



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
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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 subcutaneous opioids
 2. A single (patient)-blinded, randomised, comparison between alfentanil and diamorphine for palliative care patients who require subcutaneous opioids
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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
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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
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Reporting group description:

Patients randomised to diamorphine continued on this treatment.

Reporting group title	Alfentanil
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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			
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			
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 2) Percentage of patients eligible 3) Percentage of patients recruited 4) Percentage of patients reaching days 3 and 7 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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20
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Reporting groups

Reporting group title	Diamorphine
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Reporting group description: -

Reporting group title	Alfentanil
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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 occurrences (all)	1 / 9 (11.11%) 1	0 / 9 (0.00%) 0	
Gastrointestinal disorders			
Nausea subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	3 / 9 (33.33%) 3	
Diarrhoea subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	2 / 9 (22.22%) 2	
Constipation subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	1 / 9 (11.11%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 September 2009	<p>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).</p> <p>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.</p> <p>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 documents. However, there are no changes to the way the study would be conducted as outlined in the original application.</p> <p>Additional information around monitoring the study has also been added to the protocol.</p> <p>The documents for the study are enclosed along with the approval letters from the MHRA.</p> <p>Standard/validated data collection tools have not been included in this application.</p> <p>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.</p> <p>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.</p>

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.

Small study, single site

Notes: