



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 Charters 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 | <p>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.</p> <ul style="list-style-type: none">• 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). <p>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.</p> |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported