# Clinical trial results:
# Diamorphine or alfentanil for subcutaneous use in hospice in-patients

## Summary

| | |
|---|---|
| EudraCT number | 2006-007053-51 |
| Trial protocol | GB |
| Global end of trial date | 17 November 2014 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 22 April 2019 |
| First version publication date | 22 April 2019 |
| Summary attachment (see zip file) | Final Publication (Paul Perkins – Diamorphine v alfentanil.PDF) |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | 003/APR06 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01049672 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Gloucestershire Hospitals NHS Foundation Trust |
| Sponsor organisation address | Leadon House, Gloucestershire Royal Hospital, Great Western Road, Gloucester, United Kingdom, GL1 3NN |
| Public contact | Sue Ryder Leckhampton Court Hospice, Sue Ryder Leckhampton Court Hospice, +44 1242230199, paul.perkins@glos.nhs.uk |
| Scientific contact | Sue Ryder Leckhampton Court Hospice, Sue Ryder Leckhampton Court Hospice, +44 1242230199, paul.perkins@glos.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 | 19 August 2016 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 17 November 2014 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

A comparison of alfentanil and diamorphine to be carried out in two parts:

1. An open-label pilot comparison between alfentanil and diamorphine for palliative care patients who require subcutaeous opiods

2. A single (patient)-blinded, randomised, comparison between alfentanil and diamorphine for palliative care patients who require subcutaeous opiods

Protection of trial subjects:

Patients were allowed breakthrough doses of analgesia in addition to background.

Background therapy:

Symptom relieving drugs in addition to the 2 experimental arms

Evidence for comparator:

It is common practice to use alfentanil for patients with renal impairment. This is not commonly done for patients without.

| | |
|---|---|
| Actual start date of recruitment | 23 June 2010 |
| 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: 18 |
| Worldwide total number of subjects | 18 |
| EEA total number of subjects | 18 |

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) | 12 |
| From 65 to 84 years | 5 |
| 85 years and over | 1 |

## Subject disposition

### Recruitment

Recruitment details:

`Recruitment - December 2010 and June 2014
Hospice in-patients in the UK

### Pre-assignment

Screening details:

562 hospice in-patients with an estimated glomerular filtration rate of 40ml/min / 1.73m2 or greater on, or about to be started on a subcutaneous syringe driver were screened. 544 did not meet the inclusion criteria (some had more than one reason)

### Pre-assignment period milestones

| | |
|---|---|
| Number of subjects started | 18 |
| Number of subjects completed | 18 |

### Period 1

| | |
|---|---|
| Period 1 title | Overall trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Diamorphine |

Arm description:

Patients randomised to diamorphine continued on this treatment.

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Diamorphine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Given by subcutaneous syringe driver

| | |
|---|---|
| **Arm title** | Alfentanil |

Arm description:

Patients randomised to alfentanil were switched to this using an approximate alfentanil:diamorphine ratio of 1:10.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Alfentanil |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection/infusion |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Via subcutaneous syringe driver

| **Number of subjects in period 1** | Diamorphine | Alfentanil |
|---|---|---|
| Started | 9 | 9 |
| Completed | 9 | 9 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Diamorphine |
| Reporting group description: | |
| Patients randomised to diamorphine continued on this treatment. | |
| Reporting group title | Alfentanil |
| Reporting group description: | |
| Patients randomised to alfentanil were switched to this using an approximate alfentanil:diamorphine ratio of 1:10. | |

| Reporting group values | Diamorphine | Alfentanil | Total |
|---|---|---|---|
| Number of subjects | 9 | 9 | 18 |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 5 | 7 | 12 |
| From 65-84 years | 3 | 2 | 5 |
| 85 years and over | 1 | 0 | 1 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 7 | 7 | 14 |
| Male | 2 | 2 | 4 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Diamorphine |
| Reporting group description: | |
| Patients randomised to diamorphine continued on this treatment. | |
| Reporting group title | Alfentanil |
| Reporting group description: | |
| Patients randomised to alfentanil were switched to this using an approximate alfentanil:diamorphine ratio of 1:10. | |
| Subject analysis set title | Feasibility |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| 1) Number of patients screened<br>2) Percentage of patients eligible<br>3) Percentage of patients recruited<br>4) Percentage of patients reaching days 3 and 7<br>5) Data completion | |

### Primary: Feasibility

| | |
|---|---|
| End point title | Feasibility |
| End point description: | |
| No of patients who survived to the end of the study | |
| End point type | Primary |
| End point timeframe: | |
| Day 3 | |

| End point values | Diamorphine | Alfentanil | Feasibility | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 9 | 9 | 9 | |
| Units: Days | 9 | 9 | 9 | |

### Statistical analyses

| | |
|---|---|
| **Statistical analysis title** | Descriptive and exploratory |
| Statistical analysis description: | |
| The analysis performed was largely descriptive and exploratory: changes were calculated and compared between the two groups, using Mann–Whitney U tests. IBM SPSS Statistics version 22.0 was used for these tests. | |
| Comparison groups | Diamorphine v Alfentanil |

| | |
|---|---|
| Number of subjects included in analysis | 18 |
| Analysis specification | Pre-specified |
| Analysis type | other[1] |
| P-value | < 0.5 [2] |
| Method | descriptive and exploratory |
| Parameter estimate | N/A |

Notes:

[1] - Feasibility

[2] - Not appropriate to calculate p values for a feasibility study

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| From patient recruitment to death | |
| Adverse event reporting additional description: | |
| Prospectively | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 20 |

| Reporting groups | |
|---|---|
| Reporting group title | Diamorphine |
| Reporting group description: - | |
| Reporting group title | Alfentanil |
| Reporting group description: - | |

| Serious adverse events | Diamorphine | Alfentanil | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | 0 | |

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

| Non-serious adverse events | Diamorphine | Alfentanil | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 5 / 9 (55.56%) | 9 / 9 (100.00%) | |
| Nervous system disorders | | | |
| Pain | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 6 / 9 (66.67%) | |
| occurrences (all) | 1 | 6 | |
| Agitation | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 9 (11.11%) | |
| occurrences (all) | 0 | 1 | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 9 (0.00%) | |
| occurrences (all) | 1 | 0 | |

| | | | |
|---|---|---|---|
| Nightmare | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 9 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 3 / 9 (33.33%) | |
| occurrences (all) | 1 | 3 | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 9 (22.22%) | |
| occurrences (all) | 0 | 2 | |
| Constipation | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 9 (11.11%) | |
| occurrences (all) | 1 | 1 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 28 September 2009 | This study was originally reviewed to be undertaken by the Chief Investigator, Dr Paul Perkins, at St John's Sue Ryder Hospice in Bedfordshire. Following the original Favourable Ethical Opinion, but prior to any study activities, Dr Perkins took a post at Leckhampton Court Sue Ryder Hospice, employed by Gloucestershire Hospitals NHS Foundation Trust (GHNHSFT).<br><br>As this is a single site study the GHNHSFT agreed to take on sponsorship of the study and this change has been reviewed and approved by the MHRA, who have issued the study with a new CTA number - 19584/0203/001.<br><br>The purpose of this amendment is to inform the REC that the sponsor has changed and to provide details to the REC and the MHRA of the corresponding changes to the study documents. The Protocol, PIS, Consent and GP letter have been changed to ensure the correct contact details and headed paper are used. There have also been some formatting changes to these documens. However, there are no changes to the way the study would be conducted as outlined in the original application.<br><br>Additional information around monitoring the study has also been added to the protocol.<br><br>The documents for the study are enclosed along with the approval letters from the MHRA.<br><br>Standard/validated data collection tools have not been included in this application.<br><br>Although not 'tracked' the changes in the documentation have been underlined. Otherwise the only differences to the original documentation are the contact details and headed paper.<br><br>This amendment was previously submitted to the REC in October 2008, but was submitted on the wrong paperwork. The amendment is only just being re-submitted due to delays clarifying arrangements with Sue Ryder Care in Leckhampton. During this time, no patients have been approached or recruited into the study. |

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.

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|---|
| Small study, single site |

Notes: