Clinical trial results:
Propofol TCI (Target Controlled Infusion) vs. Midazolam plus Fentanyl for moderate sedation during gastrointestinal procedures: a double-blind randomized controlled trial.

Summary

EudraCT number	2012-001755-40
Trial protocol	IT
Global end of trial date	04 March 2014

Results information

Result version number	v1 (current)
This version publication date	13 May 2021
First version publication date	13 May 2021

Trial information

Trial identification

Sponsor protocol code	Prop/TCI/2012

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02062177
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	IRCCS Ospedale San Raffaele
Sponsor organisation address	Via Olgettina, 60, Milano, Italy, 20132
Public contact	Division of Gastroenterology and Gastrointestinal Endoscopy, IRCCS Ospedale San Raffaele, 0039 0226432744, fanti.lorella@hsr.it
Scientific contact	Division of Gastroenterology and Gastrointestinal Endoscopy, IRCCS Ospedale San Raffaele, 0039 0226432744, fanti.lorella@hsr.it

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	04 March 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 March 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare propofol TCI and midazolam i.v. boluses with respect to their effectiveness and safety for maintaining moderate sedation during esophagogastroduodenoscopies (EGD) and colonoscopies. Both sedation regimens were administered bythe endoscopist.

Protection of trial subjects:

Approval by the local Ethics Committee was obtained before the beginning of the study and written informed consent was obtained from all patients at time of enrolment.
All procedures were performed by a single experienced endoscopist using a standard technique with a high definition videoendoscope. The endoscopist had performed more than 100 propofol sedations during endoscopy before.
All medical and nursing staff members are ACLS-certified and have received non-anaesthesiologist training for sedation for gastrointestinal endoscopy, including the basic principles of sedation and practical training in NAPS.
During colonoscopy, moderate sedation was maintained throughout the scope-in phase, the most painful phase of the procedure, whereas sedative administration was discontinued upon caecal intubation.
During EGD, sedative administration was discontinued uponcompletion of the exam.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 May 2012
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	Italy: 140
Worldwide total number of subjects	140
EEA total number of subjects	140

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)	105
From 65 to 84 years	35
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This randomized double-blind controlled trial involved 140 consecutive outpatients scheduled to undergo EGD or colonoscopy. On arrival in the endoscopy suite patients were randomly assigned to one of two groups according to a previously computer-generated list

Pre-assignment

Screening details:

On patient’s arrival in the endoscopy suite a peripheral intravenous cannula was inserted. Throughout endoscopy electrocardiogram and pulse oximetry (SpO2) were continuously monitored, and non-invasive arterial blood pressure was monitored every 5 min

Period 1

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

Blinding implementation details:

Sedation was administered, under the endoscopist’s supervision, by a gastroenterology attending fellow (GR) not directly involved in the procedure, who was the only one not blinded towards the randomized sedation regimen. Because of the well-known different physical appearance of study drugs, a fabric curtain was drawn across the patient’s arm, concealing the i.v. line and the TCI pump both to the patient and to the endoscopist.

Arms

Are arms mutually exclusive?	Yes
Arm title	Group S (Standard Sedation)

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Midazolam
Investigational medicinal product code	IPNOVEL
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

Intravenous bolus 0.04 mg/kg if aged <70, 0.03 mg/kg if aged >=70, followed by 1 mg i.v. bolus up to a maximum of 5 mg.

Investigational medicinal product name	Fentanyl
Investigational medicinal product code	FENTANYL
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Patients in both groups (Group S and Group P) undergoing colonoscopy received also i.v. fentanyl (1 ug/kg) for pain control.

Arm title	Group P (Propofol TCI Sedation)

Arm description: -

Arm type	Experimental

Investigational medicinal product name	Propofol
Investigational medicinal product code	DIPRIVAN
Other name	
Pharmaceutical forms	Emulsion for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Target concentration was initially set at 1.2–1.6 g/ml (side effect concentration), according topatient's body weight and general condition, then titrated with 0.1 ug/ml increments up to a maximum of 2 ug/ml.

Number of subjects in period 1	Group S (Standard Sedation)	Group P (Propofol TCI Sedation)
Started	70	70
Completed	70	70

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	140	140	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	0		
standard deviation	± 0	-	
Gender categorical Units: Subjects			
Female	62	62	
Male	78	78	

Subject analysis sets	
Subject analysis set title	Group S - EGD
Subject analysis set type	Per protocol
Subject analysis set description: Seventy consecutive patients, undergoing EGD were prospectively enrolled and randomized (Group S)	
Subject analysis set title	Group P - EGD
Subject analysis set type	Per protocol
Subject analysis set description: Seventy consecutive patients, undergoing EGD were prospectively enrolled and randomized (Group P)	
Subject analysis set title	Group S - Colonoscopy
Subject analysis set type	Per protocol
Subject analysis set description: Seventy consecutive patients undergoing colonoscopy were prospectively randomized (Group S)	
Subject analysis set title	Group P - Colonoscopy
Subject analysis set type	Per protocol
Subject analysis set description: Seventy consecutive patients undergoing colonoscopy were prospectively randomized (Group P)	

Reporting group values	Group S - EGD	Group P - EGD	Group S - Colonoscopy
Number of subjects	35	35	35
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	52.3	47.8	58.6
standard deviation	± 18.1	± 17.5	± 11.6

Gender categorical Units: Subjects			
Female	13	14	19
Male	22	21	16

Reporting group values	Group P - Colonoscopy		
Number of subjects	35		
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	57.2		
standard deviation	± 13.8		
Gender categorical Units: Subjects			
Female	16		
Male	19		

End points

End points reporting groups

Reporting group title	Group S (Standard Sedation)
Reporting group description: -	
Reporting group title	Group P (Propofol TCI Sedation)
Reporting group description: -	
Subject analysis set title	Group S - EGD
Subject analysis set type	Per protocol
Subject analysis set description:	
Seventy consecutive patients, undergoing EGD were prospectively enrolled and randomized (Group S)	
Subject analysis set title	Group P - EGD
Subject analysis set type	Per protocol
Subject analysis set description:	
Seventy consecutive patients, undergoing EGD were prospectively enrolled and randomized (Group P)	
Subject analysis set title	Group S - Colonoscopy
Subject analysis set type	Per protocol
Subject analysis set description:	
Seventy consecutive patients undergoing colonoscopy were prospectively randomized (Group S)	
Subject analysis set title	Group P - Colonoscopy
Subject analysis set type	Per protocol
Subject analysis set description:	
Seventy consecutive patients undergoing colonoscopy were prospectively randomized (Group P)	

Primary: Patient Satisfaction (VAS)

End point title	Patient Satisfaction (VAS)
End point description:	
When completely awake, patients were asked to rate the pain/disconfort they experienced and their satisfaction about sedation on a 100 mm visual analogue scale (VAS)	
End point type	Primary
End point timeframe:	
40 minutes	

End point values	Group S - EGD	Group P - EGD	Group S - Colonoscopy	Group P - Colonoscopy
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	35	35	35	35
Units: millimeter(s)				
arithmetic mean (standard deviation)	76.5 (± 25.2)	93.8 (± 18.2)	85.5 (± 14.4)	95 (± 9.3)

Statistical analyses

Statistical analysis title	Groups comparation
Comparison groups	Group S - EGD v Group P - EGD v Group S - Colonoscopy v Group P - Colonoscopy

Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Secondary: Endoscopist Satisfaction (VAS)

End point title	Endoscopist Satisfaction (VAS)

End point description:

A 100 mm visual analogue scale (VAS) was used by the gastroenterology fellow to assess technical difficulty of examination and satisfaction with sedation as reported bythe endoscopist

End point type	Secondary

End point timeframe:

At the end of the procedure

End point values	Group S - EGD	Group P - EGD	Group S - Colonoscopy	Group P - Colonoscopy
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	35	35	35	35
Units: millimeter(s)				
arithmetic mean (standard deviation)	82.8 (± 21.2)	92.7 (± 14.3)	87.2 (± 12)	98.3 (± 11.4)

Statistical analyses

Statistical analysis title	Groups comparation
Comparison groups	Group S - EGD v Group P - EGD v Group S - Colonoscopy v Group P - Colonoscopy
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Secondary: Patient Satisfaction (VAS) 24h

End point title	Patient Satisfaction (VAS) 24h

End point description:

Patients were contacted by telephone 24–72 h after dischargeand asked again about their satisfaction about sedation, rated on averbal rating scale (0 = no satisfaction; 100 = complete satisfaction)

End point type	Secondary

End point timeframe:

24-72 h after the procedures

End point values	Group S - EGD	Group P - EGD	Group S - Colonoscopy	Group P - Colonoscopy
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	35	35	35	35
Units: millimeter(s)				
arithmetic mean (standard deviation)	77.3 (± 27.2)	92.6 (± 20.2)	87.7 (± 16.2)	97.3 (± 9.3)

Statistical analyses

Statistical analysis title	Groups comparation
Comparison groups	Group S - EGD v Group P - EGD v Group S - Colonoscopy v Group P - Colonoscopy
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Secondary: Time to discharge

End point title	Time to discharge

End point description:

End point type	Secondary

End point timeframe:

At discharge

End point values	Group S - EGD	Group P - EGD	Group S - Colonoscopy	Group P - Colonoscopy
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	35	35	35	35
Units: minute				
arithmetic mean (standard deviation)	3.9 (± 9.2)	1.1 (± 0.7)	5 (± 10.2)	1.1 (± 0.3)

Statistical analyses

Statistical analysis title	Groups comparation
Comparison groups	Group S - EGD v Group P - EGD v Group S - Colonoscopy v Group P - Colonoscopy

Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Secondary: Repeat Endoscopy

End point title	Repeat Endoscopy

End point description:

Patients were contacted by telephone 24–72 h after dischargeand asked if they would request the same anaestheticregimen for future endoscopies.

End point type	Secondary

End point timeframe:

24-72 h after discharge

End point values	Group S - EGD	Group P - EGD	Group S - Colonoscopy	Group P - Colonoscopy
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	35	35	35	35
Units: percent				
number (not applicable)	71.4	94.3	85.7	97.1

Statistical analyses

Statistical analysis title	Groups comparation
Comparison groups	Group S - EGD v Group P - EGD v Group S - Colonoscopy v Group P - Colonoscopy
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Chi-squared

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From enrolment to 24-72h after discharge	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	CTCAE
Dictionary version	3.0
Reporting groups	
Reporting group title	Group S (Standard Sedation)
Reporting group description: -	
Reporting group title	Group P (Propofol TCI Sedation)
Reporting group description: -	

Serious adverse events	Group S (Standard Sedation)	Group P (Propofol TCI Sedation)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 70 (0.00%)	0 / 70 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Group S (Standard Sedation)	Group P (Propofol TCI Sedation)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 70 (10.00%)	1 / 70 (1.43%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	3 / 70 (4.29%)	1 / 70 (1.43%)	
occurrences (all)	99999999	99999999	
Bradycardia			
subjects affected / exposed	1 / 70 (1.43%)	0 / 70 (0.00%)	
occurrences (all)	99999999	99999999	
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	3 / 70 (4.29%)	0 / 70 (0.00%)	
occurrences (all)	99999999	99999999	

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/25840875