



Clinical trial results:

A Clinical Study of ColoAd1 Administered by Sub-Acute Fractionated Intravenous Injection: Dose Escalation in Metastatic Epithelial Solid Tumours and Randomised Controlled Trial in Metastatic Colorectal Cancer

Summary

EudraCT number	2012-001067-79
Trial protocol	ES GB BE
Global end of trial date	29 April 2016

Results information

Result version number	v1 (current)
This version publication date	11 May 2017
First version publication date	11 May 2017
Summary attachment (see zip file)	Summary of secondary endpoints (Summary of secondary endpoints.pdf)

Trial information

Trial identification

Sponsor protocol code	ColoAd1-1001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02028442
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	PsiOxus Therapeutics Ltd
Sponsor organisation address	154B Brook Drive, Abingdon, United Kingdom, OX14 4SD
Public contact	Chief Medical Officer, PsiOxus Therapeutics Ltd, +44 (0)1235835328, HMJ@Psioxus.com
Scientific contact	Chief Medical Officer, PsiOxus Therapeutics Ltd, +44 (0)1235835328, HMJ@Psioxus.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	29 April 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 April 2016
Global end of trial reached?	Yes
Global end of trial date	29 April 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Phase I:

To evaluate the safety and tolerability of ColoAd1, when administered by sub-acute fractionated intravenous (IV) injection to subjects with advanced or metastatic epithelial solid tumours not responding to standard therapy or for whom no standard treatment exists

To determine the maximally-tolerated dose and/or maximum-feasible dose of ColoAd1 when administered by sub-acute fractionated IV injection to subjects with advanced or metastatic epithelial solid tumours not responding to standard therapy or for whom no standard treatment exists, and to recommend a dose for phase II studies.

Phase Ib:

To select a suitable schedule and dose for repeat cycle IV administration of ColoAd1 in subjects with metastatic colorectal (mCRC) cancer or urothelial cell cancer

Phase II: Not performed

To evaluate progression free survival in subjects with mCRC when ColoAd1 is administered IV as intensification of first line chemotherapy compared with first line chemotherapy alone

Protection of trial subjects:

The trial was conducted in compliance with the Declaration of Helsinki, the International Conference on Harmonisation guidelines on Good Clinical Practice and other applicable regulatory requirements. All personal data collected during the study were managed by the Investigator and study staff with adequate precautions to ensure confidentiality of those data, and in accordance with national local laws and regulations on personal data protection.

This was a first-in-human study and measures were put in place to minimise risk to subjects:

- Subjects with immunosuppressed background were excluded and concurrent administration of immunosuppressants was prohibited
- Subjects were eligible only when they had recovered to \leq Grade 1 from toxicities (excluding alopecia) of previous systemic treatment or radiotherapy.
- Only subjects with a good performance status (ECOG of 0 or 1) and those with adequate bone marrow, liver and renal functions and normal international normalised ratio were eligible for the study
- The Phase I part of the study was conducted by experienced Investigators in Phase I units with experience of novel therapeutic agents in Phase I studies
- All subjects in the Phase I Dose Escalation Stage were hospitalised until Day 6 to allow close monitoring during and after all administrations of ColoAd1
- Although the risk of virus shedding was thought to be minimal due to the highly attenuated nature of the virus subjects were excluded unless alternate living arrangements could be made for household contacts that were pregnant, <1year old or had severe immunosuppression
- A Clinical Events Committee, which included an independent oncologist, reviewed the safety data from each cohort of the Phase I part of the study to determine the dose for the next cohort. Additionally a Data and Safety Monitoring Committee constituted according to regulatory guidelines reviewed the safety data at the end of the Phase I part of the study

Background therapy:

None

Evidence for comparator:

The Phase II part of the study which involved comparison of sequential treatment with ColoAd1 and chemotherapy with chemotherapy alone was not performed

Actual start date of recruitment	20 September 2012
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: 32
Country: Number of subjects enrolled	Belgium: 29
Worldwide total number of subjects	61
EEA total number of subjects	61

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)	40
From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Phase I: Dose escalation using 3+3 design. 1st subject consented in Belgium 20SEP12. 1st subject in Spain 14JAN13. Then dose expansion group 9 subjects & repeat cycle group 6 subjects.

Phase Ib: Comparison weekly & 3 weekly dosing schedules. 1st subject 27OCT14. Study terminated after 6 evaluable subjects each group.

Sites: 3 Belgium 3 Spain 0 UK

Pre-assignment

Screening details:

Phase 1: 50 Screened, 37 enrolled & dosed. 13 screen failures: 8 inadequate renal function, 2 inadequate hepatic function, 2 compliance, 1 ECOG score

Phase I: 31 screened, 24 enrolled & dosed. 7 screen failures: 5 inadequate renal function one also with inadequate bone marrow function, 2 other excluded medical conditions

Period 1

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

Blinding implementation details:

Open label in both Phase I and Phase Ib.

CT scans read centrally by blinded independent assessor.

Arms

Arm title	Overall study
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Arm description:

Phase 1: 3+3 design evaluating different doses, total of 7 cohorts (Cohorts 1-7) followed by dose expansion cohort (Cohort 10) and a repeat cycle cohort (Cohort 8). No Cohort 9.

Phase Ib: weekly versus 3-weekly dose schedule comparison, total 5 cohorts

Arm type	Experimental
Investigational medicinal product name	ColoAd1
Investigational medicinal product code	
Other name	INN: Enadenotucirev
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Cohort 1: 1x10¹⁰ viral particles (vp) by IV infusion over 5 minutes

Cohort 2: 1x10¹¹ vp by IV infusion over 5 minutes

Cohort 3: 1x10¹² vp by IV infusion over 5 minutes*

Cohort 4: 1x10¹³ vp by IV infusion over 5 minutes*

Cohort 5: 3x10¹² vp by IV infusion over 5 minutes

Cohort 6: 3x10¹² vp by IV infusion over 20 minutes*

Cohort 7: 6x10¹² vp by IV infusion over 40 minutes

In all cohorts three infusions given separated by 48 hours on Days 1, 3 and 5 (one cycle)

* one subject retreated at a later date with one cycle

Cohort 8: 6x10¹² vp by IV infusion over 40 minutes Days 1, 3 and 5 every 3 weeks for 3 or 4 cycles

Cohort 10: 6x10¹² vp by IV infusion over 40 minutes single cycle, 3 subjects retreated

Phase Ib: 1 x 10¹², 3 x 10¹² or 6 x 10¹² vp on Days 1, 3 and 5 every 3 weeks for up to 6 cycles or 3 x 10¹² or 6 x 10¹² vp on Days 1, 3, 5 then 8 then weekly for up to 6 3 week cycles by IV infusion

Number of subjects in period 1	Overall study
Started	61
Completed	36
Not completed	25
Consent withdrawn by subject	2
Physician decision	1
Disease progression	16
Adverse event, non-fatal	6

Baseline characteristics

Reporting groups

Reporting group title	Overall study
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Reporting group description: -

Reporting group values	Overall study	Total	
Number of subjects	61	61	
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)	40	40	
From 65-84 years	21	21	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	60.14		
full range (min-max)	36 to 79	-	
Gender categorical			
Units: Subjects			
Female	15	15	
Male	46	46	
Race			
Units: Subjects			
Caucasian	61	61	

Subject analysis sets

Subject analysis set title	Safety analysis set
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Subject analysis set type	Safety analysis
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Subject analysis set description:

Safety analysis set included all subjects who received at least a partial dose

Reporting group values	Safety analysis set		
Number of subjects	61		
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)	40		
From 65-84 years	21		
85 years and over			
Age continuous			
Units: years			
arithmetic mean	60.14		
full range (min-max)	36 to 79		
Gender categorical			
Units: Subjects			
Female	15		
Male	46		
Race			
Units: Subjects			
Caucasian	61		

End points

End points reporting groups

Reporting group title	Overall study
Reporting group description:	
Phase 1: 3+3 design evaluating different doses, total of 7 cohorts (Cohorts 1-7) followed by dose expansion cohort (Cohort 10) and a repeat cycle cohort (Cohort 8). No Cohort 9. Phase Ib: weekly versus 3-weekly dose schedule comparison, total 5 cohorts	
Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis
Subject analysis set description:	
Safety analysis set included all subjects who received at least a partial dose	

Primary: Safety and tolerability - adverse events, laboratory data and vital signs

End point title	Safety and tolerability - adverse events, laboratory data and vital signs ^[1]
End point description:	
Tables attached of all adverse events occurring in 5% or more of subjects overall also broken down by dose groups: < 1 x 10 ¹² , 1-3 x 10 ¹² and > 3x 10 ¹² viral particles. Also attached are a summary of adverse events, laboratory data and vital signs.	
End point type	Primary
End point timeframe:	
From time of first dose until 56 days after last dose for cohorts 1-7 and 10 in Phase I and from first dose until 28 days after last dose for cohort 8 in Phase I and Phase Ib	

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 analysis performed. Only descriptive summaries were prepared due to the small numbers in each cohort of this exploratory study.

Continuous variables were summarised using the number of observations, mean, standard deviation (SD), median, minimum, and maximum. Categorical variables were summarised using number of observations, frequency and percentages of patients.

End point values	Overall study	Safety analysis set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	61	61		
Units: Number of subjects				
number (not applicable)	61	61		

Attachments (see zip file)	Adverse events in 5% or more of subjects.pdf
	Summary of adverse events.pdf
	Summary of laboratory test data.pdf
	Summary of vital signs data.pdf

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Phase I cohorts 1-7 and 10 from first dose until 56 days after last dose

Phase 1 cohort 8 and Phase Ib from first dose until 28 days after last dose

Adverse event reporting additional description:

See attachment for full list of adverse events in $\geq 5\%$ subjects.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.1
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Reporting groups

Reporting group title	Overall study
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Reporting group description:

Data from the two phases of study integrated. Due to small numbers of subjects in dose groups, adverse events summarised for those in $\geq 5\%$ subjects overall. Deaths in survival FU included.

Serious adverse events	Overall study		
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 61 (32.79%)		
number of deaths (all causes)	47		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Ataxia			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Encephalopathy			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Paraplegia			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chills			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Malaise			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	3 / 61 (4.92%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Scleritis			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain upper			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Gastrointestinal obstruction			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	3 / 61 (4.92%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Subileus			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Female genital tract fistula			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Jaundice cholestatic			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatic failure			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Respiratory, thoracic and mediastinal disorders			
Acute lung injury			

subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 1		
Hypoxia			
subjects affected / exposed	3 / 61 (4.92%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Interstitial lung disease			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Glomerulonephritis membranoproliferative			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nephrotic syndrome			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Anal abscess			

subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Overall study		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	61 / 61 (100.00%)		
General disorders and administration site conditions			
Chills	Additional description: See attachment for full list of non-serious adverse events in ≥ 5% subjects. The two most common listed here.		
subjects affected / exposed	41 / 61 (67.21%)		
occurrences (all)	88		
Pyrexia	Additional description: See attachment for full list of non-serious adverse events in ≥ 5% subjects. The two most common listed here.		
subjects affected / exposed	45 / 61 (73.77%)		
occurrences (all)	125		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 August 2012	Amendment implemented before the start of study to incorporate requested during Competent Authority review to clarify and adequately define criteria for dose limiting toxicities, the period of adverse event follow up and timepoints for pharmacokinetic blood sampling during Phase I
22 January 2013	<p>To clarify requirements and procedures for retreatment of subjects with ColoAd1, to clarify the eligibility criterion relating to renal function, to clarify how disease related toxicities should be considered, when assessing dose limiting toxicities and to clarify adverse event and serious adverse event reporting exemptions.</p> <p>To change the Medical Monitor from Dr Hamina Patel to Dr John Beadle</p>
18 April 2013	<p>To update the dose escalation schedule and to introduce the possibility of extending the duration of infusion of ColoAd1 based on a review of the literature and the safety data generated at this point due to the occurrence of dose limiting toxicities at the 1×10^{13} vp dose and possible correlation with pharmacokinetic and cytokine profile data</p> <p>To add assessments of viral kinetics, viral shedding and cytokines in the Phase I Dose Expansion Cohort</p> <p>To clarify the roles of the Clinical Events Committee and Data and Safety Monitoring Committee for the choice of the doses to be used for the Phase I Dose Expansion Cohort, the Phase II Dose Feasibility and the randomised Phase II stages</p> <p>To change the Medical Monitor from Dr John Beadle to Dr Christine Wilkinson Blanc</p>
22 September 2013	<p>To introduce the Repeat Cycle Cohort (Cohort 8)</p> <p>To update the eligibility criteria and timing for retreatment</p> <p>To update the inclusion criterion relating to adequate renal function to define absence of clinically significant haematuria on urinalysis as dipstick <2+ instead of dipstick <1+ or <3 red blood cells per high-power field on microscopic analysis and absence of clinically significant proteinuria on urinalysis as dipstick <2+ instead of dipstick <1+ or <150 mg per day on 24 hour urine collection or urine protein-creatinine ratio <30 mg/mmol creatinine. The original criterion had been set to reflect the potential renal tropism of Ad11, this criterion was relaxed as no renal adverse events or urinalysis changes had been seen at this point</p> <p>To update the inclusion criterion relating to the maximum number of prior systemic therapies for advanced disease allowed for colorectal cancer subjects selected for the Phase I Dose Expansion Cohort. Treatment of subjects with tumours that are EGFR positive usually includes an anti-EGFR therapy either combined with other therapeutic agents or alone. The inclusion criterion originally allowed three prior systemic therapies and was updated to allow four prior systemic therapies if one of them was an anti-EGFR single agent or combined to a previously administered chemotherapy regimen</p> <p>To allow flexibility in the pre-medication with ibuprofen</p>

11 August 2014	<p>To introduce Phase Ib to expand the repeat dosing investigation to compare a weekly schedule with the 3 weekly schedule included previously performed in a homogeneous population of subjects with mCRC or UCC</p> <p>To update the inclusion criteria relating to adequate renal function to define absence of clinically significant haematuria on urinalysis as dipstick $\leq 2+$ instead of dipstick $< 2+$ and absence of clinically significant proteinuria on urinalysis as dipstick $\leq 2+$ instead of dipstick $< 2+$ to match the usual definition of these criteria in oncology as there had been no renal adverse effects in the subjects treated at that point</p> <p>To allow for the collection of tissue samples from unplanned surgery biopsies performed within 90 days of first administration of ColoAd1 as analysis of collected tissue, tumour or normal tissue may allow for further understanding of the delivery and expression of ColoAd1</p> <p>To relax the contact exclusions and the precautions to be taken with household contacts based upon shedding data from the Phase I Dose Escalation and Dose Expansion Stages</p>
14 November 2014	<p>To include the following mandatory laboratory safety assessments prior to the Day 8 and Day 15 infusions of ColoAd1 in the weekly schedule which had been omitted in error in the previous version and to introduce optional assessments on Day 3 and Day 5 of Cycle 2 onwards in the 3 weekly schedule:</p> <ul style="list-style-type: none"> -Cycle 1: mandatory assessments on Day 8 and Day 15 for all subjects -Further cycles: mandatory assessments on Day 8 and Day 15 for the first 12 subjects and optional assessments based on investigators clinical judgment on days 8 and 15 for subsequent subjects <p>To specify the dose adjustments to be performed if DLTs were observed in Phase Ib</p> <p>To introduce the possibility of a dose reduction under the 3 weekly schedule as well as under the weekly schedule if the dose recommended for Phase II was not tolerated under the weekly schedule</p> <p>To update the primary objective for Phase Ib to specify that it is to determine both a schedule and dose for further studies with repeat cycle administration</p> <p>To assess a small cohort of subjects at the dose immediately below the dose recommended for Phase II (three subjects under each schedule) to provide information to support intra-subject dose reductions and future combination studies</p> <p>To further relax the eligibility criteria relating to adequate renal function by removing haematuria and proteinuria as measured on dipstick urinalysis as an exclusion criterion as no safety signals relating to renal function had been observed. The removal of this exclusion enabled an assessment of safety in a broader and more representative population of cancer subjects, e.g. inclusion of subjects with UCC</p> <p>To allow for antipyretic prophylaxis with ibuprofen to be administered with two different schedules to reflect standard practice at some centres</p>

17 July 2015	<p>To allow for the treatment of subjects beyond six cycles in Phase Ib of the study (in subjects not progressing by the end of Cycle 6 and in the absence of cumulative or residual toxicities Grade 2 or higher related to prior administrations of ColoAd1). The original selection of six cycles was made arbitrarily based upon previous clinical studies with cancer therapies and at the time of the amendment there was no preclinical or clinical data precluding this. A potential subject starting Cycle 6 with stable disease was also on the study at this time</p> <p>To remove the mandatory requirement to treat a cohort of subjects at a dose below the recommended Phase II dose for single cycle monotherapy in the weekly schedule. This was to be performed at the discretion of the CEC</p> <p>To remove the requirement for mandatory biopsies in at least two subjects in each repeat cycle schedule in Phase Ib. Biopsies proved to be a burden for subjects and as the endpoints of the study were primarily based upon safety and blood assays to compare the repeat dosing schedules it was deemed this would not affect subject safety or data integrity</p> <p>A urine dipstick to detect proteinuria was introduced 24 hours before each administration of ColoAd1 from Day 8 of Cycle 1 in the weekly schedule of Phase Ib following review of a DLT of nephrotic syndrome under this dosing schedule by the Clinical Events Committee and Data and Safety Monitoring Committee. In subjects with proteinuria 2+ or more, a 24 hour urine collection was included prior to the administration of ColoAd1. If proteinuria was >1 g/24 hour, administration was discussed with the Sponsor's Medical Monitor</p> <p>To introduce tumour assessment using the immune-related Response Criteria (irRC) Version 1 criteria in addition to Response Evaluation Criteria in Solid Tumours (RECIST) Version 1.1</p>
18 February 2016	<p>The main reason for the amendment was to remove the restriction requiring equal numbers of subjects with urothelial cell cancer and metastatic colorectal cancer in Phase Ib per treatment schedule. This amendment was approved but no subjects were treated under this amendment as the study was terminated. Two subjects in safety follow-up after treatment discontinuation were re-consented, however no protocol specific procedures outlined in the amendment were performed.</p> <p>The Medical Monitor was changed to Dr Hilary McElwaine-Johnn.</p>

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.

There were 9 cohorts in Phase I & 5 cohorts in Phase Ib, all with small numbers (3-9) of subjects. To aid interpretation, safety data from both phases have been integrated and reported in 3 dose groups <1x10¹², 1-3x10¹² & >3 x10¹² vp and overall.

Notes: