Clinical trial results:
A pilot study to assess the efficacy of intravenous iron isomaltoside 1000 (Monofer®) in the management of anaemia associated with the palliative management of upper gastrointestinal adenocarcinoma

Summary

EudraCT number	2013-000209-22
Trial protocol	GB
Global end of trial date	28 August 2017

Results information

Result version number	v1 (current)
This version publication date	22 September 2018
First version publication date	22 September 2018
Summary attachment (see zip file)	End of study report (IRON trial 12GA029 End of Study Report.pdf)

Trial information

Trial identification

Sponsor protocol code	12GA029

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01927328
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Nottingham University Hospitals NHS Trust
Sponsor organisation address	Derby Road, Nottingham, United Kingdom,
Public contact	Austin Acheson, Nottingham University Hospitals NHS Trust , +44 01159249924, researchsponsor@nuh.nhs.uk
Scientific contact	Austin Acheson, Nottingham University Hospitals NHS Trust , +44 01159249924, researchsponsor@nuh.nhs.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 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 August 2017
Global end of trial reached?	Yes
Global end of trial date	28 August 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the feasibility of a larger trial, ie determine study size, ensure logistics adequate, to review patient uptake etc.

Protection of trial subjects:

The study was conducted in full conformity with the current revision of the Declaration of Helsinki (last amended October 2000, with additional footnotes added 2002 and 2004).

The study was conducted in full conformity with relevant regulations and with the ICH Guidelines for Good Clinical Practice (CPMP/ICH/135/95) July 1996.

The protocol, informed consent form, participant information sheet and all substantial amendments to the original approved documents were submitted to the Research Ethics Committee (REC), regulatory authorities (MHRA in the UK), and host institution(s) and received formal written approval.

The study was conducted in accordance with GCP principles and NUH processes.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	07 July 2013
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: 27
Worldwide total number of subjects	27
EEA total number of subjects	27

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	27
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were identified from the oesophagogastric MDT meetings. Included were adult patients with a proven histological diagnosis of oesophagogastric adenocarcinoma, anaemia (<12 g/dL in women and <13 g/dL in men) and a treatment decision for palliative chemotherapy.

Pre-assignment

Screening details:

Patients were randomised 1:1 to each group using random allocations concealed in opaque envelopes. Patients in the control arm had their anaemia managed by traditional regimens as decided by the clinical oncology team. The patients in the intravenous iron group received intravenous iron isomaltoside 1000 (Monofer ®). Doses were calculated using the

Pre-assignment period milestones

Number of subjects started	27
Number of subjects completed	27

Period 1

Period 1 title	Recruitment
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	Yes
Arm title	Intravenous iron

Arm description:

Intravenous Iron Isomaltoside 1000 (Monofer ®) (IIM)

Arm type	Experimental
Investigational medicinal product name	Iron Isomaltoside 1000 (Monofer ®)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

The study intervention treatment is intravenous Iron Isomaltoside 1000 (Monofer ®) (IIM). It will be administered in line with the product Summary of Product Characteristics Guidelines (SPC). Doses will be calculated by the Ganzoni equation of cumulative iron deficit. To replenish iron stores by a single infusion, doses up to 20mg/kg body weight of iron may be administered per week. The IIM is diluted in 250ml 0.9% sodium chloride and infused over a period of 60 minutes. The patient will be observed by clinical staff during the administration of the drug.

Arm title	Standard care

Arm description:

Standard clinical care as per the treating physician

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Intravenous iron	Standard care
Started	14	13
Completed	11	13
Not completed	3	0
Adverse event, serious fatal	1	-
Physician decision	2	-

Period 2

Period 2 title	Cycle 1 chemotherapy
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	Yes
Arm title	Intravenous iron

Arm description:

Intravenous Iron Isomaltoside 1000 (Monofer ®) (IIM)

Arm type	Experimental
Investigational medicinal product name	Iron Isomaltoside 1000 (Monofer ®)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

The study intervention treatment is intravenous Iron Isomaltoside 1000 (Monofer ®) (IIM). It will be administered in line with the product Summary of Product Characteristics Guidelines (SPC). Doses will be calculated by the Ganzoni equation of cumulative iron deficit. To replenish iron stores by a single infusion, doses up to 20mg/kg body weight of iron may be administered per week. The IIM is diluted in 250ml 0.9% sodium chloride and infused over a period of 60 minutes. The patient will be observed by clinical staff during the administration of the drug.

Arm title	Standard care

Arm description:

Standard clinical care as per the treating physician

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2	Intravenous iron	Standard care
Started	11	13
Completed	11	13

Period 3	
Period 3 title	Cycle 2 chemotherapy
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	Yes
Arm title	Intravenous iron

Arm description:

Intravenous Iron Isomaltoside 1000 (Monofer ®) (IIM)

Arm type	Experimental
Investigational medicinal product name	Iron Isomaltoside 1000 (Monofer ®)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

The study intervention treatment is intravenous Iron Isomaltoside 1000 (Monofer ®) (IIM). It will be administered in line with the product Summary of Product Characteristics Guidelines (SPC). Doses will be calculated by the Ganzoni equation of cumulative iron deficit. To replenish iron stores by a single infusion, doses up to 20mg/kg body weight of iron may be administered per week. The IIM is diluted in 250ml 0.9% sodium chloride and infused over a period of 60 minutes. The patient will be observed by clinical staff during the administration of the drug.

Arm title	Standard care

Arm description:

Standard clinical care as per the treating physician

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 3	Intravenous iron	Standard care
Started	11	13
Completed	11	13

Period 4	
Period 4 title	Cycle 3 chemotherapy
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	Yes
Arm title	Intravenous iron

Arm description:

Intravenous Iron Isomaltoside 1000 (Monofer ®) (IIM)

Arm type	Experimental
Investigational medicinal product name	Iron Isomaltoside 1000 (Monofer ®)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

The study intervention treatment is intravenous Iron Isomaltoside 1000 (Monofer ®) (IIM). It will be administered in line with the product Summary of Product Characteristics Guidelines (SPC). Doses will be calculated by the Ganzoni equation of cumulative iron deficit. To replenish iron stores by a single infusion, doses up to 20mg/kg body weight of iron may be administered per week. The IIM is diluted in 250ml 0.9% sodium chloride and infused over a period of 60 minutes. The patient will be observed by clinical staff during the administration of the drug.

Arm title	Standard care

Arm description:

Standard clinical care as per the treating physician

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 4	Intravenous iron	Standard care
Started	11	13
Completed	11	13

Baseline characteristics

Reporting groups	
Reporting group title	Intravenous iron
Reporting group description:	
Intravenous Iron Isomaltoside 1000 (Monofer ®) (IIM)	
Reporting group title	Standard care
Reporting group description:	
Standard clinical care as per the treating physician	

Reporting group values	Intravenous iron	Standard care	Total
Number of subjects	14	13	27
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			
median	68	69	
full range (min-max)	38 to 79	48 to 85	-
Gender categorical			
Units: Subjects			
Female	4	2	6
Male	10	11	21
Haemoglobin			
Units: g/dL			
arithmetic mean	9.96	11.45	
standard deviation	± 1.6	± 1.79	-
Ferritin			
Units: ng/mL			
arithmetic mean	105	161	
standard deviation	± 120	± 123	-
Transferrin saturations			
Units: Percentage			
arithmetic mean	11.1	11.9	
standard deviation	± 8.7	± 4.8	-

End points

End points reporting groups

Reporting group title	Intravenous iron
Reporting group description: Intravenous Iron Isomaltoside 1000 (Monofer ®) (IIM)	
Reporting group title	Standard care
Reporting group description: Standard clinical care as per the treating physician	
Reporting group title	Intravenous iron
Reporting group description: Intravenous Iron Isomaltoside 1000 (Monofer ®) (IIM)	
Reporting group title	Standard care
Reporting group description: Standard clinical care as per the treating physician	
Reporting group title	Intravenous iron
Reporting group description: Intravenous Iron Isomaltoside 1000 (Monofer ®) (IIM)	
Reporting group title	Standard care
Reporting group description: Standard clinical care as per the treating physician	
Reporting group title	Intravenous iron
Reporting group description: Intravenous Iron Isomaltoside 1000 (Monofer ®) (IIM)	
Reporting group title	Standard care
Reporting group description: Standard clinical care as per the treating physician	

Primary: Blood transfusions

End point title	Blood transfusions
End point description:	
End point type	Primary
End point timeframe: At each cycle of chemotherapy	

End point values	Intravenous iron	Standard care	Intravenous iron	Standard care
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	12	8	10
Units: Units	5	3	0	4

End point values	Intravenous	Standard care		

	iron			
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	10		
Units: Units	0	0		

Statistical analyses

Statistical analysis title	Chi squared
Comparison groups	Intravenous iron v Standard care v Intravenous iron v Standard care v Intravenous iron v Standard care
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.594
Method	Chi-squared

Secondary: Haemoglobin

End point title	Haemoglobin

End point description:

End point type	Secondary

End point timeframe:

Haemoglobin at each cycle of chemotherapy

End point values	Intravenous iron	Standard care	Intravenous iron	Standard care
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	12	8	10
Units: g/dL				
arithmetic mean (standard deviation)	10.15 (± 1.49)	11.08 (± 1.10)	10.79 (± 0.99)	10.83 (± 1.15)

End point values	Intravenous iron	Standard care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	10		
Units: g/dL				
arithmetic mean (standard deviation)	10.60 (± 1.19)	10.7 (± 1.49)		

Statistical analyses

No statistical analyses for this end point

Secondary: Ferritin

End point title	Ferritin

End point description:

End point type	Secondary

End point timeframe:

At each cycle of chemotherapy

End point values	Intravenous iron	Standard care	Intravenous iron	Standard care
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	12	8	10
Units: ng/mL				
arithmetic mean (standard deviation)	1015 (± 880)	200 (± 170)	581 (± 489)	264 (± 213)

End point values	Intravenous iron	Standard care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	10		
Units: ng/mL				
arithmetic mean (standard deviation)	558 (± 637)	340 (± 325)		

Statistical analyses

No statistical analyses for this end point

Secondary: Transferrin saturations

End point title	Transferrin saturations

End point description:

End point type	Secondary

End point timeframe:

At each cycle of chemotherapy

End point values	Intravenous iron	Standard care	Intravenous iron	Standard care
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	12	8	10
Units: Percentage				
arithmetic mean (standard deviation)	26.3 (± 29)	12.1 (± 4.2)	20.7 (± 8.6)	18.3 (± 8.1)

End point values	Intravenous iron	Standard care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	10		
Units: Percentage				
arithmetic mean (standard deviation)	14 (± 7)	19 (± 9)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
At each cycle of chemotherapy	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	1

Reporting groups	
Reporting group title	Intravenous iron
Reporting group description:	
Intravenous Iron Isomaltoside 1000 (Monofer ®) (IIM)	
Reporting group title	Standard care
Reporting group description:	
Standard clinical care as per the treating physician	

Serious adverse events	Intravenous iron	Standard care	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 11 (81.82%)	7 / 13 (53.85%)	
number of deaths (all causes)	5	2	
number of deaths resulting from adverse events	2	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastatic Gastric cancer			
subjects affected / exposed	3 / 11 (27.27%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Vascular disorders			
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Insertion of oesophageal stent			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			

Neutropenia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 11 (9.09%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	2 / 11 (18.18%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Shortness of breath			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Cellulitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (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			
Septicaemia			
subjects affected / exposed	0 / 11 (0.00%)	2 / 13 (15.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 11 (0.00%)	1 / 13 (7.69%)	
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	Intravenous iron	Standard care	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
Gastrointestinal disorders			
Diarrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 13 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported