Clinical trial results:
Intraoperative imaging of colon cancer using a fluorescent peptide (EMI-137) against the c-Met receptor

Summary

EudraCT number	2016-003128-22
Trial protocol	GB
Global end of trial date	29 August 2019

Results information

Result version number	v1 (current)
This version publication date	28 June 2020
First version publication date	28 June 2020
Summary attachment (see zip file)	EMI-137 Final report (END OF TRIAL REPORT DECEMBER 2019_final_PDF.pdf)

Trial information

Trial identification

Sponsor protocol code	GS16/87090

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Sponsor's Number: GS16/87090

Notes:

Sponsors

Sponsor organisation name	University of Leeds
Sponsor organisation address	Worsley Building, Leeds, United Kingdom, LS2 9JT
Public contact	Clinical Research Fellow, The University of Leeds, gemmaarmstrong@doctors.org.uk
Scientific contact	Clinical Research Fellow, The University of Leeds, gemmaarmstrong@doctors.org.uk

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	28 August 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 August 2019
Global end of trial reached?	Yes
Global end of trial date	29 August 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of this study is to investigate the ability of a fluorescent medical product called EMI-137 to produce visible fluorescence in colon cancer during laparoscopic (keyhole) surgery.

Protection of trial subjects:

Patients will be identified via the colorectal cancer MDT and approached to participate in the study. The research team will ensure that recruited patients meet all of the eligibility criteria. Patients will receive written and verbal information, and allowed at least 24 hours to consider their participation. Participating patients will provide written, informed consent. Consent will be obtained by an appropriately delegated member of team, any time up to the morning of surgery, prior to administration of the IMP. It is permissible to take trial specific consent at the same time as consent for the planned colonic resection. The patient's general practitioner will be informed of their involvement. Pre-operative patient demographics will be collected, including gender, age, BMI, baseline FBC, U&Es, LFTs and clotting profile, co-morbidities, ASA grade, and medication. All patients will undergo routine preoperative assessment, to include colonic imaging, and staging CT scan of chest, abdomen and pelvis. The planned procedure and radiological staging will be documented.

Background therapy:

Colorectal cancer (CRC) is the fourth most common malignancy in the UK. In 2013, 41,112 cases were diagnosed. CRC is strongly related to age, with nearly 60% of cases diagnosed in patients over the age of 70 years. CRC continues to be the second highest cause of cancer related mortality in the UK, accounting for 10% of all cancer related deaths [1]. In the most deprived social groups this figure is greater. CRC mortality is 30% higher in males from the poorest areas than in their age-standardised counterparts from the least deprived areas. CRC poses significant disease burden, with the NHS continuing to see a year on year rise in cases, often in an older population with significant co-morbidities [1].
The anatomical distribution of CRC varies slightly between the genders and with age. However, there is a left-sided predominance, with over 30% of CRC seen in the rectum/rectosigmoid junction and a further quarter in the sigmoid or descending colon [1].
Survival rates in CRC are strongly correlated to the stage at diagnosis. One year survival data from 2012 shows 98% of patients presenting with stage I disease were alive after one year compared to only 46% with stage IV disease [2]. Long-term survival can usually only be achieved with curative resection. This involves segmental colectomy and en-bloc resection of the draining lymph node field. Currently there is significant variance of opinion regarding the radicality of resection and, in particular the extent of lymphadenectomy [3]. A method of accurately visualising the tumour and any associated metastatic lymph nodes in real-time would be invaluable for intra-operative decision making, allowing the surgeon to tailor the radicality of resection to the stage of disease.

Evidence for comparator: -

Actual start date of recruitment	01 August 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 9
Worldwide total number of subjects	9
EEA total number of subjects	9

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)	0
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The first patient was recruited to the trial on 14th February 2018. Patients suitable for participation in this study were identified via the local MDT meeting. They were approached during their routine clinic with verbal & written info about the trial. Patients who fulfilled the eligibility criteria were asked to give informed written consent.

Pre-assignment

Screening details:

patients were screened as per the eligibility criteria listed in the protocol, prior to surgery.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Baseline Arm

Arm description: -

Arm type	Experimental
Investigational medicinal product name	EMI-137
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

EMI-137 will be administrated by intravenous bolus at a dose of 0.02mg/kg to 0.13mg/kg body weight. The expected trial dose is 0.13mg/kg. This may be adjusted during the course of the clinical trial with evolving results from background to signal ratio.
No placebo or comparative drug will be used.

Arm title	End Data

Arm description: -

Arm type	Experimental
Investigational medicinal product name	EMI-137
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

EMI-137 will be administrated by intravenous bolus at a dose of 0.02mg/kg to 0.13mg/kg body weight. The expected trial dose is 0.13mg/kg. This may be adjusted during the course of the clinical trial with evolving results from background to signal ratio.
No placebo or comparative drug will be used.

Number of subjects in period 1	Baseline Arm	End Data
Started	1	8
Completed	1	8

Baseline characteristics

Reporting groups

Reporting group title	Main Trial Period

Reporting group description: -

Reporting group values	Main Trial Period	Total	
Number of subjects	9	9	
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)	0	0	
From 65-84 years	9	9	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	72		
standard deviation	± 3.9	-	
Gender categorical Units: Subjects			
Female	4	4	
Male	5	5	

End points

End points reporting groups

Reporting group title	Baseline Arm
Reporting group description: -	
Reporting group title	End Data
Reporting group description: -	

Primary: Tumour fluorescence

End point title	Tumour fluorescence[1]
End point description:	
End point type	Primary
End point timeframe: measured at time of surgery	

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: Please see attached End of Trial Report for information on all statistical analysis performed.

End point values	Baseline Arm	End Data		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	8		
Units: patients	1	8		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
All participants safety data was reviewed at every trial visit.	
Assessment type	Systematic

Dictionary used	
Dictionary name	CTCAE
Dictionary version	4.0

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Please see attached End of Trial Report for all safety data.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 December 2017	Introduction of the Union for International Cancer Control TNM v8 classification system Tumour Node Metastasis (TNM) v8.0 classification system on 1st January 2018 at LTHT necessitated a substantial amendment to the trial protocol. Regulatory approval was granted for this prior to trial commencement by REC and MHRA on 5th January and 10th January 2018 respectively.
29 January 2018	The Investigator Brochure (IB) and Investigational Medicinal Product Dossier (IMPD) were updated by the Industrial Partner and drug supplier Edinburgh Molecular Imaging Ltd (EM Ltd) to incorporate batch re-test results and new safety information discovered. This facilitated shelf-life extension of the EMI-137 batch supplied to LTHT. MHRA approved the first substantial amendment to these supporting documents on 25th March 2018.
15 February 2019	The expected recruitment period was extended by a further six months. This was approved on 15th February 2019.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported