Clinical trial results:
Phase 3 Study of ADXS11-001 Administered Following Chemoradiation as Adjuvant Treatment for High Risk Locally Advanced Cervical Cancer: AIM2CERV (Advaxis IMmunotherapy 2 prevent CERVical recurrence)

Summary

EudraCT number	2015-004844-20
Trial protocol	ES PL
Global end of trial date	31 July 2019

Results information

Result version number	v1 (current)
This version publication date	16 February 2024
First version publication date	16 February 2024

Trial information

Trial identification

Sponsor protocol code	ADXS001-02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02853604
WHO universal trial number (UTN)	-
Other trial identifiers	IND number: 013712

Notes:

Sponsors

Sponsor organisation name	Advaxis, Inc
Sponsor organisation address	9 Deer Park Drive, New Jersey, United States,
Public contact	Regulatory Affairs, Advaxis, Inc, +34 91 4322630, du@advaxis.com
Scientific contact	Regulatory Affairs, Advaxis, Inc, +34 91 4322630, du@advaxis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 July 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 July 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To compare the disease free survival (DFS) of ADXS11-001 to placebo administered in the adjuvant setting following concurrent chemotherapy and radiotherapy (CCRT) administered with curative intent to subjects with high-risk locally advanced squamous, adenosquamous, or adenocarcinoma of the cervix (HRLACC).

Protection of trial subjects:

1. Nausea and vomiting should be treated aggressively with prophylactic antiemetic therapy prior to each infusion and every 8 hours as needed. Subjects should also be strongly encouraged to maintain liberal oral fluid intake.
2. Close monitoring of blood pressure at baseline and during the post-infusion period to prevent grade 3 and 4 hypotension.
3. The study treatment dose will not be modified (i.e., reduced or increased). However, treatment may be delayed or discontinued for drug related severe and life-threatening toxicities.
4. Treatment may be delayed at the discretion of the investigator for adverse events that are not drug-related, but which would either put the subject at risk from treatment, adversely affect the efficacy of study treatment, confound the interpretation of study results, or prevent the assessment of study results.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 November 2016
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	Argentina: 2
Country: Number of subjects enrolled	Brazil: 11
Country: Number of subjects enrolled	United States: 20
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Malaysia: 3
Country: Number of subjects enrolled	Mexico: 3
Country: Number of subjects enrolled	Russian Federation: 17
Country: Number of subjects enrolled	Serbia: 11
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 2
Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	Taiwan: 5
Country: Number of subjects enrolled	Ukraine: 23

Worldwide total number of subjects	110
EEA total number of subjects	12

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)	102
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants completed cisplatin-based combination chemotherapy and radiation (CCRT) before enrollment into the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants with locally advanced cervical cancer at higher risk for recurrence (HRLACC) received ADXS11-001 matching placebo by intravenous infusion for approximately 60 minutes every 3 weeks for 3 doses (Weeks 1, 4 and 7) and thereafter, every 8 weeks for 5 doses (Weeks 15, 23, 31, 39, and 47) during treatment phase or until disease recurrence. Participants received a 7-day course placebo matching to either trimethoprim/sulfamethoxazole or ampicillin starting 72 hours post treatment in prime and maintenance phase.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

intravenous infusion for approximately 60 minutes every 3 weeks for 3 doses (Weeks 1, 4 and 7) and thereafter, every 8 weeks for 5 doses (Weeks 15, 23, 31, 39, and 47) during treatment phase or until disease recurrence. Participants received a 7-day course placebo matching to either trimethoprim/sulfamethoxazole or ampicillin starting 72 hours post treatment in prime and maintenance phase.

Arm title	ADXS11-001

Arm description:

Participants with HRLACC received ADXS11-001 at a dose of 1x10^9 colony forming units (CFU) by intravenous infusion for approximately 60 minutes every 3 weeks for 3 doses (Weeks 1, 4 and 7) and thereafter, every 8 weeks for 5 doses (Weeks 15, 23, 31, 39, and 47) during treatment phase or until disease recurrence. Participants received a 7-day course of either trimethoprim/sulfamethoxazole or ampicillin starting 72 hours post treatment in prime and maintenance phase.

Arm type	Experimental
Investigational medicinal product name	ADXS11-001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received ADXS11-001 at a dose of 1x10^9 colony forming units (CFU) by intravenous infusion for approximately 60 minutes every 3 weeks for 3 doses (Weeks 1, 4 and 7) and thereafter, every 8 weeks for 5 doses (Weeks 15, 23, 31, 39, and 47) during treatment phase or until disease

recurrence. Participants received a 7-day course of either trimethoprim/sulfamethoxazole or ampicillin starting 72 hours post treatment in prime and maintenance phase.

Number of subjects in period 1	Placebo	ADXS11-001
Started	37	73
Completed	9	21
Not completed	28	52
Consent withdrawn by subject	12	35
Death	1	5
Progressive Disease	-	2
Miscellaneous	11	2
Lost to follow-up	4	8

Baseline characteristics

Reporting groups	
Reporting group title	Placebo

Reporting group description:

Participants with locally advanced cervical cancer at higher risk for recurrence (HRLACC) received ADXS11-001 matching placebo by intravenous infusion for approximately 60 minutes every 3 weeks for 3 doses (Weeks 1, 4 and 7) and thereafter, every 8 weeks for 5 doses (Weeks 15, 23, 31, 39, and 47) during treatment phase or until disease recurrence. Participants received a 7-day course placebo matching to either trimethoprim/sulfamethoxazole or ampicillin starting 72 hours post treatment in prime and maintenance phase.

Reporting group title	ADXS11-001

Reporting group description:

Participants with HRLACC received ADXS11-001 at a dose of 1x10^9 colony forming units (CFU) by intravenous infusion for approximately 60 minutes every 3 weeks for 3 doses (Weeks 1, 4 and 7) and thereafter, every 8 weeks for 5 doses (Weeks 15, 23, 31, 39, and 47) during treatment phase or until disease recurrence. Participants received a 7-day course of either trimethoprim/sulfamethoxazole or ampicillin starting 72 hours post treatment in prime and maintenance phase.

Reporting group values	Placebo	ADXS11-001	Total
Number of subjects	37	73	110
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	46	49.3	
standard deviation	± 10.34	± 10.83	-
Gender categorical Units: Subjects			
Female	37	73	110
Male	0	0	0

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Participants with locally advanced cervical cancer at higher risk for recurrence (HRLACC) received ADXS11-001 matching placebo by intravenous infusion for approximately 60 minutes every 3 weeks for 3 doses (Weeks 1, 4 and 7) and thereafter, every 8 weeks for 5 doses (Weeks 15, 23, 31, 39, and 47) during treatment phase or until disease recurrence. Participants received a 7-day course placebo matching to either trimethoprim/sulfamethoxazole or ampicillin starting 72 hours post treatment in prime and maintenance phase.

Reporting group title	ADXS11-001

Reporting group description:

Participants with HRLACC received ADXS11-001 at a dose of 1x10^9 colony forming units (CFU) by intravenous infusion for approximately 60 minutes every 3 weeks for 3 doses (Weeks 1, 4 and 7) and thereafter, every 8 weeks for 5 doses (Weeks 15, 23, 31, 39, and 47) during treatment phase or until disease recurrence. Participants received a 7-day course of either trimethoprim/sulfamethoxazole or ampicillin starting 72 hours post treatment in prime and maintenance phase.

Primary: Disease Free Survival (DFS)

End point title	Disease Free Survival (DFS)[1]

End point description:

DFS was defined as the time from randomization until death or recurrence. The date of recurrence was defined as the date of the first time point when recurrence of disease was determined. The determination of recurrence should occur by definitive pathologic tissue confirmation (e.g., biopsy/fine needle aspirate). However, in those cases where it was not medically feasible to obtain a tissue sample then radiographic evidence, when confirmed by independent radiology review, was used to determine recurrence.

End point type	Primary

End point timeframe:

From the time of randomization to recurrence or death (Maximum duration: 44.7 months)

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 Sponsor terminated the study early based on a business decision (not related to safety or efficacy reasons). Upon early study termination, all subjects randomized in the study were moved to the End of Treatment visit. Therefore, efficacy evaluations including disease-free survival (DFS) and overall survival were not performed on any subject.

End point values	Placebo	ADXS11-001		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: month				
median (full range (min-max))	(to)	(to)		

Notes:

[2] - The study was terminated early due to business reasons, therefore, no efficacy data was collected.

[3] - The study was terminated early due to business reasons, therefore, no efficacy data was collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment Emergent Adverse Events

End point title	Number of Participants With Treatment Emergent Adverse Events

End point description:

End point type	Secondary

End point timeframe:

From first dose of study drug until end of study (Up to 44.7 months)

End point values	Placebo	ADXS11-001		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	72		
Units: participants	30	62		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

Overall survival was defined as the time from the date of randomization until death due to any cause.

End point type	Secondary

End point timeframe:

From the date of randomization until death due to any cause (Maximum duration: 44.7 months)

End point values	Placebo	ADXS11-001		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[4]	0[5]		
Units: month				
median (full range (min-max))	(to)	(to)		

Notes:

[4] - The study was terminated early due to business reasons, therefore, no efficacy data was collected.

[5] - The study was terminated early due to business reasons, therefore, no efficacy data was collected.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug until end of study (Up to 44.7 months)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants with locally advanced cervical cancer at higher risk for recurrence (HRLACC) received ADXS11-001 matching placebo by intravenous infusion for approximately 60 minutes every 3 weeks for 3 doses (Weeks 1, 4 and 7) and thereafter, every 8 weeks for 5 doses (Weeks 15, 23, 31, 39, and 47) during treatment phase or until disease recurrence. Participants received a 7-day course placebo matching to either trimethoprim/sulfamethoxazole or ampicillin starting 72 hours post treatment in prime and maintenance phase.

Reporting group title	ADXS11-001

Reporting group description:

Participants with HRLACC received ADXS11-001 at a dose of 1x10^9 colony forming units (CFU) by intravenous infusion for approximately 60 minutes every 3 weeks for 3 doses (Weeks 1, 4 and 7) and thereafter, every 8 weeks for 5 doses (Weeks 15, 23, 31, 39, and 47) during treatment phase or until disease recurrence. Participants received a 7-day course of either trimethoprim/sulfamethoxazole or ampicillin starting 72 hours post treatment in prime and maintenance phase.

Serious adverse events	Placebo	ADXS11-001	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 37 (21.62%)	13 / 72 (18.06%)	
number of deaths (all causes)	1	5	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 37 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 37 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			

Chest discomfort			
subjects affected / exposed	1 / 37 (2.70%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	1 / 37 (2.70%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 37 (0.00%)	2 / 72 (2.78%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Female genital tract fistula			
subjects affected / exposed	1 / 37 (2.70%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Genital haemorrhage			
subjects affected / exposed	0 / 37 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vulval disorder			
subjects affected / exposed	1 / 37 (2.70%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 37 (2.70%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			

subjects affected / exposed	0 / 37 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Radiation proctitis			
subjects affected / exposed	1 / 37 (2.70%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Seizure			
subjects affected / exposed	1 / 37 (2.70%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 37 (2.70%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 37 (0.00%)	2 / 72 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal haemorrhage			
subjects affected / exposed	1 / 37 (2.70%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			

subjects affected / exposed	0 / 37 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 37 (2.70%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 37 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 37 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 37 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 37 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urogenital fistula			
subjects affected / exposed	0 / 37 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 37 (2.70%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Muscular weakness			
subjects affected / exposed	1 / 37 (2.70%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Kidney infection			
subjects affected / exposed	1 / 37 (2.70%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	ADXS11-001	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 37 (83.78%)	64 / 72 (88.89%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 37 (5.41%)	4 / 72 (5.56%)	
occurrences (all)	2	7	
Hypotension			
subjects affected / exposed	5 / 37 (13.51%)	14 / 72 (19.44%)	
occurrences (all)	7	22	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	5 / 37 (13.51%)	1 / 72 (1.39%)	
occurrences (all)	5	1	
Chills			

subjects affected / exposed	0 / 37 (0.00%)	23 / 72 (31.94%)	
occurrences (all)	0	57	
Fatigue			
subjects affected / exposed	5 / 37 (13.51%)	14 / 72 (19.44%)	
occurrences (all)	8	22	
Hyperthermia			
subjects affected / exposed	0 / 37 (0.00%)	10 / 72 (13.89%)	
occurrences (all)	0	38	
Oedema peripheral			
subjects affected / exposed	4 / 37 (10.81%)	1 / 72 (1.39%)	
occurrences (all)	5	1	
Pain			
subjects affected / exposed	2 / 37 (5.41%)	5 / 72 (6.94%)	
occurrences (all)	2	11	
Peripheral swelling			
subjects affected / exposed	2 / 37 (5.41%)	0 / 72 (0.00%)	
occurrences (all)	2	0	
Pyrexia			
subjects affected / exposed	1 / 37 (2.70%)	27 / 72 (37.50%)	
occurrences (all)	1	63	
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	1 / 37 (2.70%)	10 / 72 (13.89%)	
occurrences (all)	2	27	
Reproductive system and breast disorders			
Dyspareunia			
subjects affected / exposed	2 / 37 (5.41%)	2 / 72 (2.78%)	
occurrences (all)	2	2	
Pelvic Pain			
subjects affected / exposed	1 / 37 (2.70%)	5 / 72 (6.94%)	
occurrences (all)	1	8	
Vaginal Discharge			
subjects affected / exposed	2 / 37 (5.41%)	3 / 72 (4.17%)	
occurrences (all)	2	3	
Vaginal Haemorrhage			

subjects affected / exposed	2 / 37 (5.41%)	1 / 72 (1.39%)	
occurrences (all)	4	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 37 (5.41%)	3 / 72 (4.17%)	
occurrences (all)	2	3	
Oropharyngeal pain			
subjects affected / exposed	2 / 37 (5.41%)	1 / 72 (1.39%)	
occurrences (all)	3	1	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 37 (5.41%)	6 / 72 (8.33%)	
occurrences (all)	2	8	
Insomnia			
subjects affected / exposed	2 / 37 (5.41%)	1 / 72 (1.39%)	
occurrences (all)	2	1	
Investigations			
C-reactive protein increased			
subjects affected / exposed	0 / 37 (0.00%)	6 / 72 (8.33%)	
occurrences (all)	0	10	
Injury, poisoning and procedural complications			
Radiation proctitis			
subjects affected / exposed	2 / 37 (5.41%)	1 / 72 (1.39%)	
occurrences (all)	3	1	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 37 (0.00%)	8 / 72 (11.11%)	
occurrences (all)	0	18	
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 37 (8.11%)	5 / 72 (6.94%)	
occurrences (all)	4	6	
Headache			
subjects affected / exposed	7 / 37 (18.92%)	20 / 72 (27.78%)	
occurrences (all)	8	43	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	4 / 37 (10.81%)	16 / 72 (22.22%)	
occurrences (all)	5	28	
Leukopenia			
subjects affected / exposed	2 / 37 (5.41%)	4 / 72 (5.56%)	
occurrences (all)	2	6	
Neutropenia			
subjects affected / exposed	1 / 37 (2.70%)	6 / 72 (8.33%)	
occurrences (all)	1	6	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	6 / 37 (16.22%)	10 / 72 (13.89%)	
occurrences (all)	18	19	
Constipation			
subjects affected / exposed	1 / 37 (2.70%)	5 / 72 (6.94%)	
occurrences (all)	1	7	
Diarrhoea			
subjects affected / exposed	7 / 37 (18.92%)	7 / 72 (9.72%)	
occurrences (all)	12	9	
Haematochezia			
subjects affected / exposed	0 / 37 (0.00%)	5 / 72 (6.94%)	
occurrences (all)	0	6	
Nausea			
subjects affected / exposed	5 / 37 (13.51%)	20 / 72 (27.78%)	
occurrences (all)	7	39	
Rectal haemorrhage			
subjects affected / exposed	3 / 37 (8.11%)	2 / 72 (2.78%)	
occurrences (all)	3	2	
Vomiting			
subjects affected / exposed	2 / 37 (5.41%)	11 / 72 (15.28%)	
occurrences (all)	2	21	
Skin and subcutaneous tissue disorders			
Rash Maculo-Papular			
subjects affected / exposed	3 / 37 (8.11%)	1 / 72 (1.39%)	
occurrences (all)	3	1	
Renal and urinary disorders			

Hydronephrosis			
subjects affected / exposed	2 / 37 (5.41%)	4 / 72 (5.56%)	
occurrences (all)	3	4	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 37 (10.81%)	7 / 72 (9.72%)	
occurrences (all)	4	14	
Back pain			
subjects affected / exposed	3 / 37 (8.11%)	9 / 72 (12.50%)	
occurrences (all)	3	14	
Muscular weakness			
subjects affected / exposed	2 / 37 (5.41%)	0 / 72 (0.00%)	
occurrences (all)	2	0	
Myalgia			
subjects affected / exposed	0 / 37 (0.00%)	6 / 72 (8.33%)	
occurrences (all)	0	14	
Pain in extremity			
subjects affected / exposed	3 / 37 (8.11%)	2 / 72 (2.78%)	
occurrences (all)	3	4	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	2 / 37 (5.41%)	4 / 72 (5.56%)	
occurrences (all)	3	4	
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 37 (5.41%)	2 / 72 (2.78%)	
occurrences (all)	4	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 May 2018	1. Subjects with a history of hysterectomy following neoadjuvant chemotherapy were excluded. 2. Antibiotic requirement during Lm surveillance consisted of a 3-week course of trimethoprim/sulfamethoxazole, ampicillin or placebo (reduced from 6 months) and 35 months of follow-up with blood testing. 3, Use of PET/CT was an acceptable method, in addition to MRI, for baseline and post-treatment assessment of the pelvis. 4. Cervical and vaginal cytology was to be performed only at screening unless necessary by the treating physician.
19 February 2019	1. Sensitivity or allergy to ampicillin was removed as an exclusion criterion. 2. Premedication regimen (antihistamine, NSAIDs, antiemetics, histamine H2-receptor antagonist) was to be given one hour prior to the procedure. 3. Patients who discontinued early for reasons other than disease occurrence were to immediately enter the follow-up period of the study. 4. Grading and management guidelines for hypotension, hypoxia, encephalopathy, organ toxicity, fever, and constitutional symptoms were added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported