Clinical trial results:
A Multicenter Study With an Open-label Phase Ib Part Followed by a Randomized, Placebo-controlled, Double-blind, Phase II Part to Evaluate Efficacy, Safety, Tolerability, and Pharmacokinetics of the DNA-PK Inhibitor Peposertib (M3814) in Combination With Capecitabine and RT in Participants With Locally Advanced Rectal Cancer

Summary

EudraCT number	2018-002275-18
Trial protocol	ES DE FR PL IT
Global end of trial date	21 February 2022

Results information

Result version number	v1 (current)
This version publication date	25 February 2023
First version publication date	25 February 2023

Trial information

Trial identification

Sponsor protocol code	MS100036_0020

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03770689
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Healthcare KGaA, Darmstadt, Germany
Sponsor organisation address	Frankfurter Strasse 250, Darmstadt, Germany, 64293
Public contact	Communication Center, Merck Healthcare KGaA, Darmstadt, Germany, +49 6151725200, service@merckgroup.com
Scientific contact	Communication Center, Merck Healthcare KGaA, Darmstadt, Germany, +49 6151725200, service@merckgroup.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	
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 February 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 February 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study was to define maximum tolerated dose (MTD), recommended Phase II dose (RP2D) safety and tolerability of Peposertib in combination with capecitabine and radiotherapy (RT).

Protection of trial subjects:

Subject protection was ensured by following high medical and ethical standards in accordance with the principles laid down in the Declaration of Helsinki, and that are consistent with Good Clinical Practice and applicable regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 March 2019
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	Spain: 8
Country: Number of subjects enrolled	United States: 11
Worldwide total number of subjects	19
EEA total number of subjects	8

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)	13
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was planned to be conducted in two phases: Phase Ib and Phase II. Phase II of the study was never initiated due to early discontinuation as per sponsor's decision.

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	Peposertib 50 mg + RT + Capecitabine:

Arm description:

Subjects received peposertib 50 milligram (mg) once daily in combination with capecitabine 825 milligram per square meter (mg/m^2) twice daily 5 days per week and radiotherapy (RT) of 50 to 50.4 Gray (Gy) to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period.

Arm type	Experimental
Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received capecitabine at a dose of 825 milligram per square meter (mg/m^2) twice daily 5 days per week up to 5.5 weeks.

Investigational medicinal product name	Peposertib
Investigational medicinal product code	
Other name	M3814, MSC2490484A
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received peposertib 50 milligram (mg) once daily 5 days per week up to 5.5 weeks.

Investigational medicinal product name	Radiotherapy (RT)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Kit for radiopharmaceutical preparation
Routes of administration	Soft tissue use

Dosage and administration details:

Subjects received RT 50 to 50.4 Gray (Gy) to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks.

Arm title	Peposertib 100 mg + RT + Capecitabine:

Arm description:

Subjects received peposertib 100 mg once daily in combination with capecitabine 825 mg/m^2 twice daily 5 days per week and RT of 50 to 50.4 Gy to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period.

Arm type	Experimental

Investigational medicinal product name	Peposertib
Investigational medicinal product code	
Other name	M3814, MSC2490484A
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received peposertib 100 milligram (mg) once daily 5 days per week up to 5.5 weeks.

Investigational medicinal product name	Radiotherapy (RT)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Kit for radiopharmaceutical preparation
Routes of administration	Soft tissue use

Dosage and administration details:

Subjects received RT 50 to 50.4 Gray (Gy) to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks.

Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received capecitabine at a dose of 825 milligram per square meter (mg/m^2) twice daily 5 days per week up to 5.5 weeks.

Arm title	Peposertib 150 mg + RT + Capecitabine:

Arm description:

Subjects received peposertib 150 mg once daily in combination with capecitabine 825 mg/m^2 twice daily 5 days per week and RT of 50 to 50.4 Gy to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period.

Arm type	Experimental
Investigational medicinal product name	Peposertib
Investigational medicinal product code	
Other name	M3814, MSC2490484A
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received peposertib 150 milligram (mg) once daily 5 days per week up to 5.5 weeks.

Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received capecitabine at a dose of 825 milligram per square meter (mg/m^2) twice daily 5 days per week up to 5.5 weeks.

Investigational medicinal product name	Radiotherapy (RT)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Kit for radiopharmaceutical preparation
Routes of administration	Soft tissue use

Dosage and administration details:

Subjects received RT 50 to 50.4 Gray (Gy) to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks.

Arm title	Peposertib 250 mg + RT + Capecitabine:

Arm description:

Subjects received peposertib 250 mg once daily in combination with capecitabine 825 mg/m^2 twice daily 5 days per week and RT of 50 to 50.4 Gy to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period.

Arm type	Experimental
Investigational medicinal product name	Peposertib
Investigational medicinal product code	
Other name	M3814, MSC2490484A
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received peposertib 250 milligram (mg) once daily 5 days per week up to 5.5 weeks.

Investigational medicinal product name	Radiotherapy (RT)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Kit for radiopharmaceutical preparation
Routes of administration	Soft tissue use

Dosage and administration details:

Subjects received RT 50 to 50.4 Gray (Gy) to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks.

Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received capecitabine at a dose of 825 milligram per square meter (mg/m^2) twice daily 5 days per week up to 5.5 weeks.

Number of subjects in period 1	Peposertib 50 mg + RT + Capecitabine:	Peposertib 100 mg + RT + Capecitabine:	Peposertib 150 mg + RT + Capecitabine:
Started	1	6	6
Pharmacokinetic Analysis Set	1	6	6
Full Analysis Set (FAS)	1	6	6
Safety Analysis Set (SAF)	1	6	6
Completed	1	6	6

Number of subjects in period 1	Peposertib 250 mg + RT + Capecitabine:
Started	6
Pharmacokinetic Analysis Set	6
Full Analysis Set (FAS)	6
Safety Analysis Set (SAF)	6
Completed	6

Baseline characteristics

Reporting groups	
Reporting group title	Peposertib 50 mg + RT + Capecitabine:
Reporting group description:	
Subjects received peposertib 50 milligram (mg) once daily in combination with capecitabine 825 milligram per square meter (mg/m^2) twice daily 5 days per week and radiotherapy (RT) of 50 to 50.4 Gray (Gy) to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period.	
Reporting group title	Peposertib 100 mg + RT + Capecitabine:
Reporting group description:	
Subjects received peposertib 100 mg once daily in combination with capecitabine 825 mg/m^2 twice daily 5 days per week and RT of 50 to 50.4 Gy to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period.	
Reporting group title	Peposertib 150 mg + RT + Capecitabine:
Reporting group description:	
Subjects received peposertib 150 mg once daily in combination with capecitabine 825 mg/m^2 twice daily 5 days per week and RT of 50 to 50.4 Gy to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period.	
Reporting group title	Peposertib 250 mg + RT + Capecitabine:
Reporting group description:	
Subjects received peposertib 250 mg once daily in combination with capecitabine 825 mg/m^2 twice daily 5 days per week and RT of 50 to 50.4 Gy to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period.	

Reporting group values	Peposertib 50 mg + RT + Capecitabine:	Peposertib 100 mg + RT + Capecitabine:	Peposertib 150 mg + RT + Capecitabine:
Number of subjects	1	6	6
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)	1	3	5
From 65-84 years	0	3	1
85 years and over	0	0	0
Sex: Female, Male Units: subjects			
Female	0	3	2
Male	1	3	4
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0

White	1	6	6
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	1	6	6
Unknown or Not Reported	0	0	0

Reporting group values	Peposertib 250 mg + RT + Capecitabine:	Total	
Number of subjects	6	19	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	4	13	
From 65-84 years	2	6	
85 years and over	0	0	
Sex: Female, Male Units: subjects			
Female	3	8	
Male	3	11	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	6	19	
More than one race	0	0	
Unknown or Not Reported	0	0	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	1	
Not Hispanic or Latino	5	18	
Unknown or Not Reported	0	0	

Subject analysis sets

Subject analysis set title	Overall Subjects
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects received peposertib 50 mg, 100 mg, 150 mg and 250 mg in their respective cohort once daily in combination with capecitabine 825 milligram per square meter (mg/m^2) twice daily 5 days per week and radiotherapy (RT) of 50 to 50.4 Gray (Gy) to the tumor area and 45 Gy to the electively irradiated

tissues in 25 to 28 fractions up to 5.5 weeks treatment period.

Subject analysis set title	All Subjects
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects received peposertib 100 mg, 150 mg and 250 mg in their respective cohort once daily in combination with capecitabine 825 milligram per square meter (mg/m^2) twice daily 5 days per week and radiotherapy (RT) of 50 to 50.4 Gray (Gy) to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period.

Subject analysis set title	Peposertib 50 mg + RT + Capecitabine
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received peposertib 50 milligram (mg) once daily in combination with capecitabine 825 milligram per square meter (mg/m^2) twice daily 5 days per week and radiotherapy (RT) of 50 to 50.4 Gray (Gy) to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period.
Number of subjects analyzed in 50 mg group for PK outcome is different than PK analysis set. Because 1 subject from peposertib 100 mg took peposertib 50 mg from Fraction Day (FD) 1 through FD 10. PK results for this subject was summarized by actual dose received (50 mg) whereas non-PK results are summarized by planned dose (100 mg). Number of subjects analyzed for 50 mg dose level in PK outputs that is 2 was therefore higher than non-PK outputs that is 1.

Subject analysis set title	Peposertib 100 mg + RT + Capecitabine
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received peposertib 100 mg once daily in combination with capecitabine 825 mg/m^2 twice daily 5 days per week and RT of 50 to 50.4 Gy to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period. Number of subjects analyzed in 100 mg group for PK outcome is different than PK analysis set because 1 subject from peposertib 100 mg took peposertib 50 mg from Fraction Day (FD) 1 through FD 10. PK results for this subject was summarized by actual dose received (50 mg) whereas non-PK results are summarized by planned dose (100 mg). Number of subjects analyzed for 100 mg dose level in PK outputs that is 5 was therefore lesser than non-PK outputs that is 6.

Subject analysis set title	Peposertib 150 mg + RT + Capecitabine
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received peposertib 150 mg once daily in combination with capecitabine 825 mg/m^2 twice daily 5 days per week and RT of 50 to 50.4 Gy to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period.

Subject analysis set title	Peposertib 250 mg + RT + Capecitabine
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received peposertib 250 mg once daily in combination with capecitabine 825 mg/m^2 twice daily 5 days per week and RT of 50 to 50.4 Gy to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period.

Reporting group values	Overall Subjects	All Subjects	Peposertib 50 mg + RT + Capecitabine
Number of subjects	19	19	2
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)	13		
From 65-84 years	6		

85 years and over			

Sex: Female, Male Units: subjects			
Female Male			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported			
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported			

Reporting group values	Peposertib 100 mg + RT + Capecitabine	Peposertib 150 mg + RT + Capecitabine	Peposertib 250 mg + RT + Capecitabine
Number of subjects	5	6	6
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Sex: Female, Male Units: subjects			
Female Male			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported			

Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported			

End points

End points reporting groups

Reporting group title	Peposertib 50 mg + RT + Capecitabine:

Reporting group description:

Subjects received peposertib 50 milligram (mg) once daily in combination with capecitabine 825 milligram per square meter (mg/m^2) twice daily 5 days per week and radiotherapy (RT) of 50 to 50.4 Gray (Gy) to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period.

Reporting group title	Peposertib 100 mg + RT + Capecitabine:

Reporting group description:

Subjects received peposertib 100 mg once daily in combination with capecitabine 825 mg/m^2 twice daily 5 days per week and RT of 50 to 50.4 Gy to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period.

Reporting group title	Peposertib 150 mg + RT + Capecitabine:

Reporting group description:

Subjects received peposertib 150 mg once daily in combination with capecitabine 825 mg/m^2 twice daily 5 days per week and RT of 50 to 50.4 Gy to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period.

Reporting group title	Peposertib 250 mg + RT + Capecitabine:

Reporting group description:

Subjects received peposertib 250 mg once daily in combination with capecitabine 825 mg/m^2 twice daily 5 days per week and RT of 50 to 50.4 Gy to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period.

Subject analysis set title	Overall Subjects
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects received peposertib 50 mg, 100 mg, 150 mg and 250 mg in their respective cohort once daily in combination with capecitabine 825 milligram per square meter (mg/m^2) twice daily 5 days per week and radiotherapy (RT) of 50 to 50.4 Gray (Gy) to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period.

Subject analysis set title	All Subjects
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects received peposertib 100 mg, 150 mg and 250 mg in their respective cohort once daily in combination with capecitabine 825 milligram per square meter (mg/m^2) twice daily 5 days per week and radiotherapy (RT) of 50 to 50.4 Gray (Gy) to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period.

Subject analysis set title	Peposertib 50 mg + RT + Capecitabine
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received peposertib 50 milligram (mg) once daily in combination with capecitabine 825 milligram per square meter (mg/m^2) twice daily 5 days per week and radiotherapy (RT) of 50 to 50.4 Gray (Gy) to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period.
Number of subjects analyzed in 50 mg group for PK outcome is different than PK analysis set.
Because 1 subject from peposertib 100 mg took peposertib 50 mg from Fraction Day (FD) 1 through FD 10. PK results for this subject was summarized by actual dose received (50 mg) whereas non-PK results are summarized by planned dose (100 mg). Number of subjects analyzed for 50 mg dose level in PK outputs that is 2 was therefore higher than non-PK outputs that is 1.

Subject analysis set title	Peposertib 100 mg + RT + Capecitabine
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received peposertib 100 mg once daily in combination with capecitabine 825 mg/m^2 twice daily 5 days per week and RT of 50 to 50.4 Gy to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period. Number of subjects analyzed in 100 mg group for PK outcome is different than PK analysis set because 1 subject from peposertib 100 mg took peposertib 50 mg from Fraction Day (FD) 1 through FD 10. PK results for this subject was summarized

by actual dose received (50 mg) whereas non-PK results are summarized by planned dose (100 mg). Number of subjects analyzed for 100 mg dose level in PK outputs that is 5 was therefore lesser than non-PK outputs that is 6.

Subject analysis set title	Peposertib 150 mg + RT + Capecitabine
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received peposertib 150 mg once daily in combination with capecitabine 825 mg/m^2 twice daily 5 days per week and RT of 50 to 50.4 Gy to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period.

Subject analysis set title	Peposertib 250 mg + RT + Capecitabine
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received peposertib 250 mg once daily in combination with capecitabine 825 mg/m^2 twice daily 5 days per week and RT of 50 to 50.4 Gy to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period.

Primary: Number of Subjects Who Experienced Dose Limiting Toxicity (DLT) Confirmed by Safety Monitoring Committee (SMC)

End point title	Number of Subjects Who Experienced Dose Limiting Toxicity (DLT) Confirmed by Safety Monitoring Committee (SMC)[1]

End point description:

DLT are treatment emergent adverse events (TEAEs) possibly related to study treatment by Investigator and/or Sponsor up to completion of treatment. DLT were based on SMC: Adverse drug reaction that is of potential clinical significance ; Any occurrence of drug-induced liver injury meeting the Hy's law criteria; Any Grade 3 toxicity excluding diarrhea, neutropenia lasting for ≤ 5 days, nausea & vomiting, Grade 3 thrombocytopenia without bleeding; Grade ≥ 4 AEs at least possibly related to study drug, irrespective of duration, excluding: Isolated Grade 4 lymphocytopenia without clinical symptoms; Neutropenia lasting for ≤ 5 days and not associated with fever; Any toxicity related to study drug that causes subject to receive > 80% of planned peposertib, capecitabine or RT dose. Dose escalation (DE) analysis set included all subjects treated in dose escalation cohorts, who received at least 80% of peposertib, 50% of capecitabine, and 80% of RT planned dose and complete DLT period.

End point type	Primary

End point timeframe:

Time from first study intervention up to 19 weeks (including 5.5 weeks of treatment and 13.5 weeks of short term safety follow-up period)

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: No statistical and comparison analysis were performed in single arm for this endpoint.

End point values	Peposertib 50 mg + RT + Capecitabine:	Peposertib 100 mg + RT + Capecitabine:	Peposertib 150 mg + RT + Capecitabine:	Peposertib 250 mg + RT + Capecitabine:
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	5	6	6
Units: subjects	0	1	1	3

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Treatment Emergent Adverse Events (TEAEs) and Treatment-Related TEAEs According to National Cancer Institute Common Terminology Criteria of Adverse Events (NCI-CTCAE) Version 5.0

End point title	Number of Subjects with Treatment Emergent Adverse Events (TEAEs) and Treatment-Related TEAEs According to National

	Cancer Institute Common Terminology Criteria of Adverse Events (NCI-CTCAE) Version 5.0

End point description:

