ISRCTN62695528 https://doi.org/10.1186/ISRCTN62695528

A large, multi-clinic study to evaluate contraceptive efficacy and safety of depot medroxyprogesterone acetate (150 mg/ml) injected under the skin every 6 months

Submission date
22/03/2022

Recruitment status
No longer recruiting

Registration date
26/05/2022

Overall study status
Completed

Last Edited
20/01/2026

Condition category
Pregnancy and Childbirth

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

Plain English summary of protocol

Background and study aims
The study is being done to find out if the existing 3-month depot medroxyprogesterone acetate (DMPA) contraceptive injection is as effective and safe when injected every 6 months under the skin instead of into the muscle. The product being tested is called '6-month DMPA SC'. A previous study of 21 women showed that injecting DMPA under the skin stopped 21 women from ovulating (i.e., producing eggs) for at least 6 months when it was given under the skin. This study will test if it prevents actual pregnancy and is safe among a larger number of women.

Who can participate?
Healthy, sexually active women aged 18 to 35 years who are willing to use 6-month DMPA SC as their only means of contraception for 12 months (i.e., receive two injections 6 months apart).

What does the study involve?
Participants in the study will receive two shots of 6-month DMPA SC (at enrollment and 6 months after the first injection) under the skin of either their abdomen or thigh. Participants will be asked to return for follow up visits at Months 3, 6 and 9, and a final visit at Month 12, and complete monthly pregnancy tests either at home or at the clinic during the study. Additional tests after the Month 12 visit to provide information on return to ovulation may be scheduled if a participant consents to participate.

What are the possible benefits and risks of participating?
There is no direct benefit from taking part in this study, however, participants may help to develop a new, longer-acting contraceptive method.
Pregnancy: Risk of pregnancy is low but unknown. Participants will be tested for pregnancy before and during the study to make sure they are not pregnant. Any positive tests will be confirmed by a blood test and/or ultrasound. The researchers will refer participants for medical care at NHS in the unlikely scenario that they become pregnant. Many studies have found that babies who are exposed to DMPA while in the womb do not have a higher risk of birth defects or

health problems.
Future fertility: Participants' typical ability to get pregnant will return when the last injection wears off. It may take as long as a year after getting the last shot of 6-month DMPA SC for this to happen.
Skin reactions: There is a chance that participants will have skin reactions where they receive the shots. No skin reactions were reported to be severe or serious during previous studies.
Irregular bleeding: Most women have irregular bleeding, spotting or no bleeding at all while using DMPA. Regular bleeding is expected to return when most of MPA is cleared from the body.
Weight gain: Some women gain weight while using DMPA (about 3-5 pounds in a year).
Sexually transmitted infections: According to WHO, it is safe for women who are at high risk of sexually transmitted infections (STIs) including human immunodeficiency virus (HIV), to use DMPA. DMPA does not protect against STIs, including HIV.
Bone mineral density: Use of DMPA for more than 2 years may weaken bones (the condition known as osteopenia which may increase the risk of broken bones). It is not expected that getting two injections of 6-month DMPA SC in this study will have any effect on bones due to the short duration of the study (12 months).
Cancer: Some studies found a slightly increased risk of breast cancer among women using 3-month DMPA for 12 months or longer. It is unlikely that getting two injections of 6-month DMPA SC in this study will lead to breast cancer.
Allergic reaction: Severe allergic reaction to DMPA, also known as anaphylactic reaction, is rare. Such reactions usually happen right after the injection. The researchers will ask participants to remain in the clinic for observation for at least 30 minutes after each injection where we have drugs to treat severe allergic reactions and easy access to emergency care in the unlikely event of such a reaction.
Additional potential side effects: acne, headache, tiredness, decreased sexual desire, breast pain, depression.
Blood draw: It is possible that participants may feel some pressure or discomfort while their blood is being drawn and they may have a small bruise where the blood was drawn. There is also a small risk of infection with a blood draw.
Ultrasound: A transvaginal ultrasound may be done to confirm a positive urine pregnancy test. This procedure is usually not painful but may cause discomfort, anxiety or embarrassment.
Gynaecological examination: This examination usually does not hurt but may cause slight discomfort, anxiety or embarrassment.
Non-medical: Potential non-medical risks in this study include a breach of confidentiality, potentially missing work to come to study visits, and answering questions about sensitive subjects like sexual history and keeping a bleeding diary. The researchers will do their best to prevent anyone outside the study from knowing about participants in this study. All attempts will be made to accommodate the participants' availability when scheduling clinic visits.
If participants have a side effect after an injection, the drug cannot be removed immediately to stop the reaction. Most of the side effects do not pose a serious risk to health and go away with time without clinical care. Participants will be provided with study team contact details and emergency contacts for the study in case they experience any of the above risks. The site team will make every attempt to resolve the issue by providing appropriate medical care and ensuring the safety of their patients.

Where is the study run from?
FHI 360 (USA)

When is the study starting and how long is it expected to run for?
March 2022 to February 2026

Who is funding the study?
FHI 360 (USA)

Who is the main contact?
Sarah Cordes
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Contact information

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Additional identifiers

Clinical Trials Information System (CTIS)
2021-004106-22

Integrated Research Application System (IRAS)
1005048

Protocol serial number
1706176

Study information

Scientific Title
A Phase III, open-label, multicenter study to evaluate contraceptive efficacy and safety of depot medroxyprogesterone acetate (150 mg/ml) injected subcutaneously every 6 months

Acronym
DMPA-XT

Study objectives
The main objective is to evaluate the contraceptive efficacy of 6-month depot medroxyprogesterone acetate (DMPA) subcutaneously (SC) injected every 6 months for 12 months in the abdomen or thigh. The primary study endpoint is the occurrence of pregnancy, as defined by a positive urine pregnancy test and confirmed by a valid method (i.e., ultrasound and /or serum human chorionic gonadotropin (hCG)). The primary efficacy endpoint will be assessed by reporting the Pearl Index (pregnancies per 100 women-years of treatment) and an associated 95% confidence interval for the Pearl Index.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 20/05/2022, South Central - Oxford B Research Ethics Committee (Ground Floor, Temple Quay House, 2 The Square, Bristol, BS1 6PN, UK; +44 (0)207 104 8360; oxfordb.rec@hra.nhs.uk), ref: 22/SC/0104

Primary study design
Interventional

Study design
Randomized parallel trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied

Contraception for up to 6 months

Interventions

Current intervention as of 22/12/2023:
Subjects will be randomly assigned using a 1:1 allocation ratio to receive both of their subcutaneous injections of 6-month DMPA SC in either the abdomen or upper thigh. 6-month DMPA SC will be administered by a trained staff member as a single subcutaneous injection in either the abdomen or thigh at a dose of 150 mg in 1 ml using a 26-gauge 3/8-inch needle.

All subjects will receive two injections of 6-month DMPA SC: the first injection during the enrollment visit which will be scheduled during the first five days of the menstrual cycle, or at the time of switching from the previous form of highly effective contraception (e.g., contraceptive patch, ring, implant, pills, copper or hormonal IUD), and the second injection during the scheduled follow-up visit at month 6 (reinjection). There will be a plus 7-day grace period for reinjection at month 6 but women may receive re-injection up to 28 days late. Subjects who are more than 28 days late for reinjection will be discontinued from the study. All subjects will have scheduled follow up visits 3, 6 (reinjection) 9, and 12 months after the first injection.

Randomization will be done using paper envelopes once eligibility is confirmed.

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Previous intervention:
Subjects will be randomly assigned using a 1:1 allocation ratio to receive both of their subcutaneous injections of 6-month DMPA SC in either the abdomen or upper thigh. 6-month DMPA SC will be administered by a trained staff member as a single subcutaneous injection in either the abdomen or thigh at a dose of 150 mg in 1 ml using a 26-gauge 3/8-inch needle.

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Randomization will be done electronically through the electronic data capture (EDC) system once eligibility is confirmed. Paper envelopes are provided to the clinical sites as a backup randomization method in the event that the EDC cannot be used.

Intervention Type

Drug

Phase

Phase III

Drug/device/biological/vaccine name(s)

Depot medroxyprogesterone acetate (DMPA)

Primary outcome(s)
The occurrence of pregnancy, defined as a positive urine pregnancy test and confirmed by a valid method (i.e., ultrasound and/or serum human chorionic gonadotropin [hCG)] at months 3, 6, 7, 9, and 12

Key secondary outcome(s)
1. Trough MPA levels, MPA accumulation, and the impact of injection site on these PK parameters. Serum MPA concentrations will be measured in the safety subset of 100 subjects on days 0 and 7 and months 1, 3, 4, 5, 6, 9, 10, 11, and 12
2. The safety of 6-month DMPA SC injected every 6 months for 12 months in the abdomen or thigh. The safety measures are:
2.1. Occurrence of adverse events (AEs) throughout the study
2.2. Use of concomitant medications throughout the study
2.3. Vital signs (blood pressure and pulse) and body weight at day 0 and months 3, 6, 9 and 12
2.4. Bleeding and spotting recorded in daily diaries throughout the study
2.5. Hemoglobin and hematocrit at screening and month 12 visits
2.6. Estradiol (E2) at day 0, months 6 and 12
2.7. Safety laboratory tests at screening and month 12 visits (in the Safety Subset of 100 subjects)
2.8. Progesterone (P) and E2 levels at day 0, months 3, 6, 9 and 12 (in the Safety Subset of 100 subjects)
2.9. Bone mineral density (BMD) prior to enrollment and at the end of study participation (in all subjects at the SA investigational center and in the Safety Subset of 100 subjects at the DR investigational center)
3. Satisfaction among users with 6-month DMPA SC injected every 6 months for 12 months in the abdomen or thigh. Satisfaction will be measured using the subject's responses to the patient satisfaction questionnaire (PSQ) at enrollment, months 6 and 12 and the subject's responses to questions about the acceptability of the bleeding pattern at months 3, 6, 9 and 12.

Completion date
18/02/2026

Eligibility

Key inclusion criteria
Current inclusion criteria as of 22/12/2023:
Women may be included in the study if they meet all of the following criteria:
1. In good general health as determined by medical history, physical and gynecological exams
2. Aged 18-35 years at treatment initiation, inclusive
3. Willing to provide informed consent, follow all study requirements and rely on 6-month DMPA SC as the only means of contraception for 12 months (i.e., two injections 6 months apart)
4. At risk of pregnancy (in a heterosexual relationship, no diagnosis of infertility, no history of tubal ligation or hysterectomy, primary partner is not vasectomized or otherwise sterile, and an average of one or more acts of vaginal intercourse per month)
5. Not pregnant and has no desire to become pregnant for at least the next 12 months
6. Regular (21-35 days) menstrual cycle (when not using hormonal contraceptives)
7. At least two normal menses since the last injection of any injectable contraceptive (if not using other hormonal contraceptives)
8. Hemoglobin ≥9.5 g/dl

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Previous inclusion criteria:
Women may be included in the study if they meet all of the following criteria:
1. In good general health as determined by medical history, physical and gynecological exams
2. Aged 18-35 years at treatment initiation, inclusive
3. Willing to provide informed consent, follow all study requirements and rely on 6-month DMPA SC as the only means of contraception for 12 months (i.e., two injections 6 months apart)
4. At risk of pregnancy (in a heterosexual relationship, no diagnosis of infertility, no history of tubal ligation or hysterectomy, primary partner is not vasectomized or otherwise sterile, and an average of one or more acts of vaginal intercourse per month)
5. Not pregnant and has no desire to become pregnant for at least the next 12 months
6. Regular (21-35 days) menstrual cycle (when not using hormonal contraceptives)
7. At least two normal menses since the last injection of any injectable contraceptive (if not using other hormonal contraceptives)
8. Hemoglobin ≥11.0 g/dl

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
35 Years

Sex
Female

Total final enrolment
748

Key exclusion criteria
Current exclusion criteria as of 22/12/2023:
Women will be excluded from participating in this study if they meet or have one or more of the following criteria:
1. Lactating
2. Hypertension with systolic BP ≥160 mm Hg or diastolic BP ≥100 mm Hg
3. Multiple risk factors for cardiovascular disease (eg, smoking, obesity,diabetes, hypertension and known dyslipidemias)
4. Current and/or history of deep venous thrombosis (DVT)/pulmonary embolism (PE)
5. Current and/or history of arterial thrombotic or thromboembolic events (ATE) (ie, myocardial infarction, ischaemic heart disease, stroke, or peripheral arterial disease)
6. Systemic lupus erythematosus
7. Migraine with aura
8. Unexplained vaginal bleeding
9. Undiagnosed mass in the breast

10. Current and/or history of breast cancer
11. Diabetes:
111. Of >20 years' duration
11.2. Complicated by nephropathy/retinopathy/neuropathy or other vascular disease
12. Cirrhosis
13. Current or history of liver tumors, benign or malignant, or active liver disease
14. Active renal disease
15. Known cervical cancer
16. History of suicide attempt
17. At high risk of sexually transmitted infections (STIs), including any of the following:
17.1. Use condoms consistently for STI prevention
17.2. Known to be HIV-positive (self or partner)
17.3. Use IV drugs (self or partner)
17.4. Diagnosis and/or treatment for an STI in the past month (self or partner), excluding recurrent herpes or condyloma
17.5. Not in a mutually monogamous relationship having lasted at least 3 months (SA investigational center only)
17.6. Tested positive for HIV, gonorrhea, chlamydia, trichomoniasis at screening (SA investigational center only)
18. Received an injection of DMPA in the past 9 months
19. Received an injection of a combined injectable contraceptive or norethisterone enanthate in the past 4 months
20. Currently uses or plans (in the next 12 months) to use a protocol-prohibited drug, another experimental drug, or any other drug that in the opinion of the center PI could complicate interpretation of study findings
21. Plans to relocate outside of study area in the next 12 months
22. Participates in another clinical study which in the opinion of the center PI would make study participation unsafe, would interfere with adherence to study requirements, or complicate data interpretation
23. Has already participated in this study
24. History of chronic alcoholism, drug dependence or abuse, psychotic states or severe neurosis or any other condition that, by the judgment of the center PI, might impair the subject's ability to cooperate
25. Current, confirmed diagnosis of COVID-19 unless they have recovered from the disease and have completed their quarantine period per local guidelines
26. Any condition (social or medical) which in the opinion of the center PI would make study participation unsafe, would interfere with adherence to study requirements, or complicate data interpretation

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Previous exclusion criteria:
Women will be excluded from participating in this study if they meet or have one or more of the following criteria:
1. Lactating
2. Hypertension with systolic BP ≥160 mm Hg or diastolic BP ≥100 mm Hg
3. Multiple risk factors for cardiovascular disease (eg, smoking, obesity, hypertension, known low high-density lipoprotein (HDL), high low-density lipoprotein (LDL), or high triglyceride levels)
4. Current and/or history of deep venous thrombosis (DVT)/pulmonary embolism (PE)
5. Current and/or history of arterial thrombotic or thromboembolic events (ATE) (ie, myocardial infarction, ischaemic heart disease, stroke, or peripheral arterial disease)
6. Hereditary or acquired predisposition for venous or arterial thrombosis
7. Systemic lupus erythematosus

8. Migraine with aura
9. Unexplained vaginal bleeding
10. Undiagnosed mass in the breast
11. Current and/or history of breast cancer
12. Diabetes:
12.1. Of >20 years' duration
12.2. Complicated by nephropathy/retinopathy/neuropathy or other vascular disease
13. Cirrhosis
14. Current or history of liver tumors, benign or malignant, or active liver disease
15. Known cervical cancer
16. Hospitalization for clinical depression or bipolar disorder in the last three years, with or without suicidal ideation
17. History of suicide attempt
18. At high risk of sexually transmitted infections (STIs), including any of the following:
18.1. Use condoms consistently for STI prevention
18.2. Known to be HIV-positive (self or partner)
18.3. Use IV drugs (self or partner)
18.4. Diagnosis and/or treatment for an STI in the past month (self or partner), excluding recurrent herpes or condyloma
18.5. Not in a mutually monogamous relationship having lasted at least 3 months (SA investigational center only)
18.6. Tested positive for HIV, gonorrhea, chlamydia, trichomoniasis at screening (SA investigational center only)
19. Received an injection of DMPA in the past 9 months
20. Received an injection of a combined injectable contraceptive or norethisterone enanthate in the past 4 months
21. Plans (in the next 12 months) to use a protocol prohibited drug, another experimental drug, or any other drug that in the opinion of the center PI could complicate interpretation of study findings
22. Plans to relocate outside of study area in the next 12 months
23. Participates in another clinical study which in the opinion of the center PI would make study participation unsafe, would interfere with adherence to study requirements, or complicate data interpretation
24. Has already participated in this study
25. History of chronic alcoholism, drug dependence or abuse, psychotic states or severe neurosis or any other condition that, by the judgment of the center PI, might impair the subject's ability to cooperate
26. Current, confirmed diagnosis of COVID-19 unless they have recovered from the disease and have completed their quarantine period per local guidelines
27. Any condition (social or medical) which in the opinion of the center PI would make study participation unsafe, would interfere with adherence to study requirements, or complicate data interpretation

Date of first enrolment
07/07/2022

Date of final enrolment
31/12/2024

Locations

Countries of recruitment
United Kingdom

Scotland

Chile

Dominican Republic

South Africa

Study participating centre
Chalmers Sexual Health Centre
2a Chalmers Street
Edinburgh
Lothian
Scotland
EH3 9ES

Study participating centre
The Gatehouse
Ayrshire Central Hospital
Irvine
Scotland
KA12 8SS

Study participating centre
Profamilia
Calle Socorro Sánchez 160
Santo Domingo
Dominican Republic
-

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Study participating centre

MatCH Research Unit
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5th Floor
430 Peter Mokaba Ridge
Overport
Durban
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4001

Study participating centre
IDIMI
Av. Sta. Rosa 1234
2do piso
Santiago
Chile
-

Sponsor information

Organisation
Family Health International 360

ROR
https://ror.org/007kp6q87

Funder(s)

Funder type
Charity

Funder Name
FHI 360

Alternative Name(s)
Family Health International

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
Current IPD sharing plan as of 07/01/2026:
IPD will be registered in a public database for use by other researchers including those outside of the study. A statement regarding the data repository is included in the informed consent. Data shared includes all quantitative data collected for the conduct of the trial, data from approved patient questionnaires, and laboratory data. Data will be archived in 21 CFR Part 11, GCP-compliant clinical database management systems once the final analysis and all publications of data are complete.

Previous IPD sharing plan:
IPD will be registered in USAID's Data Development Library (DDL) (https://data.usaid.gov) for use by other researchers including those outside of the study within 30 days of the primary peer-reviewed publication. A statement regarding the data repository is included in the informed consent. Data shared includes all quantitative data collected for the conduct of the trial, data from approved patient questionnaires, and laboratory data. Data will be archived in 21 CFR Part 11, GCP-compliant clinical database management systems once the final analysis and all publications of data are complete.

IPD sharing plan summary
Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No