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A prospective single-centre single-arm open-label study of the long-term use of a LHRH agonist (Decapeptyl SR 11.25mg) in combination with livial add-back therapy in the management of chronic cyclical pelvic pain in pre-menopausal women

Submission date
29/04/2010

Recruitment status
No longer recruiting

Registration date
29/04/2010

Overall study status
Completed

Last Edited
20/05/2019

Condition category
Signs and Symptoms

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
Decapeptyl is a synthetic (man-made) hormone that stops the ovaries producing the hormone oestrogen. It can be used to treat disorders that are dependent on oestrogen being present, such as endometriosis and chronic cyclical pelvic pain (CCPP). Endometriosis is the presence of endometrial tissue outside the uterus, most commonly in the pelvis and abdomen. This tissue is affected by cyclical changes in hormones like the usual endometrial tissue. This tissue grows further when supplied with oestrogen, forming lesions which cause pain. It is thought that if the surges in hormones are suppressed, the lesions won't be triggered and pain won't occur. Decapeptyl is currently licensed for short-term use (up to 6 months) for CCPP, but not for long-term use because oestrogen depletion can cause unwanted side effects such as hot flushes, vaginal dryness, headache and brittle bones. One proposed strategy to limit the unwanted side effects is to 'add back' oestrogen at a constant low dose – not enough to promote any flares in CCPP, but enough to prevent or significantly reduce the side effects. The aim of this study is to test the safety and effectiveness of an injection of Decapeptyl every 3 months when given with a daily hormone replacement therapy (HRT) tablet (Livial) for 2 years.

Who can participate?
Women aged between 18 and 45 with a clinical diagnosis of CCPP of at least 6 months duration (with or without evidence of endometriosis).

What does the study involve?
There will be 11 visits to hospital during the course of the study. At the first visit your medical history and medication use will be recorded and you will be asked to complete two pain questionnaires and three quality of life questionnaires. A blood sample will be taken and a bone

scan will be performed. At the next visit a physical examination and urine pregnancy test will be performed, your blood pressure and pulse will be measured, you will complete pain and quality of life questionnaires, and symptoms of oestrogen deficiency will be noted. You will be given an injection of Decapeptyl and will be given enough Livial tablets to last until the next visit. You will then return for repeat Decapeptyl injections every 3 months until Month 21, at which time the last Decapeptyl injection will be administered. At these visits you will also be given further supplies of Livial. There will be follow-up visits 6, 12, 18 and 24 months after the first injection. A final follow-up assessment will be conducted 6 months after stopping treatment (at Month 30). At each follow-up visit pain and general health questionnaires will be completed and symptoms of oestrogen deficiency will be noted. Physical examinations, blood pressure and pulse measurements, bone scans and blood samples will be repeated at months 12, 24 and 30. Other medications and adverse events are recorded at each visit.

What are the possible benefits and risks of participating?
Decapeptyl has a number of reported side effects. At the beginning of treatment the symptoms of endometriosis (pelvic pain, dysmenorrhoea) may get worse. These symptoms should disappear in one or two weeks. Genital bleeding may occur in the month following the first injection. Adverse reactions could include hot flushes, sweating, sleep disturbances, headache, mood changes, vaginal dryness, painful sexual intercourse, and decreased libido. Transient pain, redness or local inflammation at the injection site may occur. The following adverse reactions have been observed during clinical trials with other formulations of the drug: breast pain, muscle cramps, joint pain, weight gain, nausea, abdominal pain or discomfort, weakness, increased blood pressure, episodes of blurred or abnormal vision, rash, swelling, and hair loss. A small loss in bone density occurs during 6 months of Decapeptyl treatment, but clinical data suggests that this loss is reversible. Livial also has a number of reported side effects. Occasionally, vaginal bleeding or spotting may occur, mainly during the first months of treatment. Other adverse events that have been observed occasionally include: dizziness, rash, itching, headache, migraine, visual disturbances (including blurred vision), stomach upset, depression, swelling, joint pain, muscle pain, and changes in liver function.

Where is the study run from?
Sheffield Teaching Hospitals NHS Trust (UK).

When is the study starting and how long is it expected to run for?
From December 2008 to June 2016.

Who is funding the study?
Ipsen Pharma (UK).

Who is the main contact?
Sheila Duffy

Contact information

Type(s)
Scientific

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Clinical Trials Information System (CTIS)
2007-001159-20

Protocol serial number
6899

Study information

Scientific Title
A prospective single-centre single-arm open-label study of the long-term use of a LHRH agonist (Decapeptyl SR 11.25mg) in combination with livial add-back therapy in the management of chronic cyclical pelvic pain in pre-menopausal women

Acronym
N/A

Study objectives
The aim of the study is to use a long acting drug called Decapeptyl SR with added hormone replacement therapy (HRT) to treat chronic cyclical pelvic pain (CCPP). Decapeptyl is currently licensed for short-term use (up to 6 months) for CCPP. The reason it is not licensed for long-term use is that there are side effects such as hot flushes, vaginal dryness, headache and brittle bones, which are due to a reduction in oestrogen levels. By adding a hormone replacement treatment, these side effects can be significantly reduced. The purpose of this study therefore is to look at the safety and effectiveness of an injection of Decapeptyl every 3 months when given with a daily HRT tablet (Livial) for 2 years.

More details can be found here: http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=6899

On 28/05/2015 the overall trial end date was changed from 01/09/2012 to 30/06/2016.

Ethics approval required
Old ethics approval format

Ethics approval(s)
MREC approved on the 05/08/2008, ref: 08/H1308/150

Study design
Open-label interventional treatment trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: Reproductive Health and Childbirth; Subtopic: Reproductive Health and Childbirth (all Subtopics); Disease: Reproductive Health & Childbirth

Interventions
This is a single-centre, single-arm, open-label study to assess the efficacy and safety of the extended use (24 months treatment) of Decapeptyl SR (11.25 mg every 3 months) when administered in combination with Livial tablets (2.5 mg daily) for the treatment of women with CCPP. Follow up length: 30 months.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Decapeptyl SR, Livial

Primary outcome(s)
To assess the impact of treatment with Decapeptyl SR plus Tibolone on CCPP throughout the 24 month treatment period

Key secondary outcome(s))
1. To assess the change in CCPP as assessed using the Short Form McGill Pain Questionnaire (SF-MPQ)
2. To assess the change in concomitant analgesic use at all assessment timepoints
3. To assess the change in Health-related Quality of Life (HR-QOL) at all assessment timepoints
4. To assess the change in overall health status at all assessment timepoints in comparison to baseline
5. To assess the change in the Disability Score and the overall Chronic Pain Grade (0 - IV)
6. To assess the change in the scores for each individual domain of the CPG Questionnaire

Completion date
30/06/2016

Eligibility

Key inclusion criteria
Patients must satisfy all of the following entry criteria before they will be allowed to participate in the study:
1. The patient must have given written (personally signed and dated) informed consent given before completing any study-related procedure, which means any assessment or evaluation that would not have formed part of their normal medical care
2. The patient must be aged between 18 and 45 years inclusive, female only
3. The patient must have a clinical diagnosis of CCPP of at least 6 months duration (with or without evidence of endometriosis)
4. The patient must have had a laparoscopy within three years prior to the Screening visit
5. The patient must have had regular menstrual cycles (between 24 and 42 days) for the 3 months prior to screening
6. Treatment with a LHRHa is indicated for the patient
7. The patient must be able to understand, and willing to comply with the requirements of the protocol

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Female

Total final enrolment
31

Key exclusion criteria
Patients who satisfy any of the following criteria must not be included in the study:
1. The patient has been treated with any LHRHa within 6 months prior to screening
2. The patient has been treated with Danazol, gestrinone or cyproterone acetate within the 6 months prior to screening or anticipated requirement during the study
3. The patient has used cyclical progestogens or combined oral contraceptives within one full menstrual cycle (including a spontaneous bleed) prior to screening, or anticipated requirement for these treatments during the study period
4. The patient is treated with any other medication for CCPP (other than simple analgesics) within three months prior to screening
5. The patient has continuous or acyclic pelvic pain

6. The patient has known metabolic bone disease
7. The patient has an abnormal full blood count or liver or renal function at screening or within the 6 months prior to screening
8. The patient has unexplained vaginal bleeding
9. The patient has a bone mineral density age adjusted T-Score of -2 or below at the screening visit
10. The patient has any other medical condition or abnormality that in the opinion of the investigator would impact upon the safety or efficacy of the study treatment or any study assessments
11. The patient is receiving concomitant treatment with coumarin or indanedione derivatives
12. The patient has a known contraindication, allergy or hypersensitivity to any of the test compounds or materials (including both Decapeptyl SR and Livial)
13. The patient is pregnant or lactating. Female patients of child-bearing potential (i.e. who are not surgically sterile) must have a negative urine pregnancy test at the baseline visit.
14. The patient is planning a pregnancy within 31 months of screening
15. The patient is of child-bearing potential and is unwilling to use adequate barrier contraception for the duration of the study
16. The patient has received any investigational drug therapy within 30 days prior to the study, or is scheduled to receive such a drug during the study period
17. The patient has previously entered this study

Date of first enrolment
11/12/2008

Date of final enrolment
31/12/2013

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Sheffield Teaching Hospitals NHS Trust
Sheffield
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Sponsor information

Organisation
Sheffield Teaching Hospitals NHS Trust (UK)

ROR

https://ror.org/018hjpz25

Funder(s)

Funder type
Industry

Funder Name
Ipsen Pharma (UK)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results				No	No