2025

Trial information

Trial identification

Sponsor protocol code	prucalopride/VNS1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02425774
WHO universal trial number (UTN)	-
Other trial identifiers	EC UZ Leuven S-number: S56328

Notes:

Sponsors

Sponsor organisation name	UZ Leuven
Sponsor organisation address	Herestraat 49, Leuven, Belgium, 3000
Public contact	Guy Boeckxstaens, KULeuven, guy.boeckxstaens@kuleuven.be
Scientific contact	Guy Boeckxstaens, KULeuven, guy.boeckxstaens@kuleuven.be

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	01 January 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 February 2016
Global end of trial reached?	Yes
Global end of trial date	27 February 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate whether prucalopride has anti-inflammatory properties.

Protection of trial subjects:

Patients signed the informed consent prior any study specific activity.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 July 2014
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	Belgium: 42
Worldwide total number of subjects	42
EEA total number of subjects	42

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	23
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Inclusion:
- patients undergoing Pylorus Preserving Pancreatico Duodenectomie (PD), or Pylorus-resecting PD for oncologic reasons
- age > 18
Exclusion:
- adjuvant radiotherapy
- intra-abdominal inflammation
- PD for chronic pancreatitis or pancreatic polypeptide producing endocrine tumor
- ASA-PS > 3
- Uncontrolled diabetes (>200mg/dl)

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Prucalopride

Arm description:

Patients were treated with 2 mg prucalopride (12 and 2 hours prior to surgery) and received sham stimulation at the start and the end of the surgery.

Arm type	Pharmacological arm
Investigational medicinal product name	Prucalopride succinate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

2h before surgery: 1*2 mg
12h before surgery: 1*2mg

Arm title	abdominal Vagus Nerve Stimulation

Arm description:

Patients received abdominal VNS (2min, 20Hz, 2.5 mA, 1ms at the start and end of the surgical procedure) + placebo

Arm type	Electrical stimulation

No investigational medicinal product assigned in this arm

Arm title	Sham stimulation/placebo

Arm description:

Patients allocated to placebo received sham stimulation at the start and end of surgery, as well as a placebo tablet 12h and 2h before the surgery.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Prucalopride	abdominal Vagus Nerve Stimulation	Sham stimulation/placebo
Started	13	16	13
Completed	10	10	10
Not completed	3	6	3
Consent withdrawn by subject	-	1	-
Screening failure	-	-	1
Inoperability	3	3	-
Protocol deviation	-	2	2

Period 2	
Period 2 title	2h post-operative
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Prucalopride - 2h postoperative

Arm description:

Patients were treated with 2 mg prucalopride (12 and 2 hours prior to surgery) and received sham stimulation at the start and the end of the surgery.

Arm type	Pharmacological arm
Investigational medicinal product name	Prucalopride succinate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

2h before surgery: 1*2 mg
12h before surgery: 1*2mg

Arm title	abdominal Vagus Nerve Stimulation -2h postoperative

Arm description:

Patients received abdominal VNS (2min, 20Hz, 2.5 mA, 1ms at the start and end of the surgical procedure) + placebo

Arm type	Electrical stimulation

No investigational medicinal product assigned in this arm

Arm title	Sham stimulation/placebo - 2h postoperative

Arm description:

Patients allocated to placebo received sham stimulation at the start and end of surgery as well as a placebo tablet at 12h and 2h before surgery.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2	Prucalopride - 2h postoperative	abdominal Vagus Nerve Stimulation - 2h postoperative	Sham stimulation/placebo - 2h postoperative
Started	10	10	10
Completed	10	10	10

Period 3	
Period 3 title	24h postoperative
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Prucalopride - 24h postoperative

Arm description:

Patients were treated with 2 mg prucalopride (12 and 2 hours prior to surgery) and received sham stimulation at the start and the end of the surgery.

Arm type	Pharmacological arm
Investigational medicinal product name	Prucalopride succinate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

2h before surgery: 1*2 mg
12h before surgery: 1*2mg

Arm title	abdominal Vagus Nerve Stimulation - 24h postoperative

Arm description:

Patients received abdominal VNS (2min, 20Hz, 2.5 mA, 1ms at the start and end of the surgical procedure) + placebo

Arm type	Electrical stimulation

No investigational medicinal product assigned in this arm

Arm title	Sham stimulation/placebo - 24h postoperative

Arm description:

Patients allocated to placebo received sham stimulation at the start and end of surgery, as well as a placebo tablet 12h and 2h before the surgery.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 3	Prucalopride - 24h postoperative	abdominal Vagus Nerve Stimulation - 24h postoperative	Sham stimulation/placebo - 24h postoperative
Started	10	10	10
Completed	10	10	10

Period 4	
Period 4 title	48h postoperative
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms	
Are arms mutually exclusive?	Yes
Arm title	Prucalopride - 48h postoperative

Arm description:

Patients were treated with 2 mg prucalopride (12 and 2 hours prior to surgery) and received sham stimulation at the start and the end of the surgery.

Arm type	Pharmacological arm
Investigational medicinal product name	Prucalopride succinate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

2h before surgery: 1*2 mg
12h before surgery: 1*2mg

Arm title	abdominal Vagus Nerve Stimulation - 48h postoperative

Arm description:

Patients received abdominal VNS (2min, 20Hz, 2.5 mA, 1ms at the start and end of the surgical procedure) + placebo

Arm type	Electrical stimulation

No investigational medicinal product assigned in this arm

Arm title	Sham stimulation/placebo - 48h postoperative

Arm description:

Patients allocated to placebo received sham stimulation at the start and end of surgery, as well as a placebo tablet 12h and 2h before the surgery.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 4	Prucalopride - 48h postoperative	abdominal Vagus Nerve Stimulation - 48h postoperative	Sham stimulation/placebo - 48h postoperative
Started	10	10	10
Completed	10	10	10

Period 5	
Period 5 title	Postoperative stay
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Prucalopride - postoperative stay

Arm description:

Patients were treated with 2 mg prucalopride (12 and 2 hours prior to surgery) and received sham stimulation at the start and the end of the surgery.

Arm type	Pharmacological arm
Investigational medicinal product name	Prucalopride succinate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

2h before surgery: 1*2 mg
12h before surgery: 1*2mg

Arm title	abdominal Vagus Nerve Stimulation - postoperative stay

Arm description:

Patients received abdominal VNS (2min, 20Hz, 2.5 mA, 1ms at the start and end of the surgical procedure) + placebo

Arm type	Electrical stimulation

No investigational medicinal product assigned in this arm

Arm title	Sham stimulation/placebo - postoperative stay

Arm description:

Patients allocated to placebo received sham stimulation at the start and end of surgery, as well as a placebo tablet 12h and 2h before the surgery.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 5	Prucalopride - postoperative stay	abdominal Vagus Nerve Stimulation - postoperative stay	Sham stimulation/placebo - postoperative stay
Started	10	10	10
Completed	10	10	10

Baseline characteristics

Reporting groups	
Reporting group title	Overall baseline period

Reporting group description: -

Reporting group values	Overall baseline period	Total	
Number of subjects	42	42	
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)	19	19	
From 65-84 years	23	23	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	22	22	
Male	20	20	

End points

End points reporting groups

Reporting group title	Prucalopride
Reporting group description:	
Patients were treated with 2 mg prucalopride (12 and 2 hours prior to surgery) and received sham stimulation at the start and the end of the surgery.	
Reporting group title	abdominal Vagus Nerve Stimulation
Reporting group description:	
Patients received abdominal VNS (2min, 20Hz, 2.5 mA, 1ms at the start and end of the surgical procedure) + placebo	
Reporting group title	Sham stimulation/placebo
Reporting group description:	
Patients allocated to placebo received sham stimulation at the start and end of surgery, as well as a placebo tablet 12h and 2h before the surgery.	
Reporting group title	Prucalopride - 2h postoperative
Reporting group description:	
Patients were treated with 2 mg prucalopride (12 and 2 hours prior to surgery) and received sham stimulation at the start and the end of the surgery.	
Reporting group title	abdominal Vagus Nerve Stimulation -2h postoperative
Reporting group description:	
Patients received abdominal VNS (2min, 20Hz, 2.5 mA, 1ms at the start and end of the surgical procedure) + placebo	
Reporting group title	Sham stimulation/placebo - 2h postoperative
Reporting group description:	
Patients allocated to placebo received sham stimulation at the start and end of surgery as well as a placebo tablet at 12h and 2h before surgery.	
Reporting group title	Prucalopride - 24h postoperative
Reporting group description:	
Patients were treated with 2 mg prucalopride (12 and 2 hours prior to surgery) and received sham stimulation at the start and the end of the surgery.	
Reporting group title	abdominal Vagus Nerve Stimulation - 24h postoperative
Reporting group description:	
Patients received abdominal VNS (2min, 20Hz, 2.5 mA, 1ms at the start and end of the surgical procedure) + placebo	
Reporting group title	Sham stimulation/placebo - 24h postoperative
Reporting group description:	
Patients allocated to placebo received sham stimulation at the start and end of surgery, as well as a placebo tablet 12h and 2h before the surgery.	
Reporting group title	Prucalopride - 48h postoperative
Reporting group description:	
Patients were treated with 2 mg prucalopride (12 and 2 hours prior to surgery) and received sham stimulation at the start and the end of the surgery.	
Reporting group title	abdominal Vagus Nerve Stimulation - 48h postoperative
Reporting group description:	
Patients received abdominal VNS (2min, 20Hz, 2.5 mA, 1ms at the start and end of the surgical procedure) + placebo	
Reporting group title	Sham stimulation/placebo - 48h postoperative
Reporting group description:	
Patients allocated to placebo received sham stimulation at the start and end of surgery, as well as a placebo tablet 12h and 2h before the surgery.	
Reporting group title	Prucalopride - postoperative stay
Reporting group description:	
Patients were treated with 2 mg prucalopride (12 and 2 hours prior to surgery) and received sham stimulation at the start and the end of the surgery.	

Reporting group title	abdominal Vagus Nerve Stimulation - postoperative stay

Reporting group description:

Patients received abdominal VNS (2min, 20Hz, 2.5 mA, 1ms at the start and end of the surgical procedure) + placebo

Reporting group title	Sham stimulation/placebo - postoperative stay

Reporting group description:

Patients allocated to placebo received sham stimulation at the start and end of surgery, as well as a placebo tablet 12h and 2h before the surgery.

Primary: Pro-inflammatory genes in muscularis tissue: IL-6

End point title	Pro-inflammatory genes in muscularis tissue: IL-6

End point description:

Relative mRNA gene-expression of IL-6 in the muscularis externa normalised to the housekeeping gene c12fr43.

Reporting groups:
- reporting group 1: PRUC, 0h
- reporting group 2: VNS, 0h
- reporting group 3: SHAM/PLAC, 0h
- reporting group 4: PRUC, 2h
- reporting group 5: VNS, 2h
- reporting group 6: SHAM/PLAC, 2h

End point type	Primary

End point timeframe:

Biopsies from the small intestine at the beginning and end of surgery.
Small intestine was removed as part of the surgery.

End point values	Prucalopride	abdominal Vagus Nerve Stimulation	Sham stimulation/placebo	Prucalopride - 2h postoperative
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[1]	10	10	9[2]
Units: relative unit(s)				
arithmetic mean (standard error)	0.0307 (± 0.1438)	0.02032 (± 0.00662)	0.0165 (± 0.006028)	0.7192 (± 0.1598)

Notes:

[1] - One significant outlier was left out (Grubb’s test for outliers).

[2] - One significant outlier was left out (Grubb’s test for outliers).

End point values	abdominal Vagus Nerve Stimulation -2h postoperative	Sham stimulation/placebo - 2h postoperative		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: relative unit(s)				
arithmetic mean (standard error)	1.044 (± 0.2095)	1.742 (± 0.4337)		

Statistical analyses

Statistical analysis title	IL-6 mRNA expr SHAM/PLAC 0h vs PRUC 0h

Statistical analysis description:

Relative mRNA expression of IL-6 in the muscularis externa, normalised to the housekeeping gene c10fr43

Comparison groups	Sham stimulation/placebo v Prucalopride
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	equivalence[3]
P-value	> 0.05
Method	ANOVA

Notes:

[3] - Repeated two-way analysis of variance (ANOVA) with Bonferroni correction for multiple testing

Statistical analysis title	IL-6 mRNA expr SHAM/PLAC 0h vs VNS 0h

Statistical analysis description:

Relative mRNA expression of IL-6 in the muscularis externa, normalised to the housekeeping gene c10fr43

Comparison groups	abdominal Vagus Nerve Stimulation v Sham stimulation/placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence[4]
P-value	> 0.05
Method	ANOVA

Notes:

[4] - Repeated two-way analysis of variance (ANOVA) with Bonferroni correction for multiple testing

Statistical analysis title	IL-6 mRNA expr VNS 0h vs PRUC 0h

Statistical analysis description:

Relative mRNA expression of IL-6 in the muscularis externa, normalised to the housekeeping gene c10fr43

Comparison groups	Prucalopride v abdominal Vagus Nerve Stimulation
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	equivalence[5]
P-value	> 0.05
Method	ANOVA

Notes:

[5] - Repeated two-way analysis of variance (ANOVA) with Bonferroni correction for multiple testing

Statistical analysis title	IL-6 mRNA expr SHAM/PLAC 2h vs PRUC 2h

Statistical analysis description:

Relative mRNA expression of IL-6 in the muscularis externa, normalised to the housekeeping gene c10fr43

Comparison groups	Prucalopride - 2h postoperative v Sham stimulation/placebo - 2h postoperative
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	equivalence[6]
P-value	< 0.05
Method	ANOVA

Notes:

[6] - Repeated two-way analysis of variance (ANOVA) with Bonferroni correction for multiple testing

Statistical analysis title	IL-6 mRNA expr SHAM/PLAC 0h vs VNS 0h

Statistical analysis description:

Relative mRNA expression of IL-6 in the muscularis externa, normalised to the housekeeping gene c10fr43

Comparison groups	abdominal Vagus Nerve Stimulation -2h postoperative v Sham stimulation/placebo - 2h postoperative
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence[7]
P-value	> 0.05
Method	ANOVA

Notes:

[7] - Repeated two-way analysis of variance (ANOVA) with Bonferroni correction for multiple testing

Statistical analysis title	IL-6 mRNA expr VNS 2h vs PRUC 2h

Statistical analysis description:

Relative mRNA expression of IL-6 in the muscularis externa, normalised to the housekeeping gene c10fr43

Comparison groups	Prucalopride - 2h postoperative v abdominal Vagus Nerve Stimulation -2h postoperative
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	equivalence[8]
P-value	> 0.05
Method	ANOVA

Notes:

[8] - Repeated two-way analysis of variance (ANOVA) with Bonferroni correction for multiple testing

Primary: Pro-inflammatory genes in muscularis tissue: IL-8

End point title	Pro-inflammatory genes in muscularis tissue: IL-8

End point description:

Relative mRNA gene-expression of IL-6 in the muscularis externa normalised to the housekeeping gene c12fr43.

Reporting groups:
- reporting group 1: PRUC, 0h
- reporting group 2: VNS, 0h
- reporting group 3: SHAM/PLAC, 0h
- reporting group 4: PRUC, 2h
- reporting group 5: VNS, 2h
- reporting group 6: SHAM/PLAC, 2h

End point type	Primary

End point timeframe:

Biopsies from the small intestine at the beginning and end of surgery.
Small intestine was removed as part of the surgery.

End point values	Prucalopride	abdominal Vagus Nerve Stimulation	Sham stimulation/placebo	Prucalopride - 2h postoperative
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[9]	10	10	9[10]
Units: relative unit(s)				
arithmetic mean (standard error)	0.001979 (± 0.0005383)	0.002539 (± 0.0009011)	0.003581 (± 0.002201)	0.3409 (± 0.1428)

Notes:

[9] - One significant outlier was left out (Grubb’s test for outliers).

[10] - One significant outlier was left out (Grubb’s test for outliers).

End point values	abdominal Vagus Nerve Stimulation -2h postoperative	Sham stimulation/placebo - 2h postoperative		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: relative unit(s)				
arithmetic mean (standard error)	0.9788 (± 0.3261)	0.9867 (± 0.3046)		

Statistical analyses

Statistical analysis title	IL-8 mRNA expr SHAM/PLAC 0h vs PRUC 0h

Statistical analysis description:

Relative mRNA expression of IL-8 in the muscularis externa, normalised to the housekeeping gene c10fr43

Comparison groups	Prucalopride v Sham stimulation/placebo
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	equivalence[11]
P-value	> 0.05
Method	ANOVA

Notes:

[11] - Repeated two-way analysis of variance (ANOVA) with Bonferroni correction for multiple testing

Statistical analysis title	IL-8 mRNA expr SHAM/PLAC 0h vs VNS 0h

Statistical analysis description:

Relative mRNA gene-expression of IL-8 in the muscularis externa normalised to the housekeeping gene c12fr43.

Comparison groups	abdominal Vagus Nerve Stimulation v Sham stimulation/placebo

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence[12]
P-value	> 0.05
Method	ANOVA

Notes:

[12] - Repeated two-way analysis of variance (ANOVA) with Bonferroni correction for multiple testing

Statistical analysis title	IL-8 mRNA expr PRUC 0h vs VNS 0h

Statistical analysis description:

Relative mRNA gene-expression of IL-8 in the muscularis externa normalised to the housekeeping gene c12fr43.

Comparison groups	Prucalopride v abdominal Vagus Nerve Stimulation
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	equivalence[13]
P-value	> 0.05
Method	ANOVA

Notes:

[13] - Repeated two-way analysis of variance (ANOVA) with Bonferroni correction for multiple testing

Statistical analysis title	IL-8 mRNA expr SHAM/PLAC 2h vs PRUC 2h
Comparison groups	Sham stimulation/placebo - 2h postoperative v Prucalopride - 2h postoperative
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	equivalence[14]
P-value	< 0.05
Method	ANOVA

Notes:

[14] - Repeated two-way analysis of variance (ANOVA) with Bonferroni correction for multiple testing

Statistical analysis title	IL-8 mRNA expr SHAM/PLAC 2h vs VNS 2h
Comparison groups	abdominal Vagus Nerve Stimulation -2h postoperative v Sham stimulation/placebo - 2h postoperative
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence[15]
P-value	> 0.05
Method	ANOVA

Notes:

[15] - Repeated two-way analysis of variance (ANOVA) with Bonferroni correction for multiple testing

Statistical analysis title	IL-8 mRNA expr PRUC 2h vs VNS 2h
Comparison groups	Prucalopride - 2h postoperative v abdominal Vagus Nerve Stimulation -2h postoperative

Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	equivalence[16]
P-value	> 0.05
Method	ANOVA

Notes:

[16] - Repeated two-way analysis of variance (ANOVA) with Bonferroni correction for multiple testing

Primary: IL-6 in serum, 0h (baseline)

End point title	IL-6 in serum, 0h (baseline)

End point description:

All statistical analysis performed for this endpoint were not significant. All analysis were pre-specified, equivalence.
The analysis was done with Kruskall-wallis with Dunn's correction per timepoint (0, 2, 24, 48 hours postoperative).
- IL-6 serum SHAM/PLAC 0h vs PRUC 0h: p>0.05
- IL-6 serum SHAM/PLAC 0h vs VNS 0h: p>0.05
- IL-6 serum PRUC 0h vs VNS 0h: p>0.05

End point type	Primary

End point timeframe:

IL-6 in serum was measured at following time points: 0h, 2h, 24h and 48h after surgery.

End point values	Prucalopride	abdominal Vagus Nerve Stimulation	Sham stimulation/placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	10	10	
Units: picogram(s)/millilitre				
median (full range (min-max))	2.36667 (0.55915 to 8.988483)	3.7465015 (0.764547 to 12.74663)	2.1877395 (0.617229 to 12.41471)	

Statistical analyses

Statistical analysis title	IL-6 serum SHAM/PLAC 0h vs PRUC 0h

Statistical analysis description:

Kruskall-Wallis with Dunn's correction per timepoint (0,2,24,48 hours)

Comparison groups	Prucalopride v Sham stimulation/placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	Kruskal-wallis

Primary: IL-6 in serum, 2h postoperative

End point title	IL-6 in serum, 2h postoperative

End point description:

All statistical analysis performed for this endpoint were not significant. All analysis were pre-specified, equivalence.
The analysis was done with Kruskall-wallis with Dunn's correction per timepoint (0, 2, 24, 48 hours postoperative).
- IL-6 serum SHAM/PLAC 2h vs PRUC 2h: p>0.05
- IL-6 serum SHAM/PLAC 2h vs VNS 2h: p>0.05
- IL-6 serum PRUC 2h vs VNS 2h: p>0.05

End point type	Primary

End point timeframe:

IL-6 in serum was measured at following time points: 0h, 2h, 24h and 48h after surgery.

End point values	Prucalopride - 2h postoperative	abdominal Vagus Nerve Stimulation -2h postoperative	Sham stimulation/placebo - 2h postoperative	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	10	10	
Units: picogram(s)/millilitre				
median (full range (min-max))	44.81418 (7.331739 to 80.13982)	42.19487 (10.7193 to 226.3681)	45.514405 (18.64029 to 176.1539)	

Statistical analyses

Statistical analysis title	IL-6 serum SHAM/PLAC 2h vs PRUC 2h
Comparison groups	Sham stimulation/placebo - 2h postoperative v Prucalopride - 2h postoperative
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	Kruskal-wallis

Primary: IL-6 in serum, 24h postoperative

End point title	IL-6 in serum, 24h postoperative

End point description:

All statistical analysis performed for this endpoint were not significant. All analysis were pre-specified, equivalence.
The analysis was done with Kruskall-wallis with Dunn's correction per timepoint (0, 2, 24, 48 hours postoperative).
- IL-6 serum SHAM/PLAC 24h vs PRUC 24h: p>0.05
- IL-6 serum SHAM/PLAC 24h vs VNS 24h: p>0.05
- IL-6 serum PRUC 24h vs VNS 24h: p>0.05

End point type	Primary

End point timeframe:

IL-6 in serum was measured at following time points: 0h, 2h, 24h and 48h after surgery.

End point values	Prucalopride - 24h postoperative	abdominal Vagus Nerve Stimulation - 24h postoperative	Sham stimulation/placebo - 24h postoperative	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	10	10	
Units: picogram(s)/millilitre				
median (full range (min-max))	38.24138 (12.13932 to 384.1603)	104.67677 (4.030243 to 228.1577)	44.35539 (16.2332 to 87.88212)	

Statistical analyses

Statistical analysis title	IL-6 serum SHAM/PLAC 24h vs PRUC 24h
Comparison groups	Prucalopride - 24h postoperative v Sham stimulation/placebo - 24h postoperative
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	Kruskal-wallis

Primary: IL-6 in serum, 48h postoperative

End point title	IL-6 in serum, 48h postoperative

End point description:

All statistical analysis performed for this endpoint were not significant. All analysis were pre-specified, equivalence.
The analysis was done with Kruskall-wallis with Dunn's correction per timepoint (0, 2, 24, 48 hours postoperative).
- IL-6 serum SHAM/PLAC 48h vs PRUC 48h: p>0.05
- IL-6 serum SHAM/PLAC 48h vs VNS 48h: p>0.05
- IL-6 serum PRUC 48h vs VNS 48h: p>0.05

End point type	Primary

End point timeframe:

IL-6 in serum was measured at following time points: 0h, 2h, 24h and 48h after surgery.

End point values	Prucalopride - 48h postoperative	abdominal Vagus Nerve Stimulation - 48h postoperative	Sham stimulation/placebo - 48h postoperative	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	10	10	
Units: picogram(s)/millilitre				
median (full range (min-max))	20.273315 (5.037318 to 116.5325)	24.37853 (6.258462 to 456.0946)	21.307805 (8.422992 to 82.77205)	

Statistical analyses

Statistical analysis title	IL-6 serum SHAM/PLAC 48h vs PRUC 48h

Statistical analysis description:

Kruskall-Wallis with Dunn's correction per timepoint (0,2,24,48 hours)

Comparison groups	Sham stimulation/placebo - 48h postoperative v Prucalopride - 48h postoperative
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	Kruskal-wallis

Primary: IL-8 in serum, 0h (baseline)

End point title	IL-8 in serum, 0h (baseline)

End point description:

All statistical analysis performed for this endpoint were not significant. All analysis were pre-specified, equivalence.
The analysis was done with Kruskall-wallis with Dunn's correction per timepoint (0, 2, 24, 48 hours postoperative).
- IL-8 serum SHAM/PLAC 0h vs PRUC 0h: p>0.05
- IL-8 serum SHAM/PLAC 0h vs VNS 0h: p>0.05
- IL-8 serum PRUC 0h vs VNS 0h: p>0.05

End point type	Primary

End point timeframe:

IL-8 in serum was measured at following time points: 0h, 2h, 24h and 48h after surgery.

End point values	Prucalopride	abdominal Vagus Nerve Stimulation	Sham stimulation/placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	10	10	
Units: picogram(s)/millilitre				
median (full range (min-max))	22.81154 (9.915079 to 106.0631)	21.90382 (10.08026 to 254.0737)	32.21309 (7.325124 to 373.6089)	

Statistical analyses

Statistical analysis title	IL-8 serum SHAM/PLAC 0h vs PRUC 0h

Statistical analysis description:

Kruskall-Wallis with Dunn's correction per timepoint (0,2,24,48 hours)

Comparison groups	Sham stimulation/placebo v Prucalopride
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	Kruskal-wallis

Primary: IL-8 in serum, 2h postoperative

End point title	IL-8 in serum, 2h postoperative

End point description:

All statistical analysis performed for this endpoint were not significant. All analysis were pre-specified, equivalence.
The analysis was done with Kruskall-wallis with Dunn's correction per timepoint (0, 2, 24, 48 hours postoperative).
- IL-8 serum SHAM/PLAC 2h vs PRUC 2h: p>0.05
- IL-8 serum SHAM/PLAC 2h vs VNS 2h: p>0.05
- IL-8 serum PRUC 2h vs VNS 2h: p>0.05

End point type	Primary

End point timeframe:

IL-8 in serum was measured at following time points: 0h, 2h, 24h and 48h after surgery.

End point values	Prucalopride - 2h postoperative	abdominal Vagus Nerve Stimulation -2h postoperative	Sham stimulation/placebo - 2h postoperative	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	10	10	
Units: picogram(s)/millilitre				
median (full range (min-max))	48.73039 (14.997 to 147.3282)	50.9942 (11.64753 to 259.1205)	84.6272 (11.72516 to 410.5159)	

Statistical analyses

Statistical analysis title	IL-8 serum SHAM/PLAC 2h vs PRUC 2h
Statistical analysis description: Kruskall-Wallis with Dunn's correction per timepoint (0,2,24,48 hours)	
Comparison groups	Prucalopride - 2h postoperative v Sham stimulation/placebo - 2h postoperative
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	Kruskal-wallis

Primary: IL-8 in serum, 24h postoperative

End point title	IL-8 in serum, 24h postoperative

End point description:

All statistical analysis performed for this endpoint were not significant. All analysis were pre-specified, equivalence.
The analysis was done with Kruskall-wallis with Dunn's correction per timepoint (0, 2, 24, 48 hours postoperative).
- IL-8 serum SHAM/PLAC 24h vs PRUC 24h: p>0.05
- IL-8 serum SHAM/PLAC 24h vs VNS 24h: p>0.05
- IL-8 serum PRUC 24h vs VNS 24h: p>0.05

End point type	Primary

End point timeframe:

IL-8 in serum was measured at following time points: 0h, 2h, 24h and 48h after surgery.

End point values	Prucalopride - 24h postoperative	abdominal Vagus Nerve Stimulation - 24h postoperative	Sham stimulation/placebo - 24h postoperative	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	10	10	
Units: picogram(s)/millilitre				
median (full range (min-max))	25.147385 (13.00137 to 174.2133)	30.29369 (6.455689 to 272.6213)	45.30166 (19.61076 to 92.94854)	

Statistical analyses

Statistical analysis title	IL-8 serum SHAM/PLAC 24h vs PRUC 24h
Statistical analysis description: Kruskall-Wallis with Dunn's correction per timepoint (0,2,24,48 hours)	
Comparison groups	Sham stimulation/placebo - 24h postoperative v Prucalopride - 24h postoperative

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	Kruskal-wallis

Primary: IL-8 in serum, 48h postoperative

End point title	IL-8 in serum, 48h postoperative

End point description:

All statistical analysis performed for this endpoint were not significant. All analysis were pre-specified, equivalence.
The analysis was done with Kruskall-wallis with Dunn's correction per timepoint (0, 2, 24, 48 hours postoperative).
- IL-8 serum SHAM/PLAC 48h vs PRUC 48h: p>0.05
- IL-8 serum SHAM/PLAC 48h vs VNS 48h: p>0.05
- IL-8 serum PRUC 48h vs VNS 48h: p>0.05

End point type	Primary

End point timeframe:

IL-8 in serum was measured at following time points: 0h, 2h, 24h and 48h after surgery.

End point values	Prucalopride - 48h postoperative	abdominal Vagus Nerve Stimulation - 48h postoperative	Sham stimulation/placebo - 48h postoperative	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	10	10	
Units: picogram(s)/millilitre				
median (full range (min-max))	16.944955 (9.331727 to 110)	17.68162 (8.990667 to 140.5201)	27.99449 (15.92338 to 42.12079)	

Statistical analyses

Statistical analysis title	IL-8 serum SHAM/PLAC 48h vs PRUC 48h

Statistical analysis description:

Kruskall-Wallis with Dunn's correction per timepoint (0,2,24,48 hours)

Comparison groups	Prucalopride - 48h postoperative v Sham stimulation/placebo - 48h postoperative
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	Kruskal-wallis

Primary: TNF-alpha in serum, 0h (baseline)

End point title	TNF-alpha in serum, 0h (baseline)

End point description:

All statistical analysis performed for this endpoint were not significant. All analysis were pre-specified, equivalence.
The analysis was done with Kruskall-wallis with Dunn's correction per timepoint (0, 2, 24, 48 hours postoperative).
- TNFα serum SHAM/PLAC 0h vs PRUC 0h: p>0.05
- TNFα serum SHAM/PLAC 0h vs VNS 0h: p>0.05
- TNFα serum PRUC 0h vs VNS 0h: p>0.05

End point type	Primary

End point timeframe:

TNFα in serum was measured at following time points: 0h, 2h, 24h and 48h after surgery.

End point values	Prucalopride	abdominal Vagus Nerve Stimulation	Sham stimulation/placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	10	10	
Units: picogram(s)/millilitre				
median (full range (min-max))	3.023515 (1.632236 to 5.544945)	3.847894 (2.377238 to 5.25516)	3.101691 (1.599626 to 12.31394)	

Statistical analyses

Statistical analysis title	TNFα serum SHAM/PLAC 0h vs PRUC 0h

Statistical analysis description:

Kruskall-Wallis with Dunn's correction per timepoint (0,2,24,48 hours)

Comparison groups	Prucalopride v Sham stimulation/placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	Kruskal-wallis

Primary: TNF-alpha in serum, 2h postoperative

End point title	TNF-alpha in serum, 2h postoperative

End point description:

All statistical analysis performed for this endpoint were not significant. All analysis were pre-specified, equivalence.
The analysis was done with Kruskall-wallis with Dunn's correction per timepoint (0, 2, 24, 48 hours postoperative).

- TNFα serum SHAM/PLAC 2h vs PRUC 2h: p>0.05
- TNFα serum SHAM/PLAC 2h vs VNS 2h: p>0.05
- TNFα serum PRUC 2h vs VNS 2h: p>0.05

End point type	Primary

End point timeframe:

TNFα in serum was measured at following time points: 0h, 2h, 24h and 48h after surgery.

End point values	Prucalopride - 2h postoperative	abdominal Vagus Nerve Stimulation -2h postoperative	Sham stimulation/placebo - 2h postoperative	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	10	10	
Units: picogram(s)/millilitre				
median (full range (min-max))	3.188469 (0.985607 to 6.316739)	3.23437 (2.080917 to 4.639587)	4.0991915 (1.224778 to 8.70794)	

Statistical analyses

Statistical analysis title	TNFα serum SHAM/PLAC 2h vs PRUC 2h

Statistical analysis description:

Kruskall-Wallis with Dunn's correction per timepoint (0,2,24,48 hours)

Comparison groups	Prucalopride - 2h postoperative v Sham stimulation/placebo - 2h postoperative
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	Kruskal-wallis

Primary: TNF-alpha in serum, 24h postoperative

End point title	TNF-alpha in serum, 24h postoperative

End point description:

All statistical analysis performed for this endpoint were not significant. All analysis were pre-specified, equivalence.
The analysis was done with Kruskall-wallis with Dunn's correction per timepoint (0, 2, 24, 48 hours postoperative).
- TNFα serum SHAM/PLAC 24h vs PRUC 24h: p>0.05
- TNFα serum SHAM/PLAC 24h vs VNS 24h: p>0.05
- TNFα serum PRUC 24h vs VNS 24h: p>0.05

End point type	Primary

End point timeframe:

TNFα in serum was measured at following time points: 0h, 2h, 24h and 48h after surgery.

End point values	Prucalopride - 24h postoperative	abdominal Vagus Nerve Stimulation - 24h postoperative	Sham stimulation/placebo - 24h postoperative	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	10	10	
Units: picogram(s)/millilitre				
median (full range (min-max))	2.7994345 (1.417976 to 4.901272)	3.0247145 (1.50724 to 9.428092)	3.85771 (2.389357 to 5.429664)	

Statistical analyses

Statistical analysis title	TNFα serum SHAM/PLAC 24h vs PRUC 24h

Statistical analysis description:

Kruskall-Wallis with Dunn's correction per timepoint (0,2,24,48 hours)

Comparison groups	Prucalopride - 24h postoperative v Sham stimulation/placebo - 24h postoperative
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	Kruskal-wallis

Primary: TNF-alpha in serum, 48h postoperative

End point title	TNF-alpha in serum, 48h postoperative

End point description:

All statistical analysis performed for this endpoint were not significant. All analysis were pre-specified, equivalence.
The analysis was done with Kruskall-wallis with Dunn's correction per timepoint (0, 2, 24, 48 hours postoperative).
- TNFα serum SHAM/PLAC 48h vs PRUC 48h: p>0.05
- TNFα serum SHAM/PLAC 48h vs VNS 48h: p>0.05
- TNFα serum PRUC 48h vs VNS 48h: p>0.05

End point type	Primary

End point timeframe:

TNFα in serum was measured at following time points: 0h, 2h, 24h and 48h after surgery.

End point values	Prucalopride - 48h postoperative	abdominal Vagus Nerve Stimulation - 48h postoperative	Sham stimulation/placebo - 48h postoperative	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	10	10	
Units: relative unit(s)				
median (full range (min-max))	3.270561 (1.367377 to 5.21516)	3.519517 (2.071589 to 10.1279)	3.8145755 (2.131474 to 5.181907)	

Statistical analyses

Statistical analysis title	TNFα serum SHAM/PLAC 48h vs PRUC 48h
Statistical analysis description:	
Kruskall-Wallis with Dunn's correction per timepoint (0,2,24,48 hours)	
Comparison groups	Prucalopride - 48h postoperative v Sham stimulation/placebo - 48h postoperative
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	Kruskal-wallis

Secondary: Time to first defecation

End point title	Time to first defecation
End point description:	
End point type	Secondary
End point timeframe:	
Number of days postoperative until first defecation are measured.	

End point values	Prucalopride - postoperative stay	abdominal Vagus Nerve Stimulation - postoperative stay	Sham stimulation/placebo - postoperative stay	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7[17]	7[18]	9[19]	
Units: day				
arithmetic mean (standard deviation)	6.125 (± 1.937)	5.75 (± 2.191)	8.208 (± 4.771)	

Notes:

[17] - Patients (3) with site specific complications were excluded from the analysis.

[18] - Patients (3) with site specific complications were excluded from the analysis.

[19] - Patients (1) with site specific complications were excluded from the analysis.

Statistical analyses

Statistical analysis title	time to first defecation: SHAM/PLAC vs PRUC
Statistical analysis description:	
One-way ANOVA with Bonferroni correction for multiple testing	
Comparison groups	Sham stimulation/placebo - postoperative stay v Prucalopride - postoperative stay
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	ANOVA

Statistical analysis title	time to first defecation: SHAM/PLAC vs VNS
Statistical analysis description:	
One-way ANOVA with Bonferroni correction for multiple testing	
Comparison groups	abdominal Vagus Nerve Stimulation - postoperative stay v Sham stimulation/placebo - postoperative stay
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	ANOVA

Statistical analysis title	time to first defecation: PRUC vs VNS
Statistical analysis description:	
One-way ANOVA with Bonferroni correction for multiple testing	
Comparison groups	Prucalopride - postoperative stay v abdominal Vagus Nerve Stimulation - postoperative stay
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	ANOVA

Secondary: Time to discharge

End point title	Time to discharge

End point description:

End point type	Secondary

End point timeframe:

Time (days) postoperative until discharge is captured

End point values	Prucalopride - postoperative stay	abdominal Vagus Nerve Stimulation - postoperative stay	Sham stimulation/placebo - postoperative stay	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7[20]	7[21]	9[22]	
Units: day				
arithmetic mean (standard deviation)	11.14 (± 3.89)	16.1 (± 2.919)	16.75 (± 5.591)	

Notes:

[20] - Patients (3) with site specific complications were excluded from the analysis.

[21] - Patients (3) with site specific complications were excluded from the analysis.

[22] - Patients (1) with site specific complications were excluded from the analysis.

Statistical analyses

Statistical analysis title	time to discharge: SHAM/PLAC vs VNS
Comparison groups	abdominal Vagus Nerve Stimulation - postoperative stay v Sham stimulation/placebo - postoperative stay
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	equivalence[23]
P-value	> 0.05
Method	ANOVA

Notes:

[23] - One-way ANOVA with Bonferroni correction for multiple testing

Statistical analysis title	time to discharge: SHAM/PLAC vs PRUC
Comparison groups	Prucalopride - postoperative stay v Sham stimulation/placebo - postoperative stay
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	equivalence[24]
P-value	< 0.05 [25]
Method	ANOVA

Notes:

[24] - One-way ANOVA with Bonferroni correction for multiple testing

[25] - Significant shorter time to discharge in the prucalopride group in comparison to the sham/placebo group.

Statistical analysis title	time to discharge: VNS vs PRUC
Comparison groups	abdominal Vagus Nerve Stimulation - postoperative stay v Prucalopride - postoperative stay

Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	equivalence[26]
P-value	> 0.05
Method	ANOVA

Notes:

[26] - One-way ANOVA with Bonferroni correction for multiple testing

Secondary: Time to first solids after surgery

End point title	Time to first solids after surgery

End point description:

End point type	Secondary

End point timeframe:

Time (days) postoperative to first solids was captured

End point values	Prucalopride - postoperative stay	abdominal Vagus Nerve Stimulation - postoperative stay	Sham stimulation/placebo - postoperative stay	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7[27]	7[28]	9[29]	
Units: day				
arithmetic mean (standard deviation)	3.765 (± 0.7732)	9.881 (± 3.19)	10.44 (± 5.741)	

Notes:

[27] - Patients (3) with site specific complications were excluded from the analysis.

[28] - Patients (3) with site specific complications were excluded from the analysis.

[29] - Patients (1) with site specific complications were excluded from the analysis.

Statistical analyses

Statistical analysis title	time to first solids: SHAM/PLAC vs PRUC

Statistical analysis description:

One-way ANOVA with Bonferroni correction for multiple testing

Comparison groups	Sham stimulation/placebo - postoperative stay v Prucalopride - postoperative stay
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.01 [30]
Method	ANOVA

Notes:

[30] - Significant shorter time until first solids in the prucalopride group in comparison to the sham/placebo group.

Statistical analysis title	time to first solids: SHAM/PLAC vs VNS

Statistical analysis description:	
One-way ANOVA with Bonferroni correction for multiple testing	
Comparison groups	Sham stimulation/placebo - postoperative stay v abdominal Vagus Nerve Stimulation - postoperative stay
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	ANOVA

Statistical analysis title	time to first solids: PRUC vs VNS
Statistical analysis description:	
One-way ANOVA with Bonferroni correction for multiple testing	
Comparison groups	Prucalopride - postoperative stay v abdominal Vagus Nerve Stimulation - postoperative stay
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05 [31]
Method	ANOVA

Notes:

[31] - Significant shorter time until first solids in the prucalopride group in comparison to the vns group.

Secondary: Time to nasogastric tube (NGT) removal

End point title	Time to nasogastric tube (NGT) removal
End point description:	
End point type	Secondary
End point timeframe:	
Time postoperative until nasogastric tube (NGT) removal was captured	

End point values	Prucalopride - postoperative stay	abdominal Vagus Nerve Stimulation - postoperative stay	Sham stimulation/placebo - postoperative stay	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7[32]	7[33]	9[34]	
Units: day				
arithmetic mean (standard deviation)	2.82 (± 0.88)	7.6 (± 4.18)	8.97 (± 6.55)	

Notes:

[32] - Patients (3) with site specific complications were excluded from the analysis.

[33] - Patients (3) with site specific complications were excluded from the analysis.

[34] - Patients (1) with site specific complications were excluded from the analysis.

Statistical analyses

Statistical analysis title	time to nasogastric tube remova: SHAM/PLAC vs PRUC

Statistical analysis description:

One-way ANOVA with Bonferroni correction for multiple testing

Comparison groups	Sham stimulation/placebo - postoperative stay v Prucalopride - postoperative stay
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05 [35]
Method	ANOVA

Notes:

[35] - Significant shorter time to gastric tube removal in prucalopride group, in comparison to the sham/placebo group.

Statistical analysis title	time to nasogastric tube removal: SHAM/PLAC vs VNS
Comparison groups	abdominal Vagus Nerve Stimulation - postoperative stay v Sham stimulation/placebo - postoperative stay
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	equivalence[36]
P-value	> 0.05
Method	ANOVA

Notes:

[36] - One-way ANOVA with Bonferroni correction for multiple testing

Statistical analysis title	time to nasogastric tube removal: PRUC vs VNS

Statistical analysis description:

One-way ANOVA with Bonferroni correction for multiple testing

Comparison groups	Prucalopride - postoperative stay v abdominal Vagus Nerve Stimulation - postoperative stay
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	ANOVA

Secondary: Time to first solids + first defecation

End point title	Time to first solids + first defecation

End point description:

Time (days) to the occurrence of both first defecation and first solid food intake, defined as the time to the later of the two events for analysis.

End point type	Secondary

End point timeframe:

Time (postoperative) to first solids and first defecation, in days was measured

End point values	Prucalopride - postoperative stay	abdominal Vagus Nerve Stimulation - postoperative stay	Sham stimulation/placebo - postoperative stay	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7[37]	7[38]	9[39]	
Units: day				
arithmetic mean (standard deviation)	6.298 (± 1.644)	9.893 (± 3.185)	10.49 (± 5.784)	

Notes:

[37] - Patients (3) with site specific complications were excluded from the analysis.

[38] - Patients (3) with site specific complications were excluded from the analysis.

[39] - Patients (1) with site specific complications were excluded from the analysis.

Statistical analyses

Statistical analysis title	time to first solids+defecation: SHAM/PLAC vs PRUC
Statistical analysis description: One-way ANOVA with Bonferroni correction for multiple testing	
Comparison groups	Prucalopride - postoperative stay v Sham stimulation/placebo - postoperative stay
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	ANOVA

Statistical analysis title	time to first solids+defecation: SHAM/PLAC vs VNS
Statistical analysis description: One-way ANOVA with Bonferroni correction for multiple testing	
Comparison groups	Sham stimulation/placebo - postoperative stay v abdominal Vagus Nerve Stimulation - postoperative stay
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	ANOVA

Statistical analysis title	time to first solids+defecation: PRUC vs VNS
Statistical analysis description: One-way ANOVA with Bonferroni correction for multiple testing	
Comparison groups	Prucalopride - postoperative stay v abdominal Vagus Nerve Stimulation - postoperative stay

Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	ANOVA

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
The adverse events were assessed daily until discharge.	
Assessment type	Systematic

Dictionary used	
Dictionary name	No dictionary used
Dictionary version	0

Reporting groups	
Reporting group title	Prucalopride
Reporting group description:	
Patients were treated with 2 mg prucalopride (12 and 2 hours prior to surgery) and received sham stimulation at the start and the end of the surgery.	
Reporting group title	abdominal Vagus Nerve Stimulation
Reporting group description:	
Patients received abdominal VNS (2min, 20Hz, 2.5 mA, 1ms at the start and end of the surgical procedure) + placebo	
Reporting group title	Sham stimulation/placebo
Reporting group description:	
Patients allocated to placebo received sham stimulation at the start and end of surgery	

Serious adverse events	Prucalopride	abdominal Vagus Nerve Stimulation	Sham stimulation/placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 10 (20.00%)	3 / 10 (30.00%)	2 / 10 (20.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Hypotension			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastroparesis postoperative			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	2 / 10 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumonia			

subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia	Additional description: Severe hypoxia leading to prolongation of hospitalisation/admission to ITE		
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 10	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Prucalopride	abdominal Vagus Nerve Stimulation	Sham stimulation/placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 10 (40.00%)	8 / 10 (80.00%)	7 / 10 (70.00%)
Investigations			
Transfusion			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 10 (20.00%)	3 / 10 (30.00%)	2 / 10 (20.00%)
occurrences (all)	3	3	2
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	3 / 10 (30.00%)
occurrences (all)	0	1	3
Skin and subcutaneous tissue disorders			
Drain site complication	Additional description: infected wounds fluid in drain		
subjects affected / exposed	3 / 10 (30.00%)	2 / 10 (20.00%)	1 / 10 (10.00%)
occurrences (all)	3	2	1
Renal and urinary disorders			

Urinary tract infection subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 2	2 / 10 (20.00%) 2	0 / 10 (0.00%) 0
Infections and infestations Catheter site infection subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 10 (0.00%) 0	2 / 10 (20.00%) 2

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