Clinical trial results:
INFLAMMATORY RESPONSE IN MAJOR INJURY & RECOMBINANT HUMAN ERYTHROPOIETIN (IRMINE) - A PILOT STUDY

Summary

EudraCT number	2015-002255-10
Trial protocol	GB
Global end of trial date	19 April 2018

Results information

Result version number	v1 (current)
This version publication date	03 June 2021
First version publication date	03 June 2021
Summary attachment (see zip file)	IRMINE Report (IRMINE FINAL REPORT 02.pdf)

Trial information

Trial identification

Sponsor protocol code	IRMINE pilot

Additional study identifiers

ISRCTN number	ISRCTN40935649
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Abertawe Bro Morgannwg University Health Board
Sponsor organisation address	ILS2, First Floor, Swansea, United Kingdom, SA2 8PP
Public contact	Professor Ian Pallister, Abertawe Bro Morgannwg University Health Board, 01792 703166, ian.pallister@hotmail.com
Scientific contact	Professor Ian Pallister, Abertawe Bro Morgannwg University Health Board, 01792 703166, ian.pallister@hotmail.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	17 May 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 April 2018
Global end of trial reached?	Yes
Global end of trial date	19 April 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Objective: The IRMINE pilot will test the trial design and logistics in preparation for a bid for a multi-centre randomised controlled trial.

The pilot will evaluate the impact of recombinant human erythropoietin (rhEPO) on recovery in adult severe blunt trauma patients who need critical care/ITU support. This will be measured in terms of reducing organ failure as a marker of mortality, reflecting the body's abnormal inflammatory/immune response to injury, which can cause damage to the patient's own tissues and organs.

Principle Research Question: Does the use of recombinant human erythropoietin (rhEPO) reduce organ failure after severe trauma in adults?

A reduction in the body's abnormal immune response may help explain the beneficial protection of rhEPO if a decrease in organ failure is seen.

Protection of trial subjects:

Stopping rules and criteria for termination as detailed in the DMC Charted and adherence to the CTA Regulation 30

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 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	United Kingdom: 4
Worldwide total number of subjects	4
EEA total number of subjects	0

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)	4
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The on-call ITU doctor identified by the delegation log will identify suitable patients that fit the inclusion / exclusion criteria for the study as they come into ITU. The Research Nurse or other authorised person will be notified as soon as possible and will begin formal screening.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	rhEPO
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

40,000 units

Arm title	rhEPO

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	rhEPO
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

40,000 unitd

Number of subjects in period 1	Placebo	rhEPO
Started	2	2
Completed	2	2

Baseline characteristics

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	rhEPO
Reporting group description: -	

Primary: Primary end point - DMOFS

End point title	Primary end point - DMOFS
End point description:	
Daily DMOFS (whilst the participant is in ITU) will be compared between those randomised to receive rhEPO versus placebo control.	
End point type	Primary
End point timeframe:	
Twice daily while on ITU or 30 days maximum	

End point values	Placebo	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	2		
Units: score				
number (not applicable)	2	2		

Statistical analyses

Statistical analysis title	Descriptive
Comparison groups	Placebo v rhEPO
Number of subjects included in analysis	4
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.05
Method	Mann-Whitney

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs reported within 24 hours

Adverse event reporting additional description:

he initial approach of reporting all adverse events was modified in line with published recommendations as following major trauma there are multiple well recognised complications which form part of the expected natural history of the disease (Cook et al., 2008). Appropriate preferred terms were identified to assure consistency in reporting.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13

Reporting groups

Reporting group title	rhEPO
Reporting group description: -	
Reporting group title	Placebo

Reporting group description: -

Serious adverse events	rhEPO	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)	1 / 2 (50.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0		
Respiratory, thoracic and mediastinal disorders			
Multiple organ failure			
subjects affected / exposed	0 / 2 (0.00%)	1 / 2 (50.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	rhEPO	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	0 / 2 (0.00%)	
Cardiac disorders			
Increased heart rate	Additional description: Both patients increased heart rate while on ITU which resolved without specific treatment		
subjects affected / exposed	2 / 2 (100.00%)	0 / 2 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 December 2017	ABMU Health Board as Sponsor have taken the decision to implement a temporary halt Swansea on 5th December 2017 due Christmas staffing resource of the Research nurses required to undertake daily bloods and CRF completion for 7 days. The Birmingham site will be given slightly longer to recruit as they recently opened to screening on Dec 5th 2017. However, as at 31st December, as Sponsor we will be requesting that Birmingham also cease screening and recruiting pending the decision of the EME funding application due to the current Trial Manager moving onto another study in early January. If funding is awarded, a new Trial Manager will be appointed & the study will be re-opened including the addition of new sites. Due to the transition to a larger scale multi-centre study, Sponsorship of the study will be transferred from ABMU Health Board to Swansea University. Advice has been sought from MHRA (Mrs Hedwig Ganguly – email dated 27.10.17 12.02pm) who advised we may halt for a funding decision and also submit a substantial amendment which covers both the re-opening of a study following the temporary halt and the change of sponsorship. • The proposed management of patients receiving treatment at time of the halt (free text). • The consequences of the temporary halt for the evaluation of the results and for overall risk benefit assessment of the investigational medicinal product (free text). Not applicable, there is no ongoing treatment, the protocol requires one dose of EPO/Placebo within 24 hours of major trauma injury only. Daily bloods taken are to measure mechanistic effect of the drug with no ongoing impact for the treatment management decisions for the patient.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported