Clinical trial results:
Characterization of nerve-modulated macrophage population in the gastrointestinal tract

Summary

EudraCT number	2018-002192-18
Trial protocol	BE
Global end of trial date	19 August 2022

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	PrucaloprideRNAseq

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02425774
WHO universal trial number (UTN)	-
Other trial identifiers	EC UZ Leuven S-number: S61248

Notes:

Sponsors

Sponsor organisation name	UZ Leuven
Sponsor organisation address	Herestraat 49, Leuven, Belgium, 3000
Public contact	Guy Boeckxstaens, KU Leuven, +32 16342883,
Scientific contact	Guy Boeckxstaens, KU Leuven, +32 16342883,

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	19 August 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 August 2022
Global end of trial reached?	Yes
Global end of trial date	19 August 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Characterization of the macrophage population subset that is modulated by enteric neurons

Protection of trial subjects:

Day untill discharge: the study nurse was available to assess occurance of any adverse events. The CRF was closed 30 days after the last intake of the study medication in case no adverse events occurred.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 July 2018
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: 16
Worldwide total number of subjects	16
EEA total number of subjects	16

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)	4
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Inclusion:
- Age > 18
- Surgical removal of small bowel or colon (due to carcinoma or divertrikels)

Exclusion:
- Adj. radiotherapy
- Pronounced intra-abdominal inflammation
- Allergy for serotonine medication
- Active IBD
- Child-Pugh C
- Creatinine clearance <50mL/min/1.73m²
- ASA-PS >3
- Uncontrolled diabetes (>200mg/dl)

Period 1

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

Blinding implementation details:

The patients were randomized by Laboratory Wolfs and the blind was remained until the analysis was performed.

Arms

Are arms mutually exclusive?	Yes
Arm title	Prucalopride

Arm description:

16h (1x 2mg) and 2h (1x2mg) before the operation

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

Dosage and administration details:

2mg, 16u voor de operatie
2mg, 2u voor de operatie
De studie-verpleegkundige is aanwezig tijdens het innemen (voor compliance)

Arm title	Placebo

Arm description:

1 tablet placebo 16h and 2h before the operation

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:

1 tablet 16u voor de operatie
1 tablet 2u voor de operatie

Number of subjects in period 1	Prucalopride	Placebo
Started	8	8
Completed	8	8

Baseline characteristics

Reporting groups	
Reporting group title	Overall baseline period

Reporting group description: -

Reporting group values	Overall baseline period	Total	
Number of subjects	16	16	
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)	4	4	
From 65-84 years	12	12	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	8	8	
Male	8	8	

End points

End points reporting groups

Reporting group title	Prucalopride
Reporting group description:	
16h (1x 2mg) and 2h (1x2mg) before the operation	
Reporting group title	Placebo
Reporting group description:	
1 tablet placebo 16h and 2h before the operation	

Primary: Percentage of monocytes

End point title	Percentage of monocytes
End point description:	
End point type	Primary
End point timeframe:	
Single cell RNA sequencing was performed following the bowel resection.	

End point values	Prucalopride	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5[1]	7[2]		
Units: percent				
arithmetic mean (standard deviation)	13.99 (± 15.09)	13.91 (± 15.46)		

Notes:

[1] - Some samples were excluded from the analysis due to bad sample quality.

[2] - Some samples were excluded from the analysis due to bad sample quality.

Statistical analyses

Statistical analysis title	%monocytes in PRUC vs PLAC
Comparison groups	Prucalopride v Placebo
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	Wilcoxon (Mann-Whitney)

Primary: Percentage of LYVE1+ macrophages

End point title	Percentage of LYVE1+ macrophages
End point description:	
LYVE1 = Lymphatic Vessel Endothelial Hyaluronan Receptor 1	

Top differentially expressed genes of this macrophage cluster shows that it matches with LYVE1+ macrophages previously described in literature.

End point type	Primary

End point timeframe:

Single cell RNA sequencing was performed following the bowel resection.

End point values	Prucalopride	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5[3]	7[4]		
Units: percent				
arithmetic mean (standard deviation)	32.85 (± 8.472)	35.25 (± 9.552)		

Notes:

[3] - Some samples were excluded from the analysis due to bad sample quality.

[4] - Some samples were excluded from the analysis due to bad sample quality.

Statistical analyses

Statistical analysis title	%LYVE+ Macs in PRUC vs PLAC
Comparison groups	Placebo v Prucalopride
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	Wilcoxon (Mann-Whitney)

Primary: Percentage of APOE+ macrophages

End point title	Percentage of APOE+ macrophages

End point description:

APOE = apolipoprotein E

End point type	Primary

End point timeframe:

Single cell RNA sequencing was performed following the bowel resection.

End point values	Prucalopride	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5[5]	7[6]		
Units: percent				
arithmetic mean (standard deviation)	21.01 (± 15.06)	13.49 (± 4.786)		

Notes:

[5] - Some samples were excluded from the analysis due to bad sample quality.

[6] - Some samples were excluded from the analysis due to bad sample quality.

Statistical analyses

Statistical analysis title	APOE+ Macs in PRUC vs PLAC
Comparison groups	Prucalopride v Placebo
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	Wilcoxon (Mann-Whitney)

Primary: Percentage of differentiating macrophages

End point title	Percentage of differentiating macrophages

End point description:

Top differentially expressed genes show this cluster has both monocyte and mature macrophage markers.

End point type	Primary

End point timeframe:

Single cell RNA sequencing was performed following the bowel resection.

End point values	Prucalopride	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5[7]	7[8]		
Units: percent				
arithmetic mean (standard deviation)	17.1 (± 3.449)	18.51 (± 6.869)		

Notes:

[7] - Some samples were excluded from the analysis due to bad sample quality.

[8] - Some samples were excluded from the analysis due to bad sample quality.

Statistical analyses

Statistical analysis title	% differentiating Macs in PRUC vs PLAC
Comparison groups	Prucalopride v Placebo

Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	Wilcoxon (Mann-Whitney)

Primary: Percentage of mitochondrial gene-enriched macrophages

End point title	Percentage of mitochondrial gene-enriched macrophages

End point description:

Top differentially expressed genes of this macrophage cluster are mitochondrial genes.

End point type	Primary

End point timeframe:

Single cell RNA sequencing was performed following the bowel resection.

End point values	Prucalopride	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5[9]	7[10]		
Units: percent				
arithmetic mean (standard deviation)	8.852 (± 6.087)	10.57 (± 7.537)		

Notes:

[9] - Some samples were excluded from the analysis due to bad sample quality.

[10] - Some samples were excluded from the analysis due to bad sample quality.

Statistical analyses

Statistical analysis title	% mitochondria enriched Macs in PRUC vs PLAC
Comparison groups	Prucalopride v Placebo
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	Wilcoxon (Mann-Whitney)

Primary: Percentage of cytokine gene-enriched macrophages

End point title	Percentage of cytokine gene-enriched macrophages

End point description:

Top differentially expressed genes of this macrophage cluster are pro-inflammatory cytokine genes.

End point type	Primary

End point timeframe:

Single cell RNA sequencing was performed following the bowel resection.

End point values	Prucalopride	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5[11]	7[12]		
Units: percent				
arithmetic mean (standard deviation)	3.753 (± 1.379)	5.234 (± 1.788)		

Notes:

[11] - Some samples were excluded from the analysis due to bad sample quality.

[12] - Some samples were excluded from the analysis due to bad sample quality.

Statistical analyses

Statistical analysis title	% Cytokine-rich Macs in PRUC vs PLAC
Comparison groups	Prucalopride v Placebo
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	Wilcoxon (Mann-Whitney)

Primary: Percentage of LYVE1+ macrophages (cluster 2)

End point title	Percentage of LYVE1+ macrophages (cluster 2)

End point description:

LYVE1 = Lymphatic Vessel Endothelial Hyaluronan Receptor 1
Top differentially expressed genes of this second LYVE1+ macrophage cluster shows high similarity to LYVE1+ macrophages previously described in literature.

End point type	Primary

End point timeframe:

Single cell RNA sequencing was performed following the bowel resection.

End point values	Prucalopride	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5[13]	7[14]		
Units: percent				
arithmetic mean (standard deviation)	2.452 (± 1.328)	3.048 (± 3.367)		

Notes:

[13] - Some samples were excluded from the analysis due to bad sample quality.

[14] - Some samples were excluded from the analysis due to bad sample quality.

Statistical analyses

Statistical analysis title	%LYVE+ Macs (2) in PRUC vs PLAC
Comparison groups	Prucalopride v Placebo
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs, SAEs, and AESIs: until 30 days after the last treatment administration or until the last follow-up visit (whichever is later).
All SAEs and AESIs: must be reported to the Sponsor within 24 hours of the event becoming known to trial personnel.

Adverse event reporting additional description:

Since our IMP has a European license, we will not report any adverse events listed in the SmPC. The patient will be followed up from the time they take the first placebo/prucalopride tablet until their discharge.

Assessment type	Systematic

Dictionary used

Dictionary name	No dictionary used
Dictionary version	0

Reporting groups

Reporting group title	Prucalopride

Reporting group description:

16h (1x 2mg) and 2h (1x2mg) before the operation

Reporting group title	Placebo

Reporting group description:

1 tablet placebo 16h and 2h before the operation

Serious adverse events	Prucalopride	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 8 (25.00%)	0 / 8 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
Gastrointestinal perforation			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroparesis postoperative			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Prucalopride	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 8 (75.00%)	5 / 8 (62.50%)	
Vascular disorders			
Thrombophlebitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Hypotension			
subjects affected / exposed	2 / 8 (25.00%)	3 / 8 (37.50%)	
occurrences (all)	2	3	
Tachycardia			
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 8 (37.50%)	0 / 8 (0.00%)	
occurrences (all)	4	0	
Gastrointestinal disorders			
Epigastric discomfort			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
C-reactive protein increased	Additional description: CRP increase without clinical focus		
subjects affected / exposed	1 / 8 (12.50%)	2 / 8 (25.00%)	
occurrences (all)	1	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 July 2019	Uitbereiding met 10 patiënten die een dundarmresectie ondergaan + uitbereiding beleid over data handling, data management en vertrouwelijkheid van gegevens.
04 July 2020	Datum!!!! Uitbereiding experimenten met NMT-seq. aanpassing naar 6 patiënten per groep en toevoeging van bloedstaal voor testing Covid-antilichamen.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported