



Targinact Study (TACS)

A Randomized Open Label Phase II Pilot Study to Compare Targinact vs. Oxycodone in Early Return of Gastrointestinal Function after Laparoscopic Colorectal Surgery (NCT02109640)

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Background



*Delayed
return of gut
function*

Poorly defined

25-30% of elective colonic resections

Multifactorial

Opioids implicated

Return of gut function fundamental to recovery



Oxycodone MR + Naloxone

Poelaert J. Clinical therapeutics 2015;37(4):784-92.



Aims

- Feasibility outcomes
 - Recruitment
 - Retention
 - Methodological consistency?



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 - Recruitment
 - Retention
 - Methodological consistency?
- Event rate
 - Laparoscopic ERAS colectomy
 - Definition?

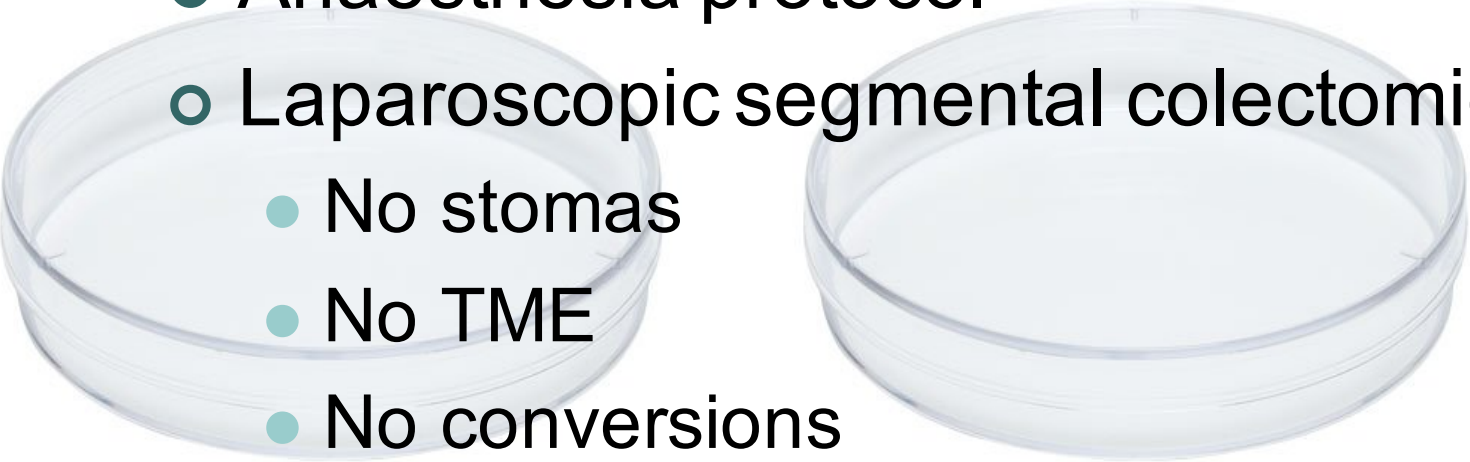


Aims

- Feasibility outcomes
 - Recruitment
 - Retention
 - Methodological consistency?
- Event rate
 - Laparoscopic ERAS colectomy
 - Definition?
- Targinact signal?



Trial design

- Patient pathway protocol
 - Anaesthesia protocol
 - Laparoscopic segmental colectomies
 - No stomas
 - No TME
 - No conversions
- 



Eligible elective laparoscopic
segmental colectomy



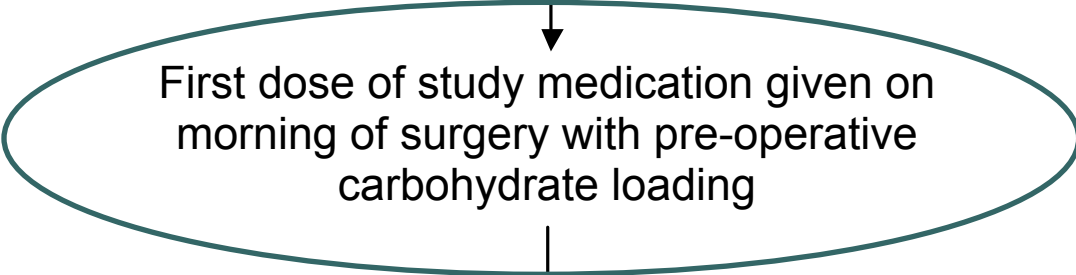
PIS given



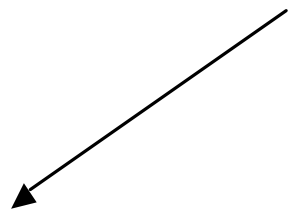
Consent at preadmission



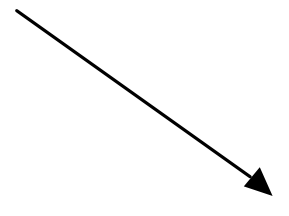
Randomisation



Surgery: laparoscopic segmental
colectomy



Post-op analgesia based
on Oxycodone



Post-op analgesia based
on Targinact

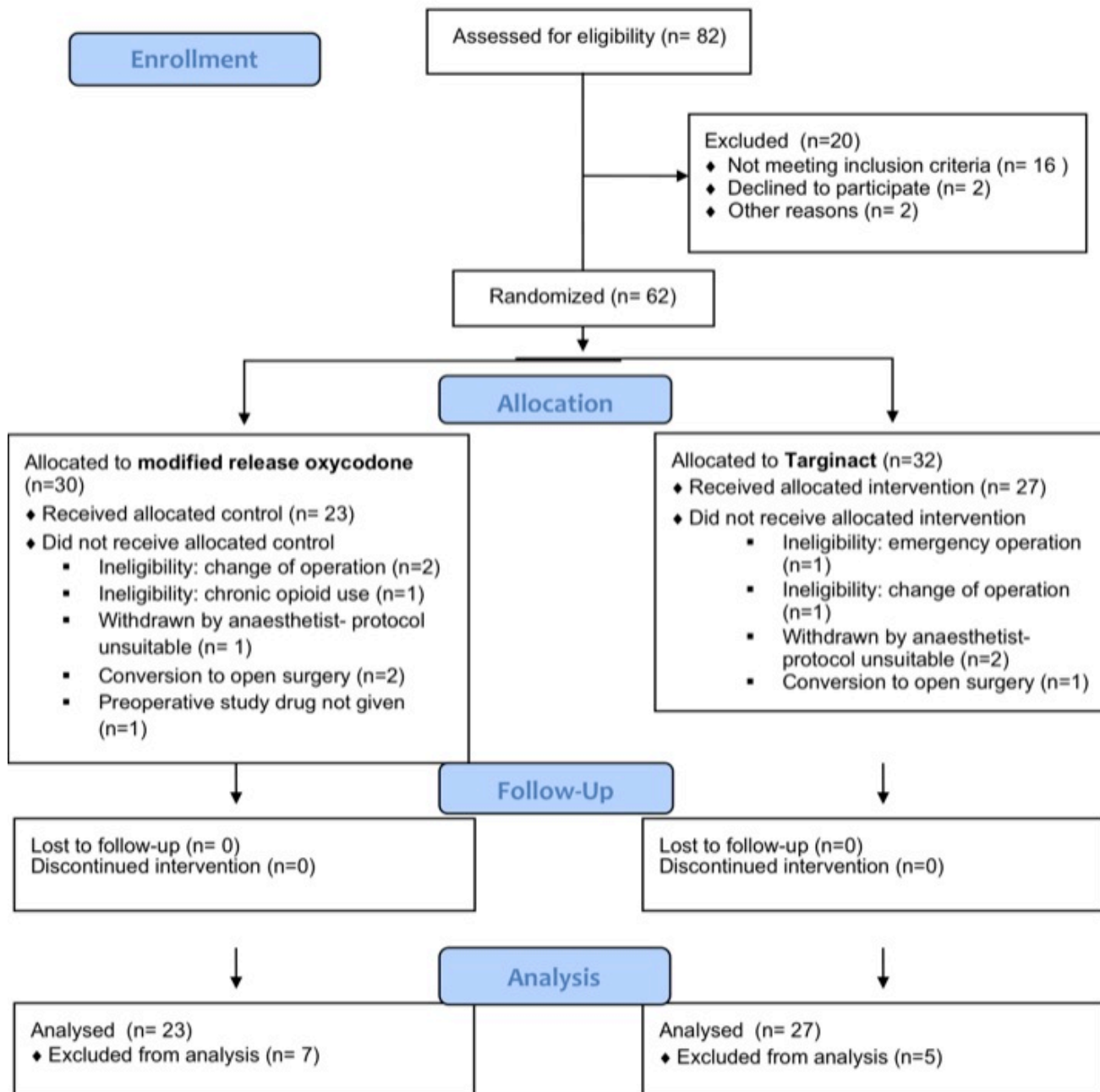


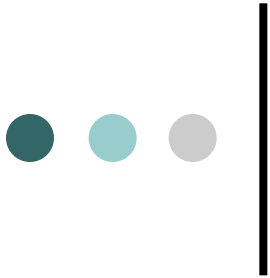
Outcome measures

- Feasibility
 - Recruitment, retention
 - Protocol compliance
- Return of gut function definition
 - Flatus or stool
 - Tolerating solid food
 - PONV<4
- PROMs
 - Pain
 - QoR



Results





Enrollment

Assessed for eligibility
(n= 82)



Excluded (n=20)
.. Not meeting inclusion criteria
(n= 16)
.. Declined to participate (n= 2)
.. Other reasons (n= 2)

Randomized (n= 62)
Stratified R v L

Allocation

Allocated to **control** (n=30)

- Received allocated control (n= 23)
- Did not receive allocated control
 - Ineligibility: change of operation (n=2)
 - Ineligibility: chronic opioid use (n=1)
 - Withdrawn by anaesthetist- protocol unsuitable (n= 1)
 - Conversion to open surgery (n=2)
 - Preoperative study drug not given (n=1)



Allocated to **intervention** (n=32)

- Received allocated intervention (n= 27)
- Did not receive allocated intervention
 - Ineligibility: emergency operation (n=1)
 - Ineligibility: change of operation (n=1)
 - Withdrawn by anaesthetist- protocol unsuitable (n=2)
 - Conversion to open surgery (n=1)





Follow-Up

Lost to follow-up (n= 0)
Discontinued intervention
(n=0)

Lost to follow-up (n=0)
Discontinued intervention
(n=0)

Analysis

Analysed (n= 23)
.. Excluded from analysis (n= 7)

Analysed (n= 27)
.. Excluded from analysis (n=5)



Patients

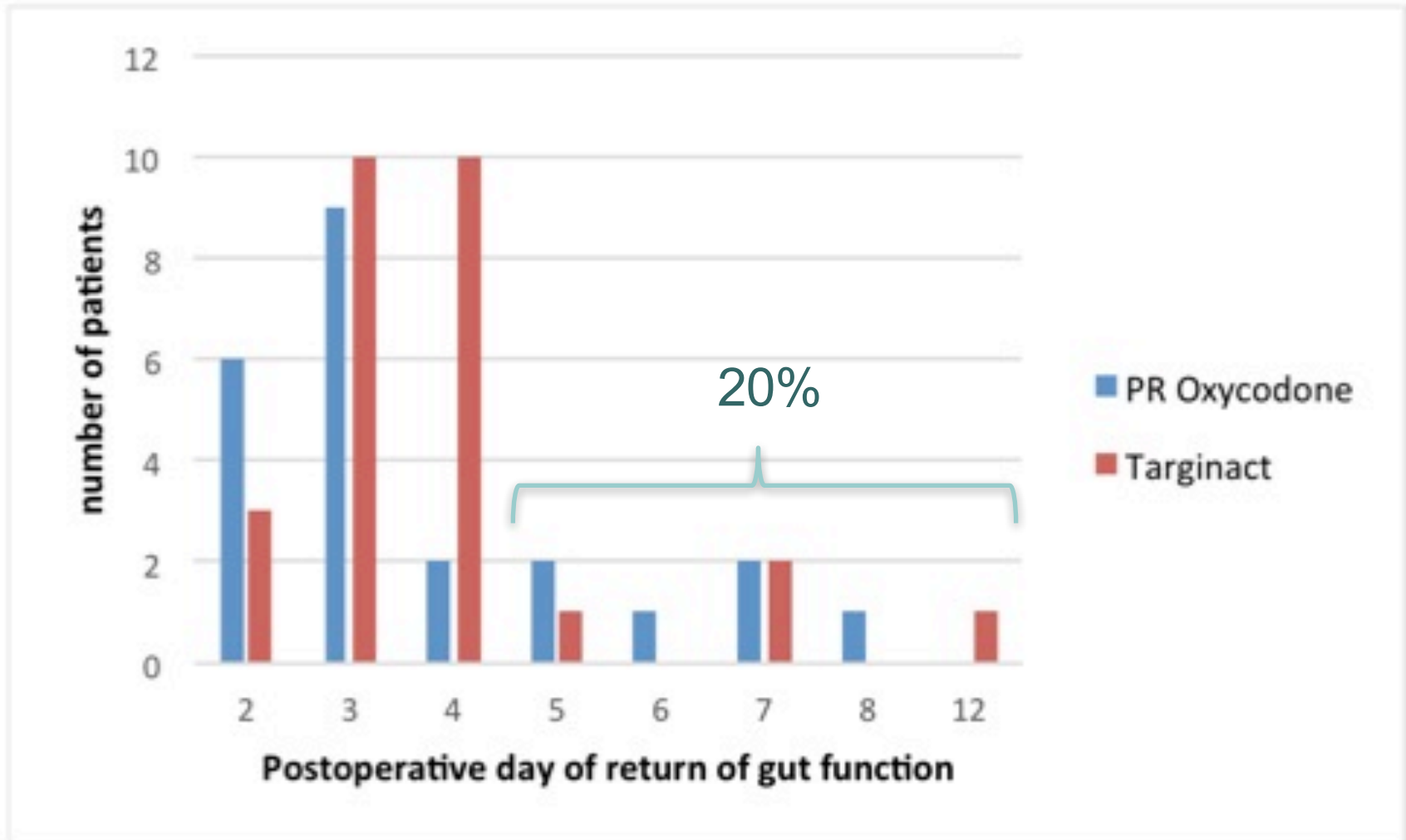
	<i>Control (n=23)</i>	<i>Intervention (n=27)</i>
Age (years)*	69(9)	68(13)
Sex ratio (F:M)	12:11	12:15
BMI*	26.9(4.9)	27.4(5.0)
WHR*	0.96 (0.1)	0.96 (0.1)
SNAQ†	16(10-19)	16(14-19)
Baseline QOR score*	127(11)	127(10)
Apfel score		
1	1	3
2	10	11
3	10	13
4	2	0
P-POSSUM*	27.7(5.6)	29.5(5.6)



Protocol compliance

	<i>Control (n=23)</i>	<i>Intervention (n=27)</i>	<i>Difference in % (95% CI)</i>	<i>P (Fisher's Exact test)</i>
Single shot spinal opiate	20/23 (87%)	27/27 (100%)	-13.0 (-32.1, 2.0)	0.090
IV lidocaine infusion	21/23 (91%)	25/27 (93%)	-1.3 (-20.2, 15.9)	1.000
IV removed day 1	21/23 (91%)	24/27 (89%)	2.4 (-17.1, 20.5)	1.000
PCA removed day 1*	21/23 (91%)	25/27 (93%)	-1.3 (-20.0, 15.9)	1.000

Day of return of gut function (flatus/stool + solid food + PONV<4)



Secondary outcomes

	<i>Control</i> (n=23)	<i>Intervention</i> (n=27)	<i>Difference</i> (95% CI)	<i>P</i>
OBAS day 3 (median (range))*	2 (0-10)	2 (0-11)	-0.09 (-0.60, 0.57)	0.68
PONV day 3 (median(range)) [†]	1 (0-6)	1 (0-5)	0.48 (-0.31, 1.27)	1.0
QoR score day 3	117 (20)	119 (23)	-1.44 (-13.7, 10.8)	0.81
Opioid consumption up to day 3 (mg of morphine equivalent)	79 (42)	70 (31)	8.5 (-12.3, 29.2)	0.42
Total opioid consumption (mg of morphine equivalent)	94 (56)	78 (36)	16.3 (-10.2, 42.8)	0.22

Sample size =
~300

Secondary outcomes

	<i>Control</i> (n=23)	<i>Intervention</i> (n=27)	<i>Difference</i> (95% CI)	<i>P</i>
Time to first flatus (hours)	51 (26)	57 (26)	-6.3 (-21.3, 8.7)	0.40
Time to first bowel movement (hours)	111 (37)	87 (38)	23.8 (2.3, 45.4)	0.03
Intraoperative IV fluids (mls)	1756 (814)	1575 (738)	179.7 (-262.1, 621.6)	0.42
Total IV fluid up to day 3 (mls)*	1887 (1228)	1946 (1747)	0.03 (-0.33, 0.39)	0.86
Total oral fluids up to day 3 (mls)	4627 (1864)	4134 (1452)	493.0 (-450.5, 1436.5)	0.3
Day of discharge (median(range)) [†]	4 (3-10)	5 (3-14)	-0.02 (-0.27, 0.23)	1.0

Sample size =
~300



Conclusions

- Recruitment
- Retention
- Protocol compliance

- 20% delayed return gut function

- Targinact
 - Negative for primary outcome
 - Testable ?beneficial effects