Clinical trial results:
A Prospective, Multi-centre, Single-Arm, Open Label Study of the Long term Use of a LHRH Agonist (Decapeptyl® SR, 11.25 mg) in Combination with Livial® Add-back Therapy in the Management of Chronic Cyclical Pelvic Pain in Pre-Menopausal Women

Summary

EudraCT number	2007-001159-20
Trial protocol	GB
Global end of trial date	09 May 2016

Results information

Result version number	v1 (current)
This version publication date	22 September 2018
First version publication date	22 September 2018

Trial information

Trial identification

Sponsor protocol code	STH14404

Additional study identifiers

ISRCTN number	ISRCTN19040577
ClinicalTrials.gov id (NCT number)	NCT00735852
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sheffield Teaching Hospitals NHS Foundation Trust
Sponsor organisation address	8 Beech Hill Road, Sheffield, United Kingdom, S10 2SB
Public contact	Mr Mostafa Metwally, Sheffield Teaching Hospitals NHS Foundation Trust, 0114 2268092, mostafa.metwally@sth.nhs.uk
Scientific contact	Mr Mostafa Metwally, Sheffield Teaching Hospitals NHS Foundation Trust, 0114 2268092, mostafa.metwally@sth.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	09 May 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 May 2016
Global end of trial reached?	Yes
Global end of trial date	09 May 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the impact of treatment with Decapeptyl SR plus Tibolone on CCPP throughout the 24 month treatment period. Changes will be determined by comparison to Baseline. Pain will be assessed using the Chronic Pain Grade (CPG) Questionnaire

Protection of trial subjects:

No specific measures were in place as these were not deemed necessary.

Background therapy:

Livial was used an add back therapy to help prevent bone loss and to help to minimise the potential side effects of the decapeptyl (menopausal symptoms).

Evidence for comparator:

No comparators were used.

Actual start date of recruitment	18 December 2008
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: 31
Worldwide total number of subjects	31
EEA total number of subjects	31

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)	31
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment period December 2008- December 2013

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	31
Number of subjects completed	27

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Consent withdrawn by subject: 1
Reason: Number of subjects	Physician decision: 1
Reason: Number of subjects	screen fail: 1
Reason: Number of subjects	lost to follow up: 1

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	treatment

Arm description:

commenced unblinded open label treatment

Arm type	Experimental
Investigational medicinal product name	Decapeptyl
Investigational medicinal product code	L02AE04
Other name	Triptorelin
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Decapeptyl 11.25 mg given IM 3 monthly for 2 years.
Prepared by mixing powder with solution immediately prior to use

Number of subjects in period 1[1]	treatment
Started	27
Completed	27

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 4 patients left the study after being consented. One was a screen fail, one withdrew consent, one was physicians decision to withdraw the patient and one was lost to follow up.

Period 2

Period 2 title	24 months
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	treatment

Arm description:

Unblinded open label treatment

Arm type	Experimental
Investigational medicinal product name	Decapeptyl
Investigational medicinal product code	L02AE04
Other name	Triptorelin
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Decapeptyl 11.25 mg given IM 3 monthly for 2 years.
Prepared by mixing powder with solution immediately prior to use

Number of subjects in period 2	treatment
Started	27
Completed	13
Not completed	14
Consent withdrawn by subject	4
Adverse event, non-fatal	4
Lack of efficacy	6

Period 3

Period 3 title	30 Months
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Follow up
Arm description: Follow up	
Arm type	Follow up
No investigational medicinal product assigned in this arm	

Number of subjects in period 3	Follow up
Started	13
Completed	13

Baseline characteristics

Reporting groups	
Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	27	27	
Age categorical			
women aged 18- 45 years inclusive			
Units: Subjects			
Adult women 18-45	27	27	
Gender categorical Units: Subjects			
Female	27	27	

End points

End points reporting groups

Reporting group title	treatment
Reporting group description: commenced unblinded open label treatment	
Reporting group title	treatment
Reporting group description: Unblinded open label treatment	
Reporting group title	Follow up
Reporting group description: Follow up	

Primary: Pain score at 24 months of treatment compared to baseline

End point title	Pain score at 24 months of treatment compared to baseline[1]
End point description: Pain scores at 24 months were compared to pain scores at baseline using the CPG questionniare	
End point type	Primary
End point timeframe: 24 months	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No further statistical analyses are available from the study team

End point values	treatment	treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	13		
Units: Pain score out of 100				
median (full range (min-max))	66.7 (30 to 93)	13.33 (0 to 36.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pain score at month 30 compared to month 24

End point title	Pain score at month 30 compared to month 24
End point description: Pain scores at 30 months were compared to scores at 24 months (i.e. 6 months following end of treatment)	
End point type	Secondary
End point timeframe: 30 months	

End point values	treatment	Follow up		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: pain score				
median (full range (min-max))	13.33 (0 to 36.3)	56.66 (6 to 80)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

until 28 days after last administration of study drug

Adverse event reporting additional description:

patients issued with study diary to record adverse events. In addition patients were asked at each study visit to report any adverse events.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Decapeptyl® SR, 11.25 mg

Reporting group description:

All study participants received the same dose for the same time period.

Serious adverse events	Decapeptyl® SR, 11.25 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 27 (22.22%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Head injury	Additional description: accident - banged head. due to presence of intracranial shunt was admitted overnight for observation		
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Ventriculo-peritoneal shunt	Additional description: Patient experienced multiple SAEs due to inpatient hospitalisation to insert and revise placement of intracranial shunt. This was due to pre existing raised intracranial pressure.		
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Haemorrhage intracranial			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	4 / 27 (14.81%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pneumonia			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urinary tract infection			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Post procedural complication	Additional description: Umbilical wound infection post surgery for placement of intracranial stent.		
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Decapeptyl® SR, 11.25 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 27 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Pyogenic granuloma subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1		
Vascular disorders Hot flush subjects affected / exposed occurrences (all)	9 / 27 (33.33%) 10		
Surgical and medical procedures Tooth extraction subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1		
General disorders and administration site conditions Injection site pain subjects affected / exposed occurrences (all) Lethargy subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) general malaise subjects affected / exposed occurrences (all) swelling of hands subjects affected / exposed occurrences (all) swelling of feet subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 2 4 / 27 (14.81%) 5 1 / 27 (3.70%) 1 3 / 27 (11.11%) 3 1 / 27 (3.70%) 1 1 / 27 (3.70%) 1		
Immune system disorders hayfever subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 3		
Reproductive system and breast disorders			

vaginal bleeding subjects affected / exposed occurrences (all)	13 / 27 (48.15%) 23		
Dyspareunia subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 2		
endometrioma subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1		
Ovarian cyst subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 2		
Pelvic pain subjects affected / exposed occurrences (all)	11 / 27 (40.74%) 24		
Breast tenderness subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 2		
Dysmenorrhoea subjects affected / exposed occurrences (all)	4 / 27 (14.81%) 5		
Vaginal discharge subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1		
Respiratory, thoracic and mediastinal disorders			
sore throat subjects affected / exposed occurrences (all)	3 / 27 (11.11%) 3		
dry cough subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1		
sinus pain subjects affected / exposed occurrences (all)	5 / 27 (18.52%) 7		
nose bleed			

subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	6		
Insomnia			
subjects affected / exposed	6 / 27 (22.22%)		
occurrences (all)	8		
Mood swings			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Loss of libido			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
Depression			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
low mood			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	3		
Investigations			
bone density decreased			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
lumbar puncture			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	2		
intracranial pressure monitoring			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
blood pressure raised			
subjects affected / exposed	4 / 27 (14.81%)		
occurrences (all)	4		
weight gain			

subjects affected / exposed	3 / 27 (11.11%)		
occurrences (all)	3		
Injury, poisoning and procedural complications			
wrist sprain			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	14 / 27 (51.85%)		
occurrences (all)	35		
Carpal tunnel syndrome			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Migraine			
subjects affected / exposed	3 / 27 (11.11%)		
occurrences (all)	5		
trapped nerve			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
faint			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
pins and needles			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Ear and labyrinth disorders			
ear ache			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		

perforated ear drum			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Eye disorders			
dry eyes			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	5 / 27 (18.52%)		
occurrences (all)	5		
Nausea			
subjects affected / exposed	4 / 27 (14.81%)		
occurrences (all)	4		
upset stomach			
subjects affected / exposed	3 / 27 (11.11%)		
occurrences (all)	8		
benign gastric polyp			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
abdominal bloating			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	5		
Constipation			
subjects affected / exposed	3 / 27 (11.11%)		
occurrences (all)	3		
heartburn			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
indigestion			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
food poisoning			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
upper abdominal pain			

subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
rectal bleeding			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
itchy skin			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	3		
Acne			
subjects affected / exposed	4 / 27 (14.81%)		
occurrences (all)	9		
Night sweats			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
skin rash			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
Swelling face			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Renal and urinary disorders			
frequency of micturition			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
kidney pain			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
aching joints			
subjects affected / exposed	7 / 27 (25.93%)		
occurrences (all)	8		
axilliary lump			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
back pain			

subjects affected / exposed	5 / 27 (18.52%)		
occurrences (all)	9		
leg pain			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
leg cramps			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Osteoarthritis			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Infections and infestations			
common cold			
subjects affected / exposed	9 / 27 (33.33%)		
occurrences (all)	19		
flu symptoms			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	3		
viral infection			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	2		
infection urinary tract			
subjects affected / exposed	3 / 27 (11.11%)		
occurrences (all)	5		
Skin infection			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
gum abscess			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
chest infection			
subjects affected / exposed	5 / 27 (18.52%)		
occurrences (all)	5		
wound infection			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		

Bronchitis			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
vaginal infection			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
oral thrush			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
thrush vaginal			
subjects affected / exposed	3 / 27 (11.11%)		
occurrences (all)	3		
Ear infection			
subjects affected / exposed	3 / 27 (11.11%)		
occurrences (all)	3		
Influenza			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
cold sores			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	2		
throat infection			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	2		
post operataive wound infection			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
tonsilitis			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
hook worm			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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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.

The current study has several limitations . The study had a significant drop out rate. This was not unexpected over a study of such long duration and may be a reflection of the fluctuation in impact of CCPP seen in this young group of patients.

Notes: