Clinical trial results:
Phase III, Prospective, Multinational, Multicenter, Randomized, Controlled, Twoarm, Double Blind Study to assess Efficacy and Safety of DPLEX Administered Concomitantly with the Standard of Care (SoC), compared to a SoC treated control arm, in prevention of post abdominal surgery incisional infection.

Summary

EudraCT number	2020-002325-28
Trial protocol	BG CZ HR HU SK PL RO
Global end of trial date	08 August 2022

Results information

Result version number	v1 (current)
This version publication date	29 September 2023
First version publication date	29 September 2023

Trial information

Trial identification

Sponsor protocol code	D-PLEX311

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04233424
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	PolyPid Ltd
Sponsor organisation address	Hasivim 18, Petach Tikva, Israel,
Public contact	Clinical Operations Manager, CTG Bulgaria EOOD, 00359 2462 72 50, simeon.georgiev@ctgcro.com
Scientific contact	Clinical Operations Manager, CTG Bulgaria EOOD, 00359 2462 72 50, simeon.georgiev@ctgcro.com

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 September 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 August 2022
Global end of trial reached?	Yes
Global end of trial date	08 August 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the antiinfective efficacy of DPLEX administered concomitantly with the Standard of Care (SoC) over a period of 30 days post operation, by preventing surgical site infection (SSI), defined as superficial and/or deep infection in the target incision, compared to the SoC treated control arm and to assess the safety of DPLEX administered concomitantly with the Standard of Care (SoC).

Protection of trial subjects:

Data was collected using eCRFs that are specifically designed for this study. The data collected on the eCRFs was captured in a clinical data management system (CDMS) that meets the technical requirements described in 21 CFR Part 11 and EU regulations. The CDMS was fully validated to ensure that it meets the scientific, regulatory, and logistical requirements of the study before it is used to capture data from this study. Before using the CDMS, all users received training on the system and study-specific training. After they are trained, users were provided with individual system access rights. Data was collected at the investigational center by appropriately designated and trained personnel, and eCRFs must be completed for each screened subject according to their source documents.
Subject identity was not discernible from the data provided on the eCRF.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	24 June 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Israel: 140
Country: Number of subjects enrolled	United States: 37
Country: Number of subjects enrolled	Moldova, Republic of: 177
Country: Number of subjects enrolled	Romania: 168
Country: Number of subjects enrolled	Poland: 17
Country: Number of subjects enrolled	Slovakia: 14
Country: Number of subjects enrolled	Croatia: 40
Country: Number of subjects enrolled	Bulgaria: 92
Country: Number of subjects enrolled	Czechia: 132
Country: Number of subjects enrolled	Hungary: 160
Worldwide total number of subjects	977
EEA total number of subjects	623

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)	453
From 65 to 84 years	496
85 years and over	28

Subject disposition

Recruitment

Recruitment details:

Subject recruitment were conducted in general surgery departments at sites in US, Europe & Israel.

Pre-assignment

Screening details:

The study population includes male and female, 18 years old and above at screening, undergoing an elective colorectal surgery involving resection, with or without a stoma formation, that includes at least 1 abdominal incision that is > 10 cm (target incision).

Pre-assignment period milestones

Number of subjects started	1038[1]
Number of subjects completed	977

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Failure to meet eligibility criteria: 37
Reason: Number of subjects	Not eligiblt to the study: 13
Reason: Number of subjects	Consent withdrawn by subject: 10
Reason: Number of subjects	Adverse event, non-fatal: 1

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 1038 subjects were screened, 977 subjects were randomized to the study that equal to worldwild number of enrolled subjects.

Period 1

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

Blinding implementation details:

The sponsor, the subjects, outcomes assessor and all staff involved in the collection and recording of the clinical and laboratory data, based on which the independent adjudication committee will perform their assessment, will be blinded to treatment assignment. In addition, all aspects of data management and clean-up will be done in blinded datasets.

Arms

Are arms mutually exclusive?	Yes
Arm title	Investigational (D-PLEX)

Arm description: -

Arm type	Experimental
Investigational medicinal product name	D-PLEX
Investigational medicinal product code	
Other name	Doxycycline new formulation
Pharmaceutical forms	Powder for implantation paste
Routes of administration	Local use

Dosage and administration details:

D-PLEX dose is individualized, pending length of the abdominal target incision, 2-3 vials (5g each, a total max of 15g) in a single application.
Application will be done at the time of initial closure of the abdominal wall target incision. Following closure of the fascia, D-PLEX reconstituted paste will be applied on the fascia suture line, followed by soft tissues of the abdominal wall along the whole length of the surgical wound (including muscle, fat

and dermis). D-PLEX will not be applied on top of the skin (suture line).

Arm title	Control (SoC)
Arm description: -	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Investigational (D-PLEX)	Control (SoC)
Started	488	489
Completed	488	489

Period 2	
Period 2 title	30 Days post-surgery
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Data analyst, Assessor, Subject

Blinding implementation details:

The sponsor, the subjects, outcomes assessor and all staff involved in the collection and recording of the clinical and laboratory data, based on which the independent adjudication committee will perform their assessment, will be blinded to treatment assignment. In addition, all aspects of data management and clean-up will be done in blinded datasets. The study site personnel, who perform the index surgery or re-intervention procedure (OR staff), will be trained not to disclose the treatment arm

Arms

Are arms mutually exclusive?	Yes
Arm title	Investigational (D-PLEX)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	D-PLEX
Investigational medicinal product code	
Other name	Doxycycline new formulation
Pharmaceutical forms	Powder for implantation paste
Routes of administration	Local use

Dosage and administration details:

D-PLEX dose is individualized, pending length of the abdominal target incision, 2-3 vials (5g each, a total max of 15g) in a single application.
Application will be done at the time of initial closure of the abdominal wall target incision. Following closure of the fascia, D-PLEX reconstituted paste will be applied on the fascia suture line, followed by soft tissues of the abdominal wall along the whole length of the surgical wound (including muscle, fat and dermis). D-PLEX will not be applied on top of the skin (suture line).

Arm title	Control (SoC)
Arm description: -	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	Investigational (D-PLEX)	Control (SoC)
Started	488	489
Completed	485	489
Not completed	3	0
Protocol deviation	3	-

Period 3

Period 3 title	60 Days post-surgery
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Blinding implementation details:

The sponsor, the subjects, outcomes assessor and all staff involved in the collection and recording of the clinical and laboratory data, based on which the independent adjudication committee will perform their assessment, will be blinded to treatment assignment. In addition, all aspects of data management and clean-up will be done in blinded datasets.

Arms

Are arms mutually exclusive?	Yes
Arm title	Investigational (D-PLEX)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	D-PLEX
Investigational medicinal product code	
Other name	Doxycycline new formulation
Pharmaceutical forms	Powder for implantation paste
Routes of administration	Local use

Dosage and administration details:

D-PLEX dose is individualized, pending length of the abdominal target incision, 2-3 vials (5g each, a total max of 15g) in a single application.
Application will be done at the time of initial closure of the abdominal wall target incision. Following closure of the fascia, D-PLEX reconstituted paste will be applied on the fascia suture line, followed by soft tissues of the abdominal wall along the whole length of the surgical wound (including muscle, fat and dermis). D-PLEX will not be applied on top of the skin (suture line).

Arm title	Control (SoC)
Arm description: -	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 3	Investigational (D-PLEX)	Control (SoC)
Started	485	489
Completed	461	458
Not completed	24	31
Adverse event, serious fatal	15	16
Consent withdrawn by subject	2	8
Physician decision	1	3
Subject refuse to visit site	2	-
Lost to follow-up	1	3
Protocol deviation	3	1

Baseline characteristics

Reporting groups	
Reporting group title	Investigational (D-PLEX)
Reporting group description: -	
Reporting group title	Control (SoC)
Reporting group description: -	

Reporting group values	Investigational (D-PLEX)	Control (SoC)	Total
Number of subjects	488	489	977
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	64.7	63.7	
standard deviation	± 12.75	± 13.27	-
Gender categorical Units: Subjects			
Female	197	198	395
Male	291	291	582

Subject analysis sets	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

this population included all abdominally-incision randomized subjects. In this population, treatment was assigned based upon the treatment to which subjects were randomized regardless of which treatment they actually received.

Subject analysis set title	Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

This population included all subjects randomized and treated with D-PLEX or SoC. In this population, treatment was assigned based upon the treatment subjects actually received regardless of the treatment to which they were randomized.

Subject analysis set title	Incision >20cm (D-PLEX arm)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The analysis set was include all subjects who have been randomized to receive D-PLEX plus SoC with target abdominal incision length >20 cm. In this analysis set, treatment was assigned based on the treatment to which subjects were randomized, regardless of which treatment they actually received.

Subject analysis set title	Incision >20cm (SoC)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The analysis set was include all subjects who have been randomized to receive SoC alone with target abdominal incision length >20 cm. In this analysis set, treatment was assigned based on the treatment to which subjects were randomized, regardless of which treatment they actually received.

Reporting group values	ITT	Safety	Incision >20cm (D-PLEX arm)
Number of subjects	974	976	212
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	64.2	64.2	64.5
standard deviation	± 13.02	± 13.03	± 11.15
Gender categorical			
Units: Subjects			
Female	395	394	70
Male	579	582	142

Reporting group values	Incision >20cm (SoC)		
Number of subjects	211		
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	64.7		
standard deviation	± 12.17		
Gender categorical			
Units: Subjects			
Female	78		
Male	133		

End points

End points reporting groups

Reporting group title	Investigational (D-PLEX)
Reporting group description: -	
Reporting group title	Control (SoC)
Reporting group description: -	
Reporting group title	Investigational (D-PLEX)
Reporting group description: -	
Reporting group title	Control (SoC)
Reporting group description: -	
Reporting group title	Investigational (D-PLEX)
Reporting group description: -	
Reporting group title	Control (SoC)
Reporting group description: -	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

this population included all abdominally-incision randomized subjects. In this population, treatment was assigned based upon the treatment to which subjects were randomized regardless of which treatment they actually received.

Subject analysis set title	Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

This population included all subjects randomized and treated with D-PLEX or SoC. In this population, treatment was assigned based upon the treatment subjects actually received regardless of the treatment to which they were randomized.

Subject analysis set title	Incision >20cm (D-PLEX arm)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The analysis set was include all subjects who have been randomized to receive D-PLEX plus SoC with target abdominal incision length >20 cm. In this analysis set, treatment was assigned based on the treatment to which subjects were randomized, regardless of which treatment they actually received.

Subject analysis set title	Incision >20cm (SoC)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The analysis set was include all subjects who have been randomized to receive SoC alone with target abdominal incision length >20 cm. In this analysis set, treatment was assigned based on the treatment to which subjects were randomized, regardless of which treatment they actually received.

Primary: Infection rate as measured by the proportion of subjects with at least one abdominal target incisional infection event

End point title	Infection rate as measured by the proportion of subjects with at least one abdominal target incisional infection event

End point description:

Infection rate as measured by the proportion of subjects with at least one abdominal target incisional infection event, occurring within 30 days post abdominal surgery and determined by a blinded independent adjudication committee. All-cause mortality and re-intervention at the primary incision site (target) due to suspected SSI or due to poor wound healing, including wound dehiscence (as verified by the blinded adjudication committee), within 30 days post index surgery will be analysed as treatment failure.

End point type	Primary

End point timeframe:

30 days post-surgery

End point values	Investigational (D-PLEX)	Control (SoC)	ITT	Incision >20cm (D-PLEX arm)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	485	489	974	212
Units: subjects				
Failure	45	59	104	17
Success	440	430	870	195

End point values	Incision >20cm (SoC)			
Subject group type	Subject analysis set			
Number of subjects analysed	211			
Units: subjects				
Failure	37			
Success	174			

Statistical analyses

Statistical analysis title	Primary analysis
Statistical analysis description: Cochran-Mantel-Haenszel Test	
Comparison groups	Investigational (D-PLEX) v Control (SoC)
Number of subjects included in analysis	974
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.152
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	-2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.7
upper limit	1

Statistical analysis title	Subgroup analysis of subjectc with incision >20
Statistical analysis description: Pre-defined subgroup analysis	
Comparison groups	Incision >20cm (D-PLEX arm) v Incision >20cm (SoC)

Number of subjects included in analysis	423
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0032 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	-9.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.5
upper limit	-3.2

Notes:

[1] - Nominal, not adjusted for multiple testing (not formal significance test)

Secondary: First key secondary endpoint

End point title	First key secondary endpoint

End point description:

Infection rate as measured by the proportion of subjects with at least one SSI event in the target incision, occurred within 30 days post abdominal index surgery, and determined by a blinded independent adjudication committee.

End point type	Secondary

End point timeframe:

30 days post-surgery

End point values	Investigational (D-PLEX)	Control (SoC)	ITT	Incision >20cm (D-PLEX arm)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	485	489	974	212
Units: subjects				
Failure	29	32	61	9
Success	440	435	875	195

End point values	Incision >20cm (SoC)			
Subject group type	Subject analysis set			
Number of subjects analysed	211			
Units: subjects				
Failure	19			
Success	177			

Statistical analyses

Statistical analysis title	First key secondary primary analysis
Comparison groups	Control (SoC) v Investigational (D-PLEX)
Number of subjects included in analysis	974
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6219
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.9
upper limit	2.3

Statistical analysis title	First key secondary analysis of subjects with >20
Comparison groups	Incision >20cm (D-PLEX arm) v Incision >20cm (SoC)
Number of subjects included in analysis	423
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.041 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	-5.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.1
upper limit	-0.2

Notes:

[2] - Nominal, not adjusted. Not a formal significance test

Secondary: Second key secondary endpoint	
End point title	Second key secondary endpoint
End point description:	
Number (percentage) of subjects with at least one score of ASEPSIS > 20 (further to an adjudicated SSI).	
End point type	Secondary
End point timeframe:	
30 days post-surgery	

End point values	Investigational (D-PLEX)	Control (SoC)	ITT	Incision >20cm (D-PLEX arm)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	485	489	936	212
Units: subjects				
Failure	8	10	18	2
Success	461	457	918	202

End point values	Incision >20cm (SoC)			
Subject group type	Subject analysis set			
Number of subjects analysed	211			
Units: subjects				
Failure	5			
Success	191			

Statistical analyses

Statistical analysis title	Second key secondary primary analysis
Comparison groups	Investigational (D-PLEX) v Control (SoC)
Number of subjects included in analysis	974
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6238
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	1.3

Statistical analysis title	Second key secondary of subjects >20cm
Comparison groups	Incision >20cm (SoC) v Incision >20cm (D-PLEX arm)
Number of subjects included in analysis	423
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.276 [3]
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	-1.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.2
upper limit	1

Notes:

[3] - Nominal, not adjusted, not formal significance test

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
60 days post-surgery	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups	
Reporting group title	Investigational arm (D-PLEX)
Reporting group description:	
Subjects randomized to the investigational arm were treated with D-PLEX during the surgery (index procedure), as an adjunct to the SoC (see below). D-PLEX was applied during the closure of the abdominal target incision. D-PLEX was not re-administered if any reintervention occurs.	
Reporting group title	Control (SoC)
Reporting group description:	
Subjects randomized to the control arm were treated only with prophylactic IV antibiotic according to SoC. Pre-operation prophylactic oral antibiotic was not allowed. Mechanical bowel preparation was at the discretion of the PI per each site's SOP	

Serious adverse events	Investigational arm (D-PLEX)	Control (SoC)	
Total subjects affected by serious adverse events			
subjects affected / exposed	69 / 478 (14.44%)	98 / 498 (19.68%)	
number of deaths (all causes)	16	17	
number of deaths resulting from adverse events	16	17	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to liver			
subjects affected / exposed	1 / 478 (0.21%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to peritoneum			
subjects affected / exposed	2 / 478 (0.42%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myeloid leukaemia			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			

Haemodynamic instability			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hypotension			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery thrombosis			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 478 (0.21%)	3 / 498 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 3	
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 478 (0.21%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Mucosal inflammation			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden cardiac death			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Female genital tract fistula			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis noninfective			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fluid collection			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic haemorrhage			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	3 / 478 (0.63%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Acute respiratory failure			
subjects affected / exposed	1 / 478 (0.21%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Hydrothorax			

subjects affected / exposed	0 / 478 (0.00%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Apnoea			
subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Emphysema			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
SARS-CoV-1 test positive			
subjects affected / exposed	1 / 478 (0.21%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oxygen saturation decreased			

subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Anastomotic leak			
subjects affected / exposed	8 / 478 (1.67%)	19 / 498 (3.82%)	
occurrences causally related to treatment / all	0 / 8	0 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic complication			
subjects affected / exposed	4 / 478 (0.84%)	3 / 498 (0.60%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 2	0 / 0	
Gastrointestinal anastomotic leak			
subjects affected / exposed	2 / 478 (0.42%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative ileus			
subjects affected / exposed	2 / 478 (0.42%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound evisceration			
subjects affected / exposed	0 / 478 (0.00%)	3 / 498 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal wound dehiscence			
subjects affected / exposed	1 / 478 (0.21%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic fistula			
subjects affected / exposed	0 / 478 (0.00%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic haemorrhage			

subjects affected / exposed	2 / 478 (0.42%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal wall wound			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia postoperative			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carcinogenicity			
subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal stoma complication			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incision site haemorrhage			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seroma			

subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suture related complication			
subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric injury			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	2 / 478 (0.42%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 2	
Cardiac failure acute			
subjects affected / exposed	1 / 478 (0.21%)	3 / 498 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 2	
Acute myocardial infarction			
subjects affected / exposed	2 / 478 (0.42%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 478 (0.21%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	0 / 478 (0.00%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Cardiopulmonary failure			

subjects affected / exposed	2 / 478 (0.42%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Cardiovascular insufficiency			
subjects affected / exposed	1 / 478 (0.21%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Acute coronary syndrome			
subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradyarrhythmia			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure congestive			
subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
Coma			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			

subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Haemorrhagic disorder			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	3 / 478 (0.63%)	6 / 498 (1.20%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	2 / 478 (0.42%)	5 / 498 (1.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 478 (0.21%)	4 / 498 (0.80%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal necrosis			
subjects affected / exposed	2 / 478 (0.42%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Intestinal fistula			
subjects affected / exposed	1 / 478 (0.21%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			

subjects affected / exposed	0 / 478 (0.00%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal fluid collection			
subjects affected / exposed	1 / 478 (0.21%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal haemorrhage			
subjects affected / exposed	1 / 478 (0.21%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mechanical ileus			
subjects affected / exposed	1 / 478 (0.21%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal perforation			
subjects affected / exposed	1 / 478 (0.21%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain lower			
subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fissure			
subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			

subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colonic fistula			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn's disease			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer perforation			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocutaneous fistula			
subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			

subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoperitoneum			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus paralytic			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctitis			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis mesenteric vessel			
subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatobiliary disorders			
Hepatorenal failure			

subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 478 (0.42%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	1 / 478 (0.21%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis noninfective			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Postoperative wound infection			
subjects affected / exposed	8 / 478 (1.67%)	6 / 498 (1.20%)	
occurrences causally related to treatment / all	0 / 8	2 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	4 / 478 (0.84%)	5 / 498 (1.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pneumonia			
subjects affected / exposed	4 / 478 (0.84%)	5 / 498 (1.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 2	
Abdominal abscess			

subjects affected / exposed	4 / 478 (0.84%)	4 / 498 (0.80%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	6 / 478 (1.26%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 478 (0.00%)	4 / 498 (0.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 478 (0.21%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
COVID-19 pneumonia			
subjects affected / exposed	1 / 478 (0.21%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic abscess			
subjects affected / exposed	2 / 478 (0.42%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related bacteraemia			
subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endotoxic shock			

subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haematoma infection			
subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mediastinitis			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical device site infection			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising fasciitis			
subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic infection			
subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perirectal abscess			
subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia acinetobacter			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Purulent discharge			

subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			
subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sepsis			
subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stoma site infection			
subjects affected / exposed	0 / 478 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 478 (0.21%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 478 (0.00%)	2 / 498 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Investigational arm (D-PLEX)	Control (SoC)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	381 / 478 (79.71%)	398 / 498 (79.92%)	
Injury, poisoning and procedural complications			
Incision site pain			
subjects affected / exposed	111 / 478 (23.22%)	118 / 498 (23.69%)	
occurrences (all)	158	167	

Procedural pain			
subjects affected / exposed	83 / 478 (17.36%)	87 / 498 (17.47%)	
occurrences (all)	87	91	
Incision site erythema			
subjects affected / exposed	52 / 478 (10.88%)	52 / 498 (10.44%)	
occurrences (all)	52	53	
Incision site discharge			
subjects affected / exposed	53 / 478 (11.09%)	37 / 498 (7.43%)	
occurrences (all)	54	37	
Incision site swelling			
subjects affected / exposed	25 / 478 (5.23%)	23 / 498 (4.62%)	
occurrences (all)	25	23	
Anastomotic leak			
subjects affected / exposed	11 / 478 (2.30%)	23 / 498 (4.62%)	
occurrences (all)	11	23	
Vascular disorders			
Hypertension			
subjects affected / exposed	11 / 478 (2.30%)	7 / 498 (1.41%)	
occurrences (all)	11	8	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	13 / 478 (2.72%)	7 / 498 (1.41%)	
occurrences (all)	15	7	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	12 / 478 (2.51%)	15 / 498 (3.01%)	
occurrences (all)	12	15	
General disorders and administration site conditions			
Pain			
subjects affected / exposed	83 / 478 (17.36%)	85 / 498 (17.07%)	
occurrences (all)	83	89	
Tenderness			
subjects affected / exposed	63 / 478 (13.18%)	64 / 498 (12.85%)	
occurrences (all)	63	66	
Feeling hot			

subjects affected / exposed	33 / 478 (6.90%)	33 / 498 (6.63%)	
occurrences (all)	33	33	
Pyrexia			
subjects affected / exposed	16 / 478 (3.35%)	23 / 498 (4.62%)	
occurrences (all)	18	23	
Swelling			
subjects affected / exposed	16 / 478 (3.35%)	23 / 498 (4.62%)	
occurrences (all)	16	23	
Asthenia			
subjects affected / exposed	5 / 478 (1.05%)	11 / 498 (2.21%)	
occurrences (all)	5	11	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	41 / 478 (8.58%)	52 / 498 (10.44%)	
occurrences (all)	42	56	
Vomiting			
subjects affected / exposed	29 / 478 (6.07%)	21 / 498 (4.22%)	
occurrences (all)	30	23	
Abdominal pain			
subjects affected / exposed	21 / 478 (4.39%)	17 / 498 (3.41%)	
occurrences (all)	21	17	
Diarrhoea			
subjects affected / exposed	19 / 478 (3.97%)	18 / 498 (3.61%)	
occurrences (all)	20	18	
Abdominal distension			
subjects affected / exposed	6 / 478 (1.26%)	11 / 498 (2.21%)	
occurrences (all)	6	11	
Infections and infestations			
Postoperative wound infection			
subjects affected / exposed	43 / 478 (9.00%)	52 / 498 (10.44%)	
occurrences (all)	45	56	
Urinary tract infection			
subjects affected / exposed	8 / 478 (1.67%)	16 / 498 (3.21%)	
occurrences (all)	8	16	
COVID-19			

subjects affected / exposed occurrences (all)	9 / 478 (1.88%) 10	13 / 498 (2.61%) 13	
Metabolism and nutrition disorders Hypokalaemia subjects affected / exposed occurrences (all)	11 / 478 (2.30%) 11	11 / 498 (2.21%) 11	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 December 2019	• Changes in study design due to re-evaluation of the overall infection rate in Europe and US regions • Implementation of HPRA recommendations
05 May 2020	Changes in study design due re-evaluation of overall infection rate in Europe and US regions and FDA recommendations.
19 August 2020	Changes in study design following FDA review of the protocol.
08 November 2021	Changes in study design following study procedures clarifications, EU regulatory authorities requests harmonized in this version.
22 February 2022	Update of study end points and sample size calculation as agreed with FDA.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported