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A study to evaluate the efficacy and safety of AMY109 in women with endometriosis

Submission date
11/10/2022

Recruitment status
No longer recruiting

Registration date
15/05/2023

Overall study status
Ongoing

Last Edited
04/10/2024

Condition category
Urological and Genital Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Endometriosis is a chronic gynaecological disorder associated with pelvic pain and infertility. The disease is not only dependent on the female hormone estrogen-dependent but is also an inflammatory gynaecological disorder Women can be treated with pain relief medication and/or hormone treatment. Sometimes the endometriosis tissue is removed by surgery to help relieve symptom. If the inflammation can be treated it is thought that pain may be reduced and infertility symptoms could improve.

This study looks at whether an experimental drug called AMY109 can reduce the inflammation and pain caused by endometriosis when it is given, either on its own, or in combination with desogestrel (a progesterone only contraceptive pill) compared to desogestrel alone. Treatment will be assigned randomly to one of three groups with a 37.5% chance of being placed in groups 1 and 2 and a 25% chance of being put into group 3.
• Group 1: AMY109 & desogestrel-placebo
• Group 2: AMY109 and desogestrel
• Group 3: AMY109-placebo & desogestrel

Placebo is a dummy drug which looks the same as the active form but contains no active ingredient.

Who can participate?
Women who are generally in good health and who have endometriosis diagnosed via a laparoscopy but who haven't yet had surgery to remove endometrial tissue within 9 months. Approximately 80 patients will be enrolled from approximately 8 centres in the United Kingdom (UK).

What does the study involve?
Eligible women from participating or referral centres will be invited to join the study. Firstly, there will be a washout period of between 4 and 12 weeks where certain medications will be stopped so that they are removed from the body. This will be followed by a screening period which could last up to 45 days to check that the participant is eligible for the study. Eligible participants will then receive AMY109 or a dummy drug for up to 52 weeks. They will also be

asked to take either desogestrel or a dummy pill every day. Four weeks after the treatment has finished, the endometriosis will be removed surgically via laparoscopy where small incisions are made near the belly button or bikini line. Follow-up visits will be on Weeks 60, 77, 89 and 105. The total duration of the study will be a maximum of 29 months, including approximately 22 hospital visits.

The severity of the endometriosis will be measured during the course of the study by using MRI scans (up to three times) and up to three trans vaginal ultrasounds (ultrasound using a probe inserted into the vagina). It will also be measured by examination of images of the endometrial tissue before and after treatment and by examination of removed endometrial tissue and fluid at the time of surgery.

Eligibility assessments at the start of the study and ongoing safety assessments will include up to three chest X-rays and up to seven electrocardiograms (ECGs). Vital signs (blood pressure, body temperature and heart rate) will be measured at every visit and blood samples will be taken to assess both the health of the participant and also to look at how the drug is processed by the body, how the body responds to the drug and whether the body is making any antibodies to the drug. The total amount of blood collected during this study may be approximately 400 mL (about 3-8 teaspoons at each visit).

Participants will have to use the pain medication provided as part of the study and also agree to use two forms of barrier contraception from consent (for example, a combination of male condom with either cap, diaphragm or sponge with spermicide).

Participants will also be asked to complete a daily diary either using an App on their own phone or a handheld device. There will be questions related to how they are feeling, quality of life, any vaginal bleeding, the level of pain experienced, and the amount of pain medication taken each day.

What are the possible benefits and risks of participating?
AMY109 is an experimental drug so there are no known health benefits at this time. Because there is limited testing in humans, there may be side effects that are not known at this time.

The most common events observed in healthy volunteers receiving AMY109 were throat pain (oropharyngeal pain), sore throat (pharyngitis), and infection of the upper respiratory tract i.e. nose, nasal cavity or throat.

The most common side effects observed in patients with endometriosis receiving AMY109 were vomiting, anaemia, diarrhoea, throat pain (oropharyngeal pain), nausea, and symptoms of common cold (nasopharyngitis).

The most common side effects observed in patients with cancer who were receiving AMY109 were fever (pyrexia), constipation, diarrhoea, increased liver enzymes (aspartate aminotransferase) and anaemia.

AMY109 is a type of drug known as a biological agent. Theoretical risks include the possibility of causing hypersensitivity, infusion reaction, or anaphylactic reaction (a type of allergic reaction that could be serious), from a mild rash to a life-threatening reaction and could also possibly make it easier to get infections (for example respiratory infections) or delay wound healing. As there may be a risk in exposing an unborn child to study drug participants have to agree to use two forms of barrier contraception throughout the study and follow up.

There are also some risks with taking desogestrel, the most common risks (noted in about 1 in 10 women) include altered mood, depressed mood, decreased sexual drive (libido), headache, nausea, acne, breast pain, irregular or no menstruation and increased body weight.

Where is the study run from?
The study is expected to run in around 8 sites in the UK

When is the study starting and how long is it expected to run for?
October 2023 to September 2026

Who is funding the study?
The study is sponsored by Chugai Pharmaceuticals Ltd (UK)

Who is the main contact?
Mr Edward Morris, edward.morris@nnuh.nhs.uk
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Contact information

Type(s)
Principal investigator

Contact name
Mr Edward Morris

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Additional identifiers

Clinical Trials Information System (CTIS)
2023-507289-14-00

Integrated Research Application System (IRAS)
1006385

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
AMY106EU, IRAS 1006385, CPMS 54010

Study information

Scientific Title

A phase II, randomized, double blind study to evaluate the efficacy and safety of AMY109 in women with endometriosis

Acronym
ACERS

Study objectives
Primary objective:
To evaluate the efficacy of both (i) AMY109 and (ii) AMY109 and desogestrel compared with (iii) desogestrel in disease severity assessed by laparoscopic appearance in women with endometriosis

Secondary objectives:
1. To evaluate the efficacy of both (i) AMY109 and (ii) AMY109 and desogestrel compared with (iii) desogestrel in disease severity assessed by magnetic resonance imaging (MRI).
2. To evaluate the efficacy of both (i) AMY109 and (ii) AMY109 and desogestrel compared with (iii) desogestrel in disease severity assessed by transvaginal ultrasound (TVUS).
3. To evaluate the efficacy of both (i) AMY109 and (ii) AMY109 and desogestrel compared with (iii) desogestrel on endometriosis associated pain.
4. To assess the safety and tolerability of both (i) AMY109 and (ii) AMY109 and desogestrel compared with (iii) desogestrel
5. To evaluate the pharmacokinetics (PK) in plasma and pharmacodynamics (PD) profile of AMY109
6. To assess the immunogenicity of AMY109 (induction of anti-AMY109 antibodies).

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 27/03/2023, North East - Newcastle & North Tyneside 2 Research Ethics Committee (NHS BT Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, United Kingdom; +44 (0)207 104 8086; newcastlenorthtyneside2.rec@hra.nhs.uk), ref: 22/ES/0045

Study design
Interventional double-blind randomized parallel-group controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Endometriosis

Interventions
Period 1: 4–12-week washout period, required for participants receiving certain types of medication.
Period 2: 21–45-day screening period, to confirm participant eligibility for the study.

Period 3: 52-week treatment period, for participants to receive study treatment.
Period 4: a post-treatment follow-up period, 52 weeks after the last dose of study drug to assess long-term safety of AMY109.

Participants will be randomised in a 3:3:2 ratio to one of the following treatment groups:
1. AMY109, and desogestrel-placebo. A placebo looks like a medicine but does not contain any active ingredients
2. AMY109 and desogestrel
3. AMY109-placebo and desogestrel
4. AMY109 or AMY109-placebo will be administered every 4 weeks intravenously (directly into the vein)
5. Desogestrel will be administered daily orally (by mouth).

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
AMY109, Desogestrel

Primary outcome(s)
Changes of total score and stage in the revised American Society of Reproductive Medicine (r-ASRM) score assessed by laparoscopy from pre-treatment to post-treatment (Baseline and Week 53)

Key secondary outcome(s))
1. Change in size of ovarian endometrioma assessed by MRI from baseline to Week 37 and 53.
2. Change in size of endometriotic nodule assessed by MRI from baseline to Week 37 and 53.
3. Change in adhesions assessed by MRI from baseline to Week 37 and 53.
4. Change of grade in the ENZIAN classification assessed by MRI from baseline to Week 37 and 53.
5. Change in the MEDL score assessed by MRI from baseline to Week 37 and 53.
6. Change in size of ovarian endometrioma from baseline to Week 25 and 53 assessed by transvaginal ultrasound (TVUS)
7.Change in size of endometriotic nodule from baseline to Week 25 and 53 assessed by TVUS
8. Change in adhesions from baseline to Week 25 and 53 assessed by TVUS
9. Change in monthly mean endometriosis associated pain scores (dysmenorrhea, dyspareunia, and NMPP) from baseline to each month as recorded by daily completion of an 11–point numerical rating scale (NRS) using an electronic diary (Baseline and then monthly up to Week 105)
10. Change in monthly mean endometriosis associated pain scores (dysmenorrhea, dyspareunia, and NMPP) from baseline to each month measured by the modified Biberoglu and Behrman Scale (mBBS) using an electronic diary on daily basis (Baseline and then monthly up to Week 105)
11. Change in monthly mean number of days of analgesics use to treat endometriosis associated pain from baseline to each month as recorded by daily completion of an electronic diary (Baseline and then monthly up to Week 105)
12. Change in monthly mean dose of analgesics use to treat endometriosis associated pain from baseline to each month as recorded by daily completion of an electronic diary (Baseline and then monthly up to Week 105)

13. Incidence and severity of adverse events (AEs), serious adverse events (SAEs), adverse events of special interest (AESIs), and adverse drug reactions up to Week 105
14. Vital signs (pulse rate, blood pressure, body temperature). Screening until Week 105.
15.12-lead electrocardiograms (ECGs). Screening until Week 53.
16. Laboratory investigations (urinalysis, hematology, blood chemistry, coagulation tests, and other investigations). Screening until Week 105
17. Plasma concentration of AMY109 and IL-8. Screening until Week 105
18. Ovarian function measured by uterine bleeding and serum level of anti-Müllerian hormone (AMH), follicle stimulating hormone (FSH), estradiol (E2), and progesterone (P4). Week 1 until Week 53
19. Plasma CA125. Week 1 until Week 53
20. Change in incidence of anti-AMY109 antibodies. Week 1 until Week 105
21. Change in plasma concentration of AMY109 and total IL-8 by anti-AMY109 antibody status (seropositive or seronegative) up to Week 105

Completion date
05/09/2026

Eligibility

Key inclusion criteria
Current inclusion criteria as of 25/04/2024:

1. Provide written informed consent and sign the Informed Consent Form
2. Female patients between 18 and 49 years of age inclusive at entering the screening period
3. Patients who have received a laparoscopic diagnosis within 9 months before entering the screening period but have not received any surgical treatment at the laparoscopic diagnosis.
4. Able to comply with study requirements in the Investigator’s judgment
5. Agree to use non-hormonal, double-barrier contraception such as a combination of male condom with either cap, diaphragm or sponge with spermicide and refrain from egg collection for preservation or donation.
6. Agree to switch from usual analgesics for dysmenorrhea, dyspareunia, and NMPP to analgesics permitted by the study protocol
7. Patients who are willing to have laparoscopic surgery after study treatment is completed and understands the surgery may be delayed by participation in the study.
8. Has at least 1 full menstrual cycle (21-38 days) during the screening period. The withdrawal bleeding while cyclically using hormonal agents is not considered regular menses
9. Has at least 21 days of e-Diary entries during the screening period and completed the e-Diary on at least 75% of days during the screening period. Note: e-Diary vendor will provide an e-Diary compliance report. The investigational site should review the report before randomization to assess eligibility.
10. Has moderate to severe endometriosis-associated NMPP (NRS score of ≥4 on ≥ 4 days of the screening period) and dysmenorrhea (NRS score of ≥4 on ≥ 2 days of the screening period)
11. Patients who are staged III/IV endometriosis according to the revised American Society of Reproductive Medicine (r-ASRM) score by central readers based on images obtained at the laparoscopic diagnosis

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Previous inclusion criteria:

1. Provide written informed consent and sign the Informed Consent Form
2. Female patients between 18 and 45 years of age inclusive at entering the screening period
3. Patient who is diagnosed as having endometriosis by laparoscopy, but have not yet received any surgical treatment at the diagnosis, within 6 months before entering the screening period and who is staged according to the revised American Society of Reproductive Medicine (r-ASRM) score by central readers based on images obtained at the laparoscopic diagnosis
4. Not suitable for surgical treatment at laparoscopic diagnosis due to severe condition of the disease
5. Able to comply with study requirements in the Investigator’s judgment
6. Agree to use non-hormonal, double-barrier contraception such as a combination of male condom with either cap, diaphragm or sponge with spermicide and refrain from egg collection for preservation or donation until 32 weeks after the last administration of AMY109 or AMY109-placebo
7. Agree to switch from usual analgesics for dysmenorrhea, dyspareunia, and NMPP to analgesics permitted by the study protocol
8. Patient is willing to have laparoscopic surgery after study treatment is completed and understands the surgery will be delayed by participation in the study. Patients must also meet the following criteria for study entry (in addition to 1-8 above):
9. Has at least 1 full menstrual cycle (21-38 days) during the screening period. The withdrawal bleeding while cyclically using hormonal agents is not considered regular menses
10. Has at least 21 days of e-Diary entries during the screening period and completed the e-Diary on at least 75% of days during the screening period.. Note: e-Diary vendor will provide an e-Diary compliance report. The investigational site should review the report before randomization to assess eligibility.
11. Has moderate to severe endometriosis-associated NMPP (NRS score of ≥4 on ≥ 4 days of the screening period) and dysmenorrhea (NRS score of ≥4 on ≥ 2 days of the screening period)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
49 years

Sex
Female

Key exclusion criteria
1. Clinically significant abnormalities in laboratory test results, physical examination, vital signs, 12-lead ECG, chest X-ray, hematology (e.g., Hemoglobin [Hb] < 90 g/L), blood chemistry, serology, and urinalysis at screening.
2. Patient has chronic pelvic pain that is not caused by endometriosis and that requires chronic analgesic or other chronic therapy, or that would interfere with the assessment of

endometriosis related pain (e.g. pelvic inflammatory disease).
3. Patient has a surgical history of hysterectomy and/or bilateral oophorectomy.
4. Prior treatment with antibody preparations (commercially available or investigational) within 6 months or 5 half-lives of the drug, whichever is longer, before entering the screening period
5. Prior treatment with anti-IL-8 antibody preparations

Date of first enrolment
10/01/2024

Date of final enrolment
31/07/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Norfolk and Norwich Hospital
Colney Lane
Norwich
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NR4 7UY

Study participating centre
Colchester Hospital
Turner Road
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CO4 5JL

Study participating centre
St Thomas Hospital
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SE1 7EH

Study participating centre
Royal Hallamshire Hospital
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Study participating centre
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369 Fulham Road
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SW10 9NH

Sponsor information

Organisation
Chugai Pharma Europe Ltd.

Funder(s)

Funder type
Industry

Funder Name
Chugai Pharmaceutical Co., Ltd

Results and Publications

Individual participant data (IPD) sharing plan
All data generated or analysed during this study will be included in the subsequent results publication

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes

Study website	Study website	11/11/2025	11/11/2025	No	Yes