Adverse event (AE) is any untoward medical occurrence in subject administered pharmaceutical product, regardless of relationship with this treatment. Therefore, an AE can be any unfavorable & unintended sign symptom, or disease temporally associated with use of a medicinal product, regardless if it is considered related to medicinal product. Serious AE: an AE that results in: death; life threatening; persistent/significant disability/incapacity; initial or prolonged inpatient hospitalization; congenital anomaly/birth defect or was otherwise considered medically important. TEAE: AE with onset after start of treatment or with onset date before the treatment start date but worsening after treatment start date. It included both serious and non-serious TEAEs. Treatment-related TEAEs: related to study intervention. Number of subjects with TEAEs and treatment related TEAEs were reported. SAF analysis set included all subjects who received at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Time from first study intervention up to long term safety follow-up period (Up to Month 35)

End point values	Peposertib 50 mg + RT + Capecitabine:	Peposertib 100 mg + RT + Capecitabine:	Peposertib 150 mg + RT + Capecitabine:	Peposertib 250 mg + RT + Capecitabine:
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	6	6	6
Units: subjects				
Subjects with TEAEs	1	6	6	6
Subjects with Treatment-Related TEAEs	1	6	6	6

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Abnormalities [Grade Greater than or equals to (>=) 3] in Laboratory Test Values

End point title	Number of Subjects With Abnormalities [Grade Greater than or equals to (>=) 3] in Laboratory Test Values

End point description:

The laboratory measurements included hematology and biochemistry values were graded with National Cancer Institute - Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 5.0 toxicity grades (where Grade 1 = mild, Grade 2 = moderate, Grade 3 = severe, Grade 4 = life threatening and Grade 5 = death). Number of subjects with abnormalities Grade >= 3 in laboratory test values were reported. SAF analysis set included all subjects who received at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Time from first study intervention up to long term safety follow-up period (Up to Month 35)

End point values	Peposertib 50 mg + RT + Capecitabine:	Peposertib 100 mg + RT + Capecitabine:	Peposertib 150 mg + RT + Capecitabine:	Peposertib 250 mg + RT + Capecitabine:
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	6	6	6
Units: subjects	1	6	6	6

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Markedly Abnormal Vital Sign Measurements

End point title	Number of Subjects With Markedly Abnormal Vital Sign Measurements

End point description:

Vital sign assessments included assessments of heart rate, diastolic blood pressure, systolic blood pressure, respiratory rate and temperature. Number of subjects with markedly abnormal vital sign measurements were reported. SAF analysis set included all subjects who received at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Time from first study intervention up to long term safety follow-up period (Up to Month 35)

End point values	Peposertib 50 mg + RT + Capecitabine:	Peposertib 100 mg + RT + Capecitabine:	Peposertib 150 mg + RT + Capecitabine:	Peposertib 250 mg + RT + Capecitabine:
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	6	6	6
Units: subjects	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Significant Abnormalities in Electrocardiogram (ECG) Findings

End point title	Number of Subjects With Clinically Significant Abnormalities in Electrocardiogram (ECG) Findings

End point description:

Electrocardiograms (ECG) was obtained after the subject has been in a semi-supine position for at least 5 min. ECG parameters included heart rate, PQ/PR duration, QRS and QT duration, QT Interval. Clinical significance was determined by the investigator. Number of subjects with clinically significant abnormalities in 12-lead ECG were reported. SAF analysis set included all subjects who received at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Time from first study intervention up to long term safety follow-up period (Up to Month 35)

End point values	Peposertib 50 mg + RT + Capecitabine:	Peposertib 100 mg + RT + Capecitabine:	Peposertib 150 mg + RT + Capecitabine:	Peposertib 250 mg + RT + Capecitabine:
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	6	6	6
Units: subjects	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Composite Pathological Complete Response (pCR)/ Clinical Complete Response (cCR)

End point title	Percentage of Subjects With Composite Pathological Complete Response (pCR)/ Clinical Complete Response (cCR)

End point description:

pCR: Absence of viable tumor cells in the primary tumor and lymph nodes. Subjects have a pCR if they undergo surgery and no residual cancer is found on histological examination of removed specimen. cCR: Subjects are considered to have a cCR if: Absence of any residual tumor in primary site and draining lymph nodes on imaging with magnetic resonance imaging; No visible lesion at endoscopy except a flat scar, telangiectasia, and/or whitening of mucosa; Absence of any palpable tumor or irregularity on digital rectal examination (DRE) and endoscopic ultrasonography (EUS); If a biopsy is negative. Subjects are considered as responders to composite endpoint pCR/cCR if subject had surgery and had pCR; subject did not undergo surgery but had cCR. Number of subjects with composite pathological complete response (pCR)/ clinical complete response (cCR) were reported. Full analysis set (FAS) include all subjects who are enrolled in the study and received at least 1 dose of treatment.

End point type	Secondary

End point timeframe:

At Week 15

End point values	Peposertib 50 mg + RT + Capecitabine:	Peposertib 100 mg + RT + Capecitabine:	Peposertib 150 mg + RT + Capecitabine:	Peposertib 250 mg + RT + Capecitabine:
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	6	6	6
Units: subjects				
number (confidence interval 95%)	0.0 (0.0 to 97.5)	1 (0.4 to 64.1)	0.0 (0.0 to 45.9)	0.0 (0.0 to 45.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Disease-free Survival

End point title	Disease-free Survival

End point description:

Disease-free Survival time, defined as the time from first treatment day to the date of the first documentation of objective progressive disease or death due to any cause, whichever occurs first. Median disease-free survival time was estimated according to Kaplan-Meier method. FAS include all subjects who are enrolled in the study and received at least 1 dose of study intervention. As per the planned analysis, Kaplan-Meier estimates were planned to be presented as overall, together with a summary of associated statistics for this endpoint.

End point type	Secondary

End point timeframe:

Time from first study intervention up to Month 35

End point values	Overall Subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	19			
Units: Months				
median (full range (min-max))	21.2 (0.0 to 23.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Pathological Complete Response (pCR)

End point title	Percentage of Subjects With Pathological Complete Response (pCR)

End point description:

pCR is defined as the absence of viable tumor cells in the primary tumor and lymph nodes. Subjects are considered to have a pCR if they undergo surgery and no residual cancer is found on histological examination of the removed specimen. FAS include all subjects who are enrolled in the study and received at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

At Week 15

End point values	Peposertib 50 mg + RT + Capecitabine:	Peposertib 100 mg + RT + Capecitabine:	Peposertib 150 mg + RT + Capecitabine:	Peposertib 250 mg + RT + Capecitabine:
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	6	6	6
Units: subjects				
number (confidence interval 95%)	0.0 (0.0 to 97.5)	0.0 (0.0 to 45.9)	0.0 (0.0 to 45.9)	0.0 (0.0 to 45.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Clinical Complete Response (cCR)

End point title	Percentage of Subjects With Clinical Complete Response (cCR)

End point description:

cCR: It is defined as subjects considered to have a cCR if: 1) Absence of any residual tumor in the primary site and draining lymph nodes on imaging with magnetic resonance; 2) No visible lesion at endoscopy except a flat scar, telangiectasia, and/or whitening of the mucosa; 3) Absence of any palpable tumor or irregularity on digital rectal examination (DRE) and endoscopic ultrasonography (EUS); 4) If a biopsy is taken, it must be negative. FAS include all subjects who are enrolled in the study and received at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

At Week 15

End point values	Peposertib 50 mg + RT + Capecitabine:	Peposertib 100 mg + RT + Capecitabine:	Peposertib 150 mg + RT + Capecitabine:	Peposertib 250 mg + RT + Capecitabine:
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	6	6	6
Units: subjects				
number (confidence interval 95%)	0.0 (0.0 to 97.5)	16.7 (0.4 to 64.1)	16.7 (0.4 to 64.1)	16.7 (0.4 to 64.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Time from Surgery to Local Recurrence

End point title	Time from Surgery to Local Recurrence

End point description:

Time from surgery to local recurrence defined as time from day of surgery to the date of the first documentation of progression of disease, flagged as local recurrence. Median time from surgery to local recurrence was estimated according to Kaplan-Meier method. FAS include all subjects who are enrolled in the study and received at least 1 dose of study intervention. Here, number of subjects analyzed signifies those subjects who underwent rectal surgery.

End point type	Secondary

End point timeframe:

Time from surgery up to Month 35

End point values	All Subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	9[2]			
Units: months				
median (full range (min-max))	9.999999 (2.8 to 15.0)			

Notes:

[2] - Due to small number of events Median and CI was not determinable. 9.99999 represents no observation.

Statistical analyses

No statistical analyses for this end point

Secondary: Time from Surgery to Distant Metastasis

End point title	Time from Surgery to Distant Metastasis

End point description:

Time from surgery to distant metastasis defined as time from day of surgery to the date of the first documentation of progression of disease, flagged as distant metastasis. Median time from surgery to distant metastasis was estimated according to Kaplan-Meier method. FAS include all subjects who are enrolled in the study and received at least 1 dose of study intervention. Here, number of subjects analyzed signifies those subjects who underwent rectal surgery.

End point type	Secondary

End point timeframe:

Time from surgery up to 35 months

End point values	All Subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	9[3]			
Units: months				
median (full range (min-max))	9.999999 (2.8 to 15.0)			

Notes:

[3] - Due to small number of events Median and CI was not determinable. 9.99999 represents no observation.

Statistical analyses

No statistical analyses for this end point

Secondary: Neoadjuvant Rectal (NAR) Score

End point title	Neoadjuvant Rectal (NAR) Score

End point description:

The NAR formula includes the clinical tumor (cT) stage, pathologic tumor (pT), and node (pN) stage according to the tumor, node, metastasis classification system for colorectal cancers. The NAR formula is as follows:

[5pN- 3 (cT- pT) + 12]2 / 9.61

NAR score ranges from 0 to 100, whereas a score close to 100 is indicative of a poorer prognosis.
FAS include all subjects who are enrolled in the study and received at least 1 dose of study intervention. Here, "Number of subjects analyzed" signifies those subjects who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

At Week 15

End point values	Peposertib 50 mg + RT + Capecitabine:	Peposertib 100 mg + RT + Capecitabine:	Peposertib 150 mg + RT + Capecitabine:	Peposertib 250 mg + RT + Capecitabine:
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[4]	2	2	5
Units: score on a scale				
arithmetic mean (standard deviation)	()	9.4 (± 7.95)	13.8 (± 1.69)	21.2 (± 12.11)

Notes:

[4] - None of the subject was analyzed for this arm.

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of Peposertib

End point title	Maximum Observed Plasma Concentration (Cmax) of Peposertib

End point description:

Cmax was obtained directly from the concentration versus time curve. One subject was assigned to receive peposertib 100 mg; however, this subject took peposertib 50 mg for FD 1 through FD 10 and then took peposertib 100 mg for remainder of study participation. PK results for this subject was summarized by actual dose received (50 mg) whereas non-PK results are summarized by planned dose (100 mg). Pharmacokinetic (PK) analysis set included subjects who received at least 1 dose of peposertib and have sufficient peposertib plasma concentration data to enable the calculation of at least 1 PK parameter. Sufficient concentration data is defined as at least 3 valid, post dose, concentration points in the PK profile to obtain any PK parameter.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 2, 3, 4 and 6 hours post-dose on Fraction Day 1 and Fraction Day 9

End point values	Peposertib 50 mg + RT + Capecitabine	Peposertib 100 mg + RT + Capecitabine	Peposertib 150 mg + RT + Capecitabine	Peposertib 250 mg + RT + Capecitabine
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[5]	5	6	6
Units: nanogram per milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)				
Fraction Day 1	()	593 (± 55.8)	728 (± 24.1)	1350 (± 55.5)
Fraction Day 9	()	653 (± 50.4)	792 (± 41.8)	1760 (± 35.6)

Notes:

[5] - None of the subject was analyzed for this arm.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-time Curve From Time Zero to Last Sampling Time (tlast) (AUC0-t) of Peposertib

End point title	Area Under the Plasma Concentration-time Curve From Time Zero to Last Sampling Time (tlast) (AUC0-t) of Peposertib

End point description:

Area under the plasma concentration vs time curve from time zero to the last sampling time t at which the concentration was at or above the lower limit of quantification (LLQ). AUC0-t was to be calculated according to the mixed log-linear trapezoidal rule. PK analysis set was used. One subject was assigned to receive peposertib 100 mg; however, this subject took peposertib 50 mg for FD 1 through FD 10 and then took peposertib 100 mg for remainder of study participation. PK results for this subject was summarized by actual dose received (50 mg) whereas non-PK results are summarized by planned dose (100 mg). Here, "n" signifies those subjects who were evaluable for specified category at given time point.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 2, 3, 4 and 6 hour post-dose on Fraction Day 1 and Fraction Day 9

End point values	Peposertib 50 mg + RT + Capecitabine	Peposertib 100 mg + RT + Capecitabine	Peposertib 150 mg + RT + Capecitabine	Peposertib 250 mg + RT + Capecitabine
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2[6]	5	6	6
Units: hour*nanogram per milliliter (h*ng/mL)				
geometric mean (geometric coefficient of variation)				
Fraction Day 1, n= 2, 5, 6, 6	9.999999 (± 9.9999)	2950 (± 69.8)	4000 (± 33.3)	7300 (± 71.1)
Fraction Day 9, n= 2, 5, 5, 6	9.999999 (± 9.9999)	3450 (± 81.9)	5540 (± 51.0)	9450 (± 50)

Notes:

[6] - 9.99999 represents that there was no observation.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Plasma Concentration (tmax) of Peposertib

End point title	Time to Reach Maximum Plasma Concentration (tmax) of Peposertib

End point description:

Time to reach the maximum plasma concentration (Tmax) was obtained directly from the concentration versus time curve. PK analysis set was used. One subject was assigned to receive peposertib 100 mg; however, this subject took peposertib 50 mg for FD 1 through FD 10 and then took peposertib 100 mg for remainder of study participation. PK results for this subject was summarized by actual dose received (50 mg) whereas non-PK results are summarized by planned dose (100 mg). PK analysis set was used. One subject was assigned to receive peposertib 100 mg; however, this subject took peposertib 50 mg for FD 1 through FD 10 and then took peposertib 100 mg for remainder of study participation. PK results for this subject was summarized by actual dose received (50 mg) whereas non-PK results are summarized by planned dose (100 mg). Here, "Number of subjects analyzed" signifies those subjects who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 2, 3, 4 and 6 hour post-dose on Fraction Day 1 and Fraction Day 9

End point values	Peposertib 50 mg + RT + Capecitabine	Peposertib 100 mg + RT + Capecitabine	Peposertib 150 mg + RT + Capecitabine	Peposertib 250 mg + RT + Capecitabine
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2[7]	5	6	6
Units: hours				
median (full range (min-max))				
Fraction Day 1	3.99999 (3 to 4)	1 (0.83 to 2)	2.33 (1.07 to 2.97)	2.43 (0.85 to 4.00)
Fraction Day 9	2.99999 (2 to 3.22)	2.05 (0.83 to 2.25)	2.09 (1.07 to 3.82)	2.01 (0.92 to 7.33)

Notes:

[7] - 3.99999 and 2.99999 represents that there was no observation

Statistical analyses

No statistical analyses for this end point

Secondary: Total Body Clearance Following Oral Administration (CL/f) of Peposertib

End point title	Total Body Clearance Following Oral Administration (CL/f) of Peposertib

End point description:

The apparent total body clearance of study intervention following extravascular administration on FD1, taking into account the fraction of dose absorbed. CL/f = Dose oral (p.o.)/AUC0-inf. The predicted AUC0-inf should be used. PK analysis set was used. Here, "Number of subjects" analyzed signifies those subjects who were evaluable for this outcome measure. Here, "Number Analyzed" signified those subjects who were evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 2, 3, 4 and 6 hour post-dose on Fraction Day 1

End point values	Peposertib 50 mg + RT + Capecitabine:	Peposertib 100 mg + RT + Capecitabine:	Peposertib 150 mg + RT + Capecitabine:	Peposertib 250 mg + RT + Capecitabine:
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[8]	5	6	5
Units: Liter per hour				
geometric mean (geometric coefficient of variation)	()	31.7 (± 74.5)	34.5 (± 41.1)	33.0 (± 87.6)

Notes:

[8] - None of the subject was analyzed for this arm.

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Volume of Distribution (Vz/f) of Peposertib

End point title	Apparent Volume of Distribution (Vz/f) of Peposertib

End point description:

The apparent volume of distribution during the terminal phase following extravascular administration, based on the fraction of dose absorbed. Vz/f = Dose/(AUC0-inf multiplied by Lambda z) following single dose. Vz/f= Dose/(AUCtau*Lambda z) following multiple dose. One subject was assigned to receive peposertib 100 mg; however, this subject took peposertib 50 mg for FD 1 through FD 10 and then took peposertib 100 mg for remainder of study participation. PK results for this subject was summarized by actual dose received (50 mg) whereas non-PK results are summarized by planned dose (100 mg). PK analysis set was used. Here, "Number of subjects" analyzed signifies those subjects who were evaluable for this outcome measure. Here, "n" signified those subjects who were evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 2, 3, 4 and 6 hour post-dose on Fraction Day 1 and Fraction Day 9

End point values	Peposertib 50 mg + RT + Capecitabine:	Peposertib 100 mg + RT + Capecitabine:	Peposertib 150 mg + RT + Capecitabine:	Peposertib 250 mg + RT + Capecitabine:
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1[9]	5	6	5
Units: Liter				
geometric mean (geometric coefficient of variation)				
Fraction Day 1, n= 0, 5, 6, 5	9.999999 (± 9.9999)	256 (± 60.3)	274 (± 25.7)	245 (± 64.1)
Fraction Day 9, n= 1, 5, 5, 5	9.999999 (± 9.9999)	261 (± 100.8)	217 (± 43.7)	234 (± 39.7)

Notes:

[9] - 9.99999 represents that there was no observation.

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Terminal Half-life (t1/2) of Peposertib

End point title	Apparent Terminal Half-life (t1/2) of Peposertib

End point description:

Terminal half-life is the time measured for the concentration to decrease by one half. Terminal half-life calculated by natural log 2 divided by lambda z. One subject was assigned to receive peposertib 100 mg; however, this subject took peposertib 50 mg for FD 1 through FD 10 and then took peposertib 100 mg for remainder of study participation. PK results for this subject was summarized by actual dose received (50 mg) whereas non-PK results are summarized by planned dose (100 mg). PK analysis set was used. Here, "Number of subjects" analyzed signifies those subjects who were evaluable for this endpoint. Here, "n" signified those subjects who were evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 2, 3, 4 and 6 hour post-dose on Fraction Day 1 and Fraction Day 9

End point values	Peposertib 50 mg + RT + Capecitabine:	Peposertib 100 mg + RT + Capecitabine:	Peposertib 150 mg + RT + Capecitabine:	Peposertib 250 mg + RT + Capecitabine:
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1[10]	5	6	5
Units: hours				
geometric mean (geometric coefficient of variation)				
Fraction Day 1, n= 0, 5, 6, 5	9.999999 (± 9.9999)	5.60 (± 22.0)	5.51 (± 29.0)	5.14 (± 28.7)
Fraction Day 9, n= 1, 5, 5, 5	9.999999 (± 9.9999)	6.28 (± 30.8)	5.04 (± 61.0)	6.12 (± 28.9)

Notes:

[10] - 9.99999 represents that there was no observation.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to long term follow-up period (Month 36)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Peposertib 50 mg + RT + Capecitabine:
Reporting group description:	
Subjects received peposertib 50 milligram (mg) once daily in combination with capecitabine 825 milligram per square meter (mg/m^2) twice daily 5 days per week and radiotherapy (RT) of 50 to 50.4 Gray (Gy) to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period.	
Reporting group title	Peposertib 100 mg + RT + Capecitabine:
Reporting group description:	
Subjects received peposertib 100 mg once daily in combination with capecitabine 825 mg/m^2 twice daily 5 days per week and RT of 50 to 50.4 Gy to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period.	
Reporting group title	Peposertib 150 mg + RT + Capecitabine:
Reporting group description:	
Subjects received peposertib 150 mg once daily in combination with capecitabine 825 mg/m^2 twice daily 5 days per week and RT of 50 to 50.4 Gy to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period.	
Reporting group title	Peposertib 250 mg + RT + Capecitabine:
Reporting group description:	
Subjects received peposertib 250 mg once daily in combination with capecitabine 825 mg/m^2 twice daily 5 days per week and RT of 50 to 50.4 Gy to the tumor area and 45 Gy to the electively irradiated tissues in 25 to 28 fractions up to 5.5 weeks treatment period.	

Serious adverse events	Peposertib 50 mg + RT + Capecitabine:	Peposertib 100 mg + RT + Capecitabine:	Peposertib 150 mg + RT + Capecitabine:
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	3 / 6 (50.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (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
Platelet count decreased			

subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (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
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (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
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 6 (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			
Diarrhoea			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (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
Enterocolitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (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
Proctitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (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
Infections and infestations			
Pneumonia			

subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (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
Sepsis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (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
Metabolism and nutrition disorders			
Hypoalbuminaemia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (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

Serious adverse events	Peposertib 250 mg + RT + Capecitabine:		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 6 (66.67%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Platelet count decreased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Accidental overdose			

subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enterocolitis			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Proctitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypoalbuminaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Peposertib 50 mg + RT + Capecitabine:	Peposertib 100 mg + RT + Capecitabine:	Peposertib 150 mg + RT + Capecitabine:
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)	5 / 6 (83.33%)	6 / 6 (100.00%)
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Peripheral embolism			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Secretion discharge			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	1 / 1 (100.00%)	5 / 6 (83.33%)	3 / 6 (50.00%)
occurrences (all)	1	5	3
Asthenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			

Dyspnoea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Psychiatric disorders			
Personality change			
subjects affected / exposed	1 / 1 (100.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Investigations			
White blood cell count decreased			
subjects affected / exposed	0 / 1 (0.00%)	2 / 6 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Weight decreased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	2 / 6 (33.33%)
occurrences (all)	0	1	2
Lymphocyte count decreased			
subjects affected / exposed	0 / 1 (0.00%)	2 / 6 (33.33%)	2 / 6 (33.33%)
occurrences (all)	0	2	2
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Radiation skin injury			
subjects affected / exposed	1 / 1 (100.00%)	3 / 6 (50.00%)	2 / 6 (33.33%)
occurrences (all)	1	3	2

Anal injury			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nervous system disorders			
Sciatica			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Dizziness postural			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Neutropenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Thrombocytopenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Anaemia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Leukopenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	1 / 1 (100.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Abdominal distension			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	1 / 1 (100.00%)	5 / 6 (83.33%)	3 / 6 (50.00%)
occurrences (all)	1	5	3
Dry mouth			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Dyschezia			
subjects affected / exposed	1 / 1 (100.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Anal incontinence			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	2 / 6 (33.33%)
occurrences (all)	0	1	2
Anal inflammation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	3 / 6 (50.00%)
occurrences (all)	0	0	3
Colitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0

Rectal ulcer			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rectal tenesmus			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Rectal haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Proctitis			
subjects affected / exposed	1 / 1 (100.00%)	2 / 6 (33.33%)	2 / 6 (33.33%)
occurrences (all)	1	2	2
Proctalgia			
subjects affected / exposed	0 / 1 (0.00%)	3 / 6 (50.00%)	3 / 6 (50.00%)
occurrences (all)	0	3	3
Nausea			
subjects affected / exposed	1 / 1 (100.00%)	4 / 6 (66.67%)	2 / 6 (33.33%)
occurrences (all)	1	4	2
Haematochezia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 1 (100.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Rash maculo-papular			
subjects affected / exposed	1 / 1 (100.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Rash papular			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin ulcer			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Dermatitis			

subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	2 / 6 (33.33%)
occurrences (all)	0	1	2
Renal and urinary disorders			
Urinary incontinence			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Urinary hesitation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Haematuria			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Micturition urgency			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Dysuria			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Bladder spasm			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Candida infection			

subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Vaginal infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hypoalbuminaemia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hyperglycaemia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Dehydration			
subjects affected / exposed	0 / 1 (0.00%)	3 / 6 (50.00%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Decreased appetite			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	3 / 6 (50.00%)
occurrences (all)	0	1	3
Hyponatraemia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypocalcaemia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Peposertib 250 mg + RT + Capecitabine:		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)		
Vascular disorders			

Hypotension subjects affected / exposed occurrences (all) Peripheral embolism subjects affected / exposed occurrences (all)	 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0		
General disorders and administration site conditions Secretion discharge subjects affected / exposed occurrences (all) Oedema peripheral subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Asthenia subjects affected / exposed occurrences (all)	 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 3 / 6 (50.00%) 3		
Reproductive system and breast disorders Pelvic pain subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all)	 0 / 6 (0.00%) 0		
Psychiatric disorders Personality change subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all)	 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0		
Investigations			

White blood cell count decreased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Weight decreased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Lymphocyte count decreased subjects affected / exposed occurrences (all)	3 / 6 (50.00%) 3		
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Platelet count decreased subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Injury, poisoning and procedural complications Radiation skin injury subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Anal injury subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Nervous system disorders Sciatica subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Dysgeusia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Dizziness postural			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Neutropenia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Thrombocytopenia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Anaemia			
subjects affected / exposed	4 / 6 (66.67%)		
occurrences (all)	4		
Leukopenia			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Abdominal distension			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	5 / 6 (83.33%)		
occurrences (all)	5		
Dry mouth			

subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Dyschezia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Abdominal pain lower				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Anal incontinence				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Anal inflammation				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Flatulence				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Constipation				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Colitis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Vomiting				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Rectal ulcer				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Rectal tenesmus				
subjects affected / exposed	5 / 6 (83.33%)			
occurrences (all)	5			
Rectal haemorrhage				
subjects affected / exposed	3 / 6 (50.00%)			
occurrences (all)	3			
Proctitis				

subjects affected / exposed	3 / 6 (50.00%)			
occurrences (all)	3			
Proctalgia				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Nausea				
subjects affected / exposed	2 / 6 (33.33%)			
occurrences (all)	2			
Haematochezia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Skin and subcutaneous tissue disorders				
Pruritus				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Rash maculo-papular				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Rash papular				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Skin ulcer				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Dermatitis				
subjects affected / exposed	2 / 6 (33.33%)			
occurrences (all)	2			
Dry skin				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Erythema				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Palmar-plantar erythrodysaesthesia syndrome				

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Renal and urinary disorders Urinary incontinence subjects affected / exposed occurrences (all) Urinary hesitation subjects affected / exposed occurrences (all) Haematuria subjects affected / exposed occurrences (all) Micturition urgency subjects affected / exposed occurrences (all) Dysuria subjects affected / exposed occurrences (all) Bladder spasm subjects affected / exposed occurrences (all)	 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0		
Infections and infestations Bacteraemia subjects affected / exposed occurrences (all) Candida infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) Vaginal infection subjects affected / exposed occurrences (all)	 0 / 6 (0.00%) 0 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1		
Metabolism and nutrition disorders			

Hypoalbuminaemia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Dehydration subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Decreased appetite subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2		
Hyponatraemia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Hypokalaemia subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2		
Hypocalcaemia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 April 2019	The key changes of the protocol were: 1. To allow for the inclusion of Stage II rectal cancer patients, who may often benefit from concurrent chemoradiation according to clinical practice. 2. To allow for the administration of induction chemotherapy, reflecting evolving clinical practice for locally advanced rectal cancer. 3. To adjust the schedule of visits and evaluations to the standard clinical practice. 4. To adjust the tumor evaluation procedures for locally advanced rectal cancer reflecting evolving clinical practice.
11 May 2020	The main purpose of this protocol amendment was to provide clearer and more detailed guidance with regards to key therapeutic interventions, such as induction or adjuvant chemotherapy regimens, study treatment specifications (e.g. radiotherapy techniques), and surgical pathology assessment for pathological complete response.
06 May 2021	The protocol amendment was issued to document the premature discontinuation of study.

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.

As decided by sponsor study was discontinued prior to the initiation of the Phase II part of the study; therefore, results only from the Phase Ib part of the study was reported.

Notes: