Clinical trial results:
Multiorgan Metabolic imaging response assessment of Abemaciclib: the MiMe-A trial

Summary

EudraCT number	2017-000123-28
Trial protocol	BE FR
Global end of trial date	20 December 2023

Results information

Result version number	v1 (current)
This version publication date	09 November 2024
First version publication date	09 November 2024
Summary attachment (see zip file)	Final Study Report (MiMe-A_Final_study_report.pdf)

Trial information

Trial identification

Sponsor protocol code	IJB-MULTI-MIME-A-2017

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03339843
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Institut Jules Bordet
Sponsor organisation address	rue Meyelemeersch 90, Anderlecht, Belgium, 1070
Public contact	CTSU, Institut Jules Bordet, ctsu.trials@bordet.be
Scientific contact	CTSU, Institut Jules Bordet, ctsu.trials@bordet.be
Sponsor organisation name	Institut Jules Bordet
Sponsor organisation address	Rue Meylemeersch 90, Anderlecht, Belgium, 1070
Public contact	Dr. Laura Polastro , Institut Jules Bordet, laura.polastro@hubruxelles.be
Scientific contact	Dr Alain Hendlisz, Institut Jules Bordet, alain.hendlisz@hubruxelles.be

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	21 November 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 November 2021
Global end of trial reached?	Yes
Global end of trial date	20 December 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the anti-tumour activity of abemaciclib in the five tumour types studied in this trial using the combination of FDG-PET/CT during the first cycle of therapy (early FDG- PET/CT) and RECIST v1.1 after 2 cycles of therapy as a screening tool.

Protection of trial subjects:

Both dose suppression (within a cycle) and cycle delay are permitted in case of clinically significant toxicities. Abemaciclib may be held up to 14 days within a cycle or at the start of next cycle to permit sufficient time recovery from the toxicity. If a dose suspension occurs, the investigator may resume abemaciclib dosing at the same dose level for the remainder of the cycle or at reduced dose (assuming resolution to at least grade 1 for the non-hematological and at least grade 2 for hematological toxicity). If the subject experiences the same toxicity with the same or greater severity requiring a dose suspension within a cycle or at start of the next cycle, the subject must be dose reduced and non rechallenged a second time at the prior dose level. Subject not recovering from toxicity within 14 days should be considered for discontinuation of abemaciclib. In exceptional circumstances, a delay > 14 days is permitted upon agreement of the Investigator and the Sponsor.
Subjects who were taking strong CYP3A inhibitors were recommended to reduce the abemaciclib dose. Very close monitoring of side effects was organized (for example medical visit after 10 days of taking abemaciclib) in order to adapt supportive treatments and doses of abemaciclib in the event of side effects.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 October 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	18 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 62
Country: Number of subjects enrolled	France: 23
Worldwide total number of subjects	85
EEA total number of subjects	85

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)	26
From 65 to 84 years	57
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Planned recruitment period : 24 months
The recruitment of a tumour cohort will be stopped when at least 13 evaluable patients have been enrolled in the cohort and have been treated until the first RECIST assessment (ie: after 2 cycles).

Pre-assignment

Screening details:

During the screening period, following signature of the Informed Consent Form and registration, the principal investigator confirms the subject's eligibility for the study by conducting the assessments described below and complete the corresponding CRF.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: Esophaegal adenocarcinoma

Arm description:

Subjects with histologically confirmed esophageal adenocarcinoma that is metastatic or unresectable and for which standard platinum regimens are no longer effective.

Arm type	Experimental
Investigational medicinal product name	Abemaciclib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Abemaciclib will be continuously administrated orally at a dose of 150mg twice daily until disease progression, until new lesions are observed at the early FDG-PET/CT, until the lack of tolerability or the subject 's consent withdrawal. One cycle is 28 days.

Arm title	Cohort 2: Esophageal squamous cell carcinoma

Arm description:

Subjects with histologically confirmed esophageal squamous cell carcinoma that is metastatic or unresectable and for which standard platinum regimens are no longer effective.

Arm type	Experimental
Investigational medicinal product name	Abemaciclib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Abemaciclib will be continuously administrated orally at a dose of 150mg twice daily until disease progression, until new lesions are observed at the early FDG-PET/CT, until the lack of tolerability or the subject 's consent withdrawal. One cycle is 28 days.

Arm title	Cohort 3: Cholangiocarcinoma

Arm description:

Subjects with histologically confirmed cholangiocarcinoma that is metastatic or unresectable and for which standard platinum regimens are no longer effective.

Arm type	Experimental

Investigational medicinal product name	Abemaciclib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Abemaciclib will be continuously administrated orally at a dose of 150mg twice daily until disease progression, until new lesions are observed at the early FDG-PET/CT, until the lack of tolerability or the subject ‘s consent withdrawal. One cycle is 28 days.

Arm title	Cohort 4: Urothelial cancer

Arm description:

Subjects with histologically confirmed urothelial cancer that is metastatic or unresectable and for which standard platinum regimens are no longer effective. Subjects must have been pre-treated with nivolumab or another immune checkpoint inhibitor.

Arm type	Experimental
Investigational medicinal product name	Abemaciclib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Abemaciclib will be continuously administrated orally at a dose of 150mg twice daily until disease progression, until new lesions are observed at the early FDG-PET/CT, until the lack of tolerability or the subject ‘s consent withdrawal. One cycle is 28 days.

Arm title	Cohort 5: Endometrial cancer

Arm description:

Subjects with histologically confirmed endometrial cancer a that is metastatic or unresectable and for which standard platinum regimens are no longer effective.

Arm type	Experimental
Investigational medicinal product name	Abemaciclib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Abemaciclib will be continuously administrated orally at a dose of 150mg twice daily until disease progression, until new lesions are observed at the early FDG-PET/CT, until the lack of tolerability or the subject ‘s consent withdrawal. One cycle is 28 days.

Number of subjects in period 1	Cohort 1: Esophaegal adenocarcinoma	Cohort 2: Esophageal squamous cell carcinoma	Cohort 3: Cholangiocarcinoma
Started	17	17	17
Completed	17	17	17

Number of subjects in period 1	Cohort 4: Urothelial cancer	Cohort 5: Endometrial cancer
Started	17	17
Completed	17	17

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1: Esophaegal adenocarcinoma
Reporting group description:	
Subjects with histologically confirmed esophageal adenocarcinoma that is metastatic or unresectable and for which standard platinum regimens are no longer effective.	
Reporting group title	Cohort 2: Esophageal squamous cell carcinoma
Reporting group description:	
Subjects with histologically confirmed esophageal squamous cell carcinoma that is metastatic or unresectable and for which standard platinum regimens are no longer effective.	
Reporting group title	Cohort 3: Cholangiocarcinoma
Reporting group description:	
Subjects with histologically confirmed cholangiocarcinoma that is metastatic or unresectable and for which standard platinum regimens are no longer effective.	
Reporting group title	Cohort 4: Urothelial cancer
Reporting group description:	
Subjects with histologically confirmed urothelial cancer that is metastatic or unresectable and for which standard platinum regimens are no longer effective. Subjects must have been pre-treated with nivolumab or another immune checkpoint inhibitor.	
Reporting group title	Cohort 5: Endometrial cancer
Reporting group description:	
Subjects with histologically confirmed endometrial cancer a that is metastatic or unresectable and for which standard platinum regimens are no longer effective.	

Reporting group values	Cohort 1: Esophaegal adenocarcinoma	Cohort 2: Esophageal squamous cell carcinoma	Cohort 3: Cholangiocarcinoma
Number of subjects	17	17	17
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	8	5	3
From 65-84 years	9	12	12
85 years and over	0	0	2
Gender categorical Units: Subjects			
Female	3	6	11
Male	14	11	6

Reporting group values	Cohort 4: Urothelial cancer	Cohort 5: Endometrial cancer	Total
Number of subjects	17	17	85

Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	5	5	26
From 65-84 years	12	12	57
85 years and over	0	0	2
Gender categorical Units: Subjects			
Female	2	17	39
Male	15	0	46

End points

End points reporting groups

Reporting group title	Cohort 1: Esophaegal adenocarcinoma
Reporting group description:	
Subjects with histologically confirmed esophageal adenocarcinoma that is metastatic or unresectable and for which standard platinum regimens are no longer effective.	
Reporting group title	Cohort 2: Esophageal squamous cell carcinoma
Reporting group description:	
Subjects with histologically confirmed esophageal squamous cell carcinoma that is metastatic or unresectable and for which standard platinum regimens are no longer effective.	
Reporting group title	Cohort 3: Cholangiocarcinoma
Reporting group description:	
Subjects with histologically confirmed cholangiocarcinoma that is metastatic or unresectable and for which standard platinum regimens are no longer effective.	
Reporting group title	Cohort 4: Urothelial cancer
Reporting group description:	
Subjects with histologically confirmed urothelial cancer that is metastatic or unresectable and for which standard platinum regimens are no longer effective. Subjects must have been pre-treated with nivolumab or another immune checkpoint inhibitor.	
Reporting group title	Cohort 5: Endometrial cancer
Reporting group description:	
Subjects with histologically confirmed endometrial cancer a that is metastatic or unresectable and for which standard platinum regimens are no longer effective.	

Primary: Overall Response (combining PERCIST and RECIST evaluations)

End point title	Overall Response (combining PERCIST and RECIST
End point description:	
Based on the protocol, a subject is considered evaluable if he/she has a clear treatment success or non-treatment success. Treatment success is defined as when a subject has metabolic response according to PERCIST with a response cut off set at 15% at the early FDG-PET/CT and a morphological disease control after 2 cycles measured by RECIST v1.1 (disease control is defined as complete response (CR), partial response (PR) or stable disease (SD)).	
End point type	Primary
End point timeframe:	
after 2 cycles	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis will be done on eligible and evaluable patients. The thresholds to go on after the interim analysis have been described above.
In case, accrual goes beyond the first step, statistical testing will be done using a chi square test (at 10% one-sided significance level). A 95% confidence interval will also be reported using an exact binomial distribution.

End point values	Cohort 1: Esophaegal adenocarcinoma	Cohort 2: Esophageal squamous cell carcinoma	Cohort 3: Cholangiocarcinoma	Cohort 4: Urothelial cancer
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	17	17	17
Units: Number				
Treatment Success	0	0	0	1

Treatment Failure	17	17	17	16

End point values	Cohort 5: Endometrial cancer			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: Number				
Treatment Success	0			
Treatment Failure	17			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Non-serious adverse events (AEs) : from first administration of abemaciclib until 28 days after the last administration of abemaciclib
Serious adverse events (SAEs) : from CF signature until initiation of abemaciclib

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Cohort 1: Esophaegal adenocarcinoma

Reporting group description:

Subjects with histologically confirmed esophageal adenocarcinoma that is metastatic or unresectable and for which standard platinum regimens are no longer effective.

Reporting group title	Cohort 2: Esophageal squamous cell carcinoma

Reporting group description:

Subjects with histologically confirmed esophageal squamous cell carcinoma that is metastatic or unresectable and for which standard platinum regimens are no longer effective.

Reporting group title	Cohort 3: Cholangiocarcinoma

Reporting group description:

Subjects with histologically confirmed cholangiocarcinoma that is metastatic or unresectable and for which standard platinum regimens are no longer effective.

Reporting group title	Cohort 4: Urothelial cancer

Reporting group description:

Subjects with histologically confirmed urothelial cancer that is metastatic or unresectable and for which standard platinum regimens are no longer effective. Subjects must have been pre-treated with nivolumab or another immune checkpoint inhibitor.

Reporting group title	Cohort 5: Endometrial cancer

Reporting group description:

Subjects with histologically confirmed endometrial cancer a that is metastatic or unresectable and for which standard platinum regimens are no longer effective.

Serious adverse events	Cohort 1: Esophaegal adenocarcinoma	Cohort 2: Esophageal squamous cell carcinoma	Cohort 3: Cholangiocarcinoma
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 17 (17.65%)	4 / 17 (23.53%)	6 / 17 (35.29%)
number of deaths (all causes)	1	2	1
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Ureteric anastomosis complication			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	2 / 17 (11.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Influenza like illness			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Bezoar			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			

subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pulmonary sepsis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Biliary sepsis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			

Decreased appetite			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic metabolic decompensation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 4: Urothelial cancer	Cohort 5: Endometrial cancer	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 17 (35.29%)	3 / 17 (17.65%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Ureteric anastomosis complication			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza like illness			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			

subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Bezoar			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 17 (11.76%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 17 (5.88%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			

subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 17 (11.76%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary sepsis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastroenteritis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic metabolic decompensation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Cohort 1: Esophaegal adenocarcinoma	Cohort 2: Esophageal squamous cell carcinoma	Cohort 3: Cholangiocarcinoma
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 17 (82.35%)	6 / 17 (35.29%)	17 / 17 (100.00%)
Vascular disorders			

Hypotension			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	2
Pallor			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Pelvic venous thrombosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Superficial vein thrombosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	11 / 17 (64.71%)	5 / 17 (29.41%)	8 / 17 (47.06%)
occurrences (all)	12	5	8
chest pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Oedema			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 17 (0.00%)	2 / 17 (11.76%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
General physical health deterioration			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Inflammation			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			

subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	2 / 17 (11.76%)
occurrences (all)	0	2	2
Influenza like illness			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Immune system disorders			
Pneumonia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Hypersensitivity			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Prostatism			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 17 (5.88%)	2 / 17 (11.76%)	0 / 17 (0.00%)
occurrences (all)	1	2	0
Epistaxis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	0 / 17 (0.00%)	2 / 17 (11.76%)	2 / 17 (11.76%)
occurrences (all)	0	2	2
Pulmonary embolism			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Nasal dryness			

subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Pulmonary haemorrhage			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Haemoptysis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Bronchopneumopathy			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Lung disorder			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Productive cough			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Confusional state			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Nervousness			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood creatine increased			

subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 17 (5.88%)	2 / 17 (11.76%)	1 / 17 (5.88%)
occurrences (all)	1	2	2
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	2 / 17 (11.76%)	1 / 17 (5.88%)	1 / 17 (5.88%)
occurrences (all)	2	1	1
White blood cell count decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Bilirubin conjugated increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Upper limb fracture			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Fall			

subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Congenital, familial and genetic disorders			
Tracheo-oesophageal fistula			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 17 (0.00%)	2 / 17 (11.76%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
Palpitations			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Arteriospasm coronary			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Tachycardia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Dysgeusia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Tremor			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			

subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Monoparesis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Altered state of consciousness			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Neutropenia			
subjects affected / exposed	1 / 17 (5.88%)	2 / 17 (11.76%)	4 / 17 (23.53%)
occurrences (all)	1	2	6
Lymphopenia			
subjects affected / exposed	0 / 17 (0.00%)	2 / 17 (11.76%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
Thrombocytopenia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	6 / 17 (35.29%)
occurrences (all)	0	1	9
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	2 / 17 (11.76%)
occurrences (all)	0	1	2
Eye disorders			
Lacrimation increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Xerophthalmia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			

Constipation			
subjects affected / exposed	1 / 17 (5.88%)	4 / 17 (23.53%)	4 / 17 (23.53%)
occurrences (all)	1	4	5
Abdominal distension			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	3 / 17 (17.65%)
occurrences (all)	0	1	3
Anal haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 17 (0.00%)	3 / 17 (17.65%)	0 / 17 (0.00%)
occurrences (all)	0	3	0
Abdominal rigidity			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Dysphagia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 17 (5.88%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Nausea			
subjects affected / exposed	5 / 17 (29.41%)	1 / 17 (5.88%)	6 / 17 (35.29%)
occurrences (all)	5	1	6
Gingival swelling			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Oral pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	1 / 17 (5.88%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Vomiting			
subjects affected / exposed	4 / 17 (23.53%)	1 / 17 (5.88%)	2 / 17 (11.76%)
occurrences (all)	4	1	2
Intestinal obstruction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Inguinal hernia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Hepatic pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	2 / 17 (11.76%)
occurrences (all)	0	1	2
Dermatitis bullous			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Pruritus			

subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Ingrowing nail			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	2 / 17 (11.76%)	2 / 17 (11.76%)	1 / 17 (5.88%)
occurrences (all)	2	2	1
Acute kidney injury			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Bladder pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Chronic kidney disease			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Cystitis haemorrhagic			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Hypothyroidism			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Arthralgia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Arthritis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Influenza			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Fungal oesophagitis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Biliary tract infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
COVID-19			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Cestode infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Fungal infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Cholangitis infective			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Pyelonephritis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	2
Tooth abscess			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1

Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Hypoalbuminaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Hypoglycaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Malnutrition			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Hyperglycaemia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	3 / 17 (17.65%)
occurrences (all)	0	1	3
Hypophosphataemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1

Non-serious adverse events	Cohort 4: Urothelial cancer	Cohort 5: Endometrial cancer	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 17 (94.12%)	16 / 17 (94.12%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Pallor			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Pelvic venous thrombosis			

subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Superficial vein thrombosis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 17 (23.53%)	8 / 17 (47.06%)	
occurrences (all)	4	8	
chest pain			
subjects affected / exposed	2 / 17 (11.76%)	0 / 17 (0.00%)	
occurrences (all)	2	0	
Malaise			
subjects affected / exposed	0 / 17 (0.00%)	4 / 17 (23.53%)	
occurrences (all)	0	4	
Oedema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Mucosal inflammation			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
General physical health deterioration			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Inflammation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Oedema peripheral			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Influenza like illness			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Pyrexia			

subjects affected / exposed	2 / 17 (11.76%)	0 / 17 (0.00%)	
occurrences (all)	2	0	
Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Immune system disorders			
Pneumonia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Hypersensitivity			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Prostatism			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 17 (11.76%)	3 / 17 (17.65%)	
occurrences (all)	2	3	
Epistaxis			
subjects affected / exposed	2 / 17 (11.76%)	0 / 17 (0.00%)	
occurrences (all)	2	0	
Dyspnoea			
subjects affected / exposed	4 / 17 (23.53%)	2 / 17 (11.76%)	
occurrences (all)	5	3	
Pulmonary embolism			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Nasal dryness			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Pulmonary haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Haemoptysis			

subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Bronchopneumopathy			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Lung disorder			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Productive cough			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Insomnia			
subjects affected / exposed	2 / 17 (11.76%)	1 / 17 (5.88%)	
occurrences (all)	2	1	
Confusional state			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Depression			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Nervousness			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Investigations			
Blood creatine increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Blood creatinine increased			

subjects affected / exposed	6 / 17 (35.29%)	4 / 17 (23.53%)	
occurrences (all)	7	4	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 17 (5.88%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Weight decreased			
subjects affected / exposed	0 / 17 (0.00%)	3 / 17 (17.65%)	
occurrences (all)	0	3	
White blood cell count decreased			
subjects affected / exposed	1 / 17 (5.88%)	3 / 17 (17.65%)	
occurrences (all)	2	3	
Bilirubin conjugated increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Blood bilirubin increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Upper limb fracture			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Fall			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Congenital, familial and genetic disorders			
Tracheo-oesophageal fistula			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	

Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Palpitations			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Arteriospasm coronary			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Tachycardia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Dizziness			
subjects affected / exposed	1 / 17 (5.88%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Headache			
subjects affected / exposed	3 / 17 (17.65%)	1 / 17 (5.88%)	
occurrences (all)	3	1	
Dysgeusia			
subjects affected / exposed	2 / 17 (11.76%)	3 / 17 (17.65%)	
occurrences (all)	3	4	
Tremor			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Paraesthesia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Monoparesis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Altered state of consciousness			

subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Neutropenia			
subjects affected / exposed	3 / 17 (17.65%)	4 / 17 (23.53%)	
occurrences (all)	4	4	
Lymphopenia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Thrombocytopenia			
subjects affected / exposed	3 / 17 (17.65%)	4 / 17 (23.53%)	
occurrences (all)	4	6	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Vertigo			
subjects affected / exposed	2 / 17 (11.76%)	0 / 17 (0.00%)	
occurrences (all)	2	0	
Eye disorders			
Lacrimation increased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Xerophthalmia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	6 / 17 (35.29%)	1 / 17 (5.88%)	
occurrences (all)	6	1	
Abdominal distension			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Abdominal pain			

subjects affected / exposed	1 / 17 (5.88%)	7 / 17 (41.18%)	
occurrences (all)	2	7	
Anal haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Abdominal pain upper			
subjects affected / exposed	2 / 17 (11.76%)	0 / 17 (0.00%)	
occurrences (all)	2	0	
Abdominal rigidity			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Dry mouth			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Dyspepsia			
subjects affected / exposed	1 / 17 (5.88%)	2 / 17 (11.76%)	
occurrences (all)	1	2	
Dysphagia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 17 (5.88%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Nausea			
subjects affected / exposed	7 / 17 (41.18%)	6 / 17 (35.29%)	
occurrences (all)	10	6	
Gingival swelling			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Oral pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Stomatitis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Vomiting			

subjects affected / exposed	8 / 17 (47.06%)	2 / 17 (11.76%)	
occurrences (all)	10	2	
Intestinal obstruction			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Flatulence			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Inguinal hernia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Hepatobiliary disorders			
Hepatic pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Dry skin			
subjects affected / exposed	0 / 17 (0.00%)	2 / 17 (11.76%)	
occurrences (all)	0	2	
Dermatitis bullous			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Pruritus			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	1 / 17 (5.88%)	1 / 17 (5.88%)	
occurrences (all)	1	2	
Ingrowing nail			

subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Skin lesion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	2 / 17 (11.76%)	0 / 17 (0.00%)	
occurrences (all)	2	0	
Acute kidney injury			
subjects affected / exposed	1 / 17 (5.88%)	2 / 17 (11.76%)	
occurrences (all)	1	2	
Bladder pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	3	0	
Dysuria			
subjects affected / exposed	1 / 17 (5.88%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Chronic kidney disease			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Cystitis haemorrhagic			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Haematuria			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Pollakiuria			
subjects affected / exposed	1 / 17 (5.88%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Hypothyroidism			

subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Arthralgia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal pain			
subjects affected / exposed	0 / 17 (0.00%)	2 / 17 (11.76%)	
occurrences (all)	0	2	
Myalgia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Arthritis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	2	
Bronchitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Influenza			
subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Fungal oesophagitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Oral herpes			

subjects affected / exposed	0 / 17 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	3 / 17 (17.65%)	1 / 17 (5.88%)	
occurrences (all)	3	1	
Biliary tract infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
COVID-19			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Cestode infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Fungal infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Cholangitis infective			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Pyelonephritis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Conjunctivitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Tooth abscess			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	

Hypoalbuminaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Hyperkalaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Hypoglycaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Malnutrition			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Hyperglycaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Hypokalaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	
Hypophosphataemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 December 2018	patient information sheet/ informed consent (including addendum)
19 February 2019	documents related to IMP or IMPD patient informatio sheet/ informed consent included addendum protocol
22 May 2019	• Addition of at least a new site or a site whose LEC did not reply initially or moved site
09 July 2019	• Addition of at least a new site or a site whose LEC did not reply initially or moved site
12 September 2019	• New/amended IDMC charter • New/amended patient information sheet / informed consent (including addendum) • New/amended protocol • New/amended patient diary
18 September 2019	• New/amended patient information sheet / informed consent (including addendum) • New/amended patient diary • New/amended protocol
15 October 2019	• Change of PI - already approved site
17 October 2019	• New/amended patient information sheet / informed consent (including addendum)
13 March 2020	• Addition of at least a new site or a site whose LEC did not reply initially or moved site • Change of PI - already approved site
13 May 2020	• Changes in the logistics of the trial, which are NOT site-related (e.g. :lab, CRO etc)
30 June 2020	• Closure of an approved site • Addition of at least a new site or a site whose LEC did not reply initially or moved site
21 October 2020	Addition of at least a new site or a site whose LEC did not reply initially or moved site

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

An interim analysis was performed on each tumour cohort in the first stage, which includes the first 13 evaluable subjects. Since there were 2 or less subjects with treatment success in these 13 evaluable subjects (futility criteria) in all cohorts,

Notes: