



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 anti-infective 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 worldild 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 standard deviation | 64.7 ± 12.75 | 63.7 ± 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 standard deviation | 64.2 ± 13.02 | 64.2 ± 13.03 | 64.5 ± 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 standard deviation | 64.7 ± 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 subjects 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 occurrences (all) | 83 / 478 (17.36%) 87 | 87 / 498 (17.47%) 91 | |
| Incision site erythema subjects affected / exposed occurrences (all) | 52 / 478 (10.88%) 52 | 52 / 498 (10.44%) 53 | |
| Incision site discharge subjects affected / exposed occurrences (all) | 53 / 478 (11.09%) 54 | 37 / 498 (7.43%) 37 | |
| Incision site swelling subjects affected / exposed occurrences (all) | 25 / 478 (5.23%) 25 | 23 / 498 (4.62%) 23 | |
| Anastomotic leak subjects affected / exposed occurrences (all) | 11 / 478 (2.30%) 11 | 23 / 498 (4.62%) 23 | |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 11 / 478 (2.30%) 11 | 7 / 498 (1.41%) 8 | |
| Cardiac disorders Tachycardia subjects affected / exposed occurrences (all) | 13 / 478 (2.72%) 15 | 7 / 498 (1.41%) 7 | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 12 / 478 (2.51%) 12 | 15 / 498 (3.01%) 15 | |
| General disorders and administration site conditions Pain subjects affected / exposed occurrences (all) | 83 / 478 (17.36%) 83 | 85 / 498 (17.07%) 89 | |
| Tenderness subjects affected / exposed occurrences (all) | 63 / 478 (13.18%) 63 | 64 / 498 (12.85%) 66 | |
| Feeling hot | | | |

| | | | |
|---|------------------------|-------------------------|--|
| subjects affected / exposed occurrences (all) | 33 / 478 (6.90%) 33 | 33 / 498 (6.63%) 33 | |
| Pyrexia subjects affected / exposed occurrences (all) | 16 / 478 (3.35%) 18 | 23 / 498 (4.62%) 23 | |
| Swelling subjects affected / exposed occurrences (all) | 16 / 478 (3.35%) 16 | 23 / 498 (4.62%) 23 | |
| Asthenia subjects affected / exposed occurrences (all) | 5 / 478 (1.05%) 5 | 11 / 498 (2.21%) 11 | |
| Gastrointestinal disorders | | | |
| Nausea subjects affected / exposed occurrences (all) | 41 / 478 (8.58%) 42 | 52 / 498 (10.44%) 56 | |
| Vomiting subjects affected / exposed occurrences (all) | 29 / 478 (6.07%) 30 | 21 / 498 (4.22%) 23 | |
| Abdominal pain subjects affected / exposed occurrences (all) | 21 / 478 (4.39%) 21 | 17 / 498 (3.41%) 17 | |
| Diarrhoea subjects affected / exposed occurrences (all) | 19 / 478 (3.97%) 20 | 18 / 498 (3.61%) 18 | |
| Abdominal distension subjects affected / exposed occurrences (all) | 6 / 478 (1.26%) 6 | 11 / 498 (2.21%) 11 | |
| Infections and infestations | | | |
| Postoperative wound infection subjects affected / exposed occurrences (all) | 43 / 478 (9.00%) 45 | 52 / 498 (10.44%) 56 | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 8 / 478 (1.67%) 8 | 16 / 498 (3.21%) 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 | <ul style="list-style-type: none">Changes in study design due to re-evaluation of the overall infection rate in Europe and US regionsImplementation 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