Clinical trial results:
A Randomized Open Label Pilot Study to Compare Targinact vs. Oxycodone in Early Return of Gastrointestinal Function after Colorectal Surgery

Summary

EudraCT number	2013-005327-16
Trial protocol	GB
Global end of trial date	01 July 2016

Results information

Result version number	v1 (current)
This version publication date	29 July 2020
First version publication date	29 July 2020
Summary attachment (see zip file)	Targinact (TACS Publication.pdf)

Trial information

Trial identification

Sponsor protocol code	NA

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02109640
WHO universal trial number (UTN)	-
Other trial identifiers	Clintrials.gov Number: NCT02109640, REC Number: 14/ES/0016

Notes:

Sponsors

Sponsor organisation name	University of Edinburgh & NHS Lothian
Sponsor organisation address	47 Little France Crescent, Edinburgh, United Kingdom, EH16 4TJ
Public contact	Hugh Paterson, University of Edinburgh, 07780 957402, hugh.paterson@ed.ac.uk
Scientific contact	Hugh Paterson, University of Edinburgh, 07780 957402, hugh.paterson@ed.ac.uk

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 July 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 September 2015
Global end of trial reached?	Yes
Global end of trial date	01 July 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to compare Targinact (prolonged release naloxone + oxycodone) with current standard treatment (oxycodone alone) in post-operative return of normal gut function after elective colorectal resectional surgery.

Protection of trial subjects:

As with all opioid analgesics, there is a risk of side effects. Initial doses of the study drug were given in hospital under regular monitoring of observations as per normal practice in post-operative patients. Participants discharged on study drug were counselled on the risks of opioid analgesics as per normal practice and advised to discontinue use at the earliest opportunity.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 December 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	United Kingdom: 62
Worldwide total number of subjects	62
EEA total number of subjects	62

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)	14
From 65 to 84 years	46
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Patients scheduled for elective laparoscopic segmental colonic resection in a single colorectal surgery unit were recruited by study staff during scheduled preoperative visits.

Pre-assignment

Screening details:

Patients scheduled for elective laparoscopic segmental colonic resection in a single colorectal surgery unit were screened for eligibility.

82 patients were assessed for eligibility. 20 of these were excluded: did not meet inclusion criteria n = 16; declined to participate n = 2; other reason n = 2. 62 patients were recruited.

Period 1

Period 1 title	Whole study period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

The statistician was blinded to which group was allocated to intervention and which to control.

Arms

Are arms mutually exclusive?	Yes
Arm title	Oxycodone

Arm description:

Post-op analgesia based on modified release oxycodone

Arm type	Active comparator
Investigational medicinal product name	Oxycodone
Investigational medicinal product code	PL 16950/0097-0100,0123,0139-0141, 0150
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

5-20mgd bd

Arm title	Targinact

Arm description:

Intervention arm

Arm type	Experimental
Investigational medicinal product name	Targinact
Investigational medicinal product code	PRD506871
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

5-20mg bd

Number of subjects in period 1	Oxycodone	Targinact
Started	30	32
Completed	23	27
Not completed	7	5
Physician decision	1	2
Conversion to open surgery	2	1
Ineligibility	3	2
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Oxycodone
Reporting group description:	
Post-op analgesia based on modified release oxycodone	
Reporting group title	Targinact
Reporting group description:	
Intervention arm	

Reporting group values	Oxycodone	Targinact	Total
Number of subjects	30	32	62
Age categorical Units: Subjects			
Adults (18-64 years)	6	7	13
From 65-84 years	16	19	35
85 years and over	1	1	2
Excluded from analysis	7	5	12
Age continuous Units: years			
median	68	71	
full range (min-max)	50 to 87	30 to 83	-
Gender categorical Units: Subjects			
Female	12	12	24
Male	11	15	26
Not recorded	7	5	12
Type of operation			
Right or left colectomy			
Units: Subjects			
Right colectomy	10	14	24
Left colectomy	13	13	26
Excluded from analysis	7	5	12

Subject analysis sets	
Subject analysis set title	Subjects receiving the intervention/control
Subject analysis set type	Per protocol

Subject analysis set description:

Analyses of the data included Fisher’s exact test for categorical data (owing to the small numbers in some of the cells), and Student’s t test, with log transformation where appropriate. Estimates of differences in proportions and means were also calculated. The randomized groups were compared for a number of clinical measures, and in general a comment is made where there was little or no difference between the groups.

All of the analyses are descriptive, no adjustment was made for multiple comparisons.

A two-sided 5 per cent significance level was applied throughout.

Participant data was anonymised prior to analysis and the analysis was conducted by an independent statistician who was blinded to the treatment.

Reporting group values	Subjects receiving the intervention/control		
Number of subjects	50		
Age categorical			
Units: Subjects			
Adults (18-64 years)	13		
From 65-84 years	35		
85 years and over	2		
Excluded from analysis	12		
Age continuous			
Units: years			
median			
full range (min-max)			
Gender categorical			
Units: Subjects			
Female	24		
Male	26		
Not recorded	12		
Type of operation			
Right or left colectomy			
Units: Subjects			
Right colectomy	24		
Left colectomy	26		
Excluded from analysis	12		

End points

End points reporting groups

Reporting group title	Oxycodone
Reporting group description:	
Post-op analgesia based on modified release oxycodone	
Reporting group title	Targinact
Reporting group description:	
Intervention arm	
Subject analysis set title	Subjects receiving the intervention/control
Subject analysis set type	Per protocol

Subject analysis set description:

Analyses of the data included Fisher's exact test for categorical data (owing to the small numbers in some of the cells), and Student's t test, with log transformation where appropriate. Estimates of differences in proportions and means were also calculated. The randomized groups were compared for a number of clinical measures, and in general a comment is made where there was little or no difference between the groups.

All of the analyses are descriptive, no adjustment was made for multiple comparisons.

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Participant data was anonymised prior to analysis and the analysis was conducted by an independent statistician who was blinded to the treatment.

Primary: Return of postoperative gut function

End point title	Return of postoperative gut function
End point description:	
Post-operative at which composite of the following achieved: tolerating oral diet; passage of flatus/faeces/minimal nausea and vomiting	
End point type	Primary
End point timeframe:	
Assessed on postoperative day 3	

End point values	Oxycodone	Targinact		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	27		
Units: number				
number (not applicable)				
Day 3	15	13		
Day 4	17	23		

Attachments (see zip file)	Postoperative day of return of gut function/Targinact.pdf

Statistical analyses

Statistical analysis title	Return of gut function day 3
Comparison groups	Oxycodone v Targinact
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.264 [1]
Method	Fisher exact
Parameter estimate	Absolute % difference
Point estimate	17.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10
upper limit	40.7

Notes:

[1] - unadjusted

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
30 days after operation	
Adverse event reporting additional description:	
Normal postoperative events such as mild nausea, pain etc excluded a priori	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups	
Reporting group title	Complications

Reporting group description:

There were two major complications in the intervention arm of the study: one intra-abdominal collection was drained percutaneously and one (day 4) anastomotic dehiscence required reoperation, repair and proximal diversion. There were no
major complications in the control arm.

Serious adverse events	Complications		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Surgical and medical procedures			
Intra-abdominal fluid collection			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Anastomotic complication			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Complications		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)		

Surgical and medical procedures Hospitalisation subjects affected / exposed occurrences (all)	 1 / 3 (33.33%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 June 2014	Change of study design from double-blinded to open label blinded design. Addition of a novel method of documenting nutritional intake (Digital Photography of Food Method). Addition of postoperative in-patient activity monitoring.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/27762434