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A clinical trial testing a new treatment called mRNA-4194 for people with Lynch syndrome

Submission date
06/03/2026

Recruitment status
Recruiting

Registration date
02/06/2026

Overall study status
Ongoing

Last Edited
02/06/2026

Condition category
Genetic Diseases

[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
This is a study testing a treatment called mRNA-4194 for people with Lynch syndrome (LS). People with LS have a change in one of their genes, meaning their bodies find it harder to stop cells becoming abnormal. This increases the risk of many types of cancer, most commonly in the bowel and, in women, the womb. Bowel cancer in LS is often preceded by a small growth of abnormal cells called a polyp, which can be identified/removed by colonoscopy.
The mRNA-4194 treatment aims to help the immune system recognise and remove these early abnormal cells before they cause cancer. It works by giving the body short-term instructions to make harmless pieces of protein found in these abnormal cells. This may help the immune system train itself to spot and destroy similar cells in future.

Who can participate?
Patients aged 18 years and over with Lynch syndrome (LS)

What does the study involve?
The trial has two parts. In Part 1, up to 30 adults will receive several injections of mRNA-4194 into a muscle over 12 weeks to help find a dose that is well tolerated and activates the immune system. Part 2 includes another 80-110 adults, who will receive several injections over 6 months and a booster injection after a year. Participants will also have blood tests and colonoscopies to check for changes in bowel lining or polyps. All participants will have regular visits for health checks, blood tests, and monitoring. Blood and tissue samples will be analysed in labs to see if mRNA-4194 can successfully train the immune system.

What are the possible benefits and risks of participating?
This trial will be the first time people are given mRNA-4194, so the side effects are unknown. Based on similar medications, the most common side effects are expected to be flu-like symptoms (tiredness, mild fever, chills, headache, muscle/joint aches) and symptoms where the injection is given (soreness, swelling, redness). Less commonly, these side effects may include more severe reactions at the injection site and allergic reactions. The trial will help doctors assess the safety of mRNA-4194 and if it could help the immune system prevent cancer in people with LS.
mRNA-4194 has not been given to human subjects before. The genetic mutations targeted by

mRNA-4194 were rigorously selected for tumour specificity, excluding common germline variants to minimize patient risk. Information on the potential toxicity associated with IM injection of mRNA 4194 is derived from non-clinical studies with mRNA-4194 and clinical studies with other mRNA therapies developed with Moderna's platform using the SM-102 lipid nanoparticles (LNPs - the carrier used to deliver the vaccine). Moderna's mRNA-LNP therapeutic cancer vaccine platform technology has been validated in studies of both individualized and off-the-shelf (OTS) therapies, which have demonstrated acceptable safety and signals of benefit in patients with solid tumours.
The intended design of the first in human trial allows for data-driven dose adjustments, with escalation or de-escalation decisions based on safety and tolerability to minimize participant risk. Selection of the dose for expansion will be informed by integrated assessment of safety and translational data, including antigen-specific T cell responses.
Adenomatous polyps ≥2 mm and <10 mm will be left in situ to permit evaluation of the biological effect of the investigational product. For participants in Part 2, additional risk is minimized by limiting retention of polyps at baseline to small polyps (<10 mm) and reducing the interval between follow-up colonoscopy procedures. The observation period in this trial, with follow-up colonoscopy at 28 weeks and 2 years after the start of study intervention, is substantially shorter than the SOC recommendation for repeat colonoscopies (every 2 years is standard), minimizing risk to study participants. The core PPI group agreed that the risk associated with leaving small polyps in situ was acceptable when considering the possible benefits of a vaccine, as long as the risks were clearly highlighted in the PIS.
There is a risk associated with additional research sample collection; blood samples could cause pain, bruising or bleeding. The trial will only be conducted at hospitals with expertise in the trials to ensure the highest standard of care for the patients.
The trial has undergone a risk assessment for Part 1 involving the operational team, oncology consultants and nursing team, along with pharmacists and statisticians. An additional risk assessment will be conducted, and a substantial modification submitted, for Part 2. The trial set-up has also involved patient involvement, with members from a PPI group who have lived experience of LS. Meetings have been held to review the patient pathway through the trial, and also discuss the visit schedule and visit burden, in addition to patient-facing documentation and their input has tailored how the trial is presented to potential patients. PPI members will also sit on the TMG.

Where is the study run from?
University of Oxford (UK)

When is the study starting and how long is it expected to run for?
March 2026 to September 2029

Who is funding the study?
Moderna (USA)

Who is the main contact?
OCTO INTERCEPT-Lynch Trial Team, octo-intercept-lynch@oncology.ox.ac.uk

Contact information

Type(s)
Principal investigator

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Additional identifiers

Integrated Research Application System (IRAS)
1012429

Sponsor's protocol code number
OCTRU484

Study information

Scientific Title
A Phase I/II open-label, dose-escalation, and dose-expansion study of mRNA-4194 in participants with Lynch syndrome

Acronym
INTERCEPT Lynch

Study objectives
The aims of the trial are to measure the safety and tolerability of novel vaccine mRNA-4194, define the recommended dose for further study, and to assess the effect of novel vaccine mRNA-4194 on immune cells and against precancerous LS-associated polyps in the colon and rectum polyp burden after priming treatment.

Ethics approval required
Ethics approval required

Ethics approval(s)

approved 05/05/2026, North East - York Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; -; york.rec@hra.nhs.uk), ref: 26/NE/0046

Primary study design
Interventional

Allocation
Non-randomized controlled trial

Masking
Open (masking not used)

Control
Uncontrolled

Assignment
Single

Purpose
Prevention

Study type(s)

Health condition(s) or problem(s) studied
Lynch syndrome (LS)

Interventions
The INTERCEPT-Lynch trial is an open-label, multicentre, Phase I/II trial of mRNA-4194 administered by intramuscular (IM) injection to participants with LS who are not known to have active cancer but are at high risk of developing MSI-H cancer due to inheritance of a germline pathogenic variant in one of the DNA MMR genes.

The trial will include two parts:

Part 1 consists of dose-escalation/de-escalation cohorts. Part 1 will enrol participants with confirmed LS. Participants will receive doses (cycles) of mRNA-4194.

Part 2 consists of dose-expansion cohort(s). Part 2 will enrol participants with confirmed LS and at least one baseline adenomatous colorectal polyp measuring ≥2 mm and <10 mm identified at SOC surveillance colonoscopy. Participants will receive doses (cycles) of mRNA-4194 administered at the dose level(s) determined from Part 1. A follow-up colonoscopy will be conducted 28 weeks after the start of priming treatment to remove retained polyps and evaluate biological endpoints, with a further colonoscopy performed at 24 months to align with the interval of surveillance colonoscopies in LS.

Part 1:
Dose range: 50 µg, 125 µg (starting dose), 250 µg, 500 µg, 1000 µg
Safety follow-up: 30 days after last dose
Immunogenicity follow-up: 28 weeks after first dose

Part 2:
Dose range: Dose(s) to be selected based on assessment of safety, immunogenicity and other translational data from participants in Part 1
Safety follow-up: 30 days after last dose
Long-term follow-up: Week 104

Randomisation process (Part 2) – if two recommended doses for expansion (RDEs) are selected
Participants will be randomised in a 1:1 ratio
Randomisation Form completed via REDCap EDC
Central CTU team to review and confirm participant eligibility
In the event of being unable to access REDCap, randomisation may be performed over the telephone with a member of the central CTU team

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
mRNA-4194

Primary outcome(s)
Part 1: Safety and tolerability of mRNA-4194 is assessed via the incidence and severity of Dose-Limiting Toxicities (DLTs), Adverse Events (AEs), Adverse Events of Special Interest (AESIs), and Serious Adverse Events (SAEs) at screening and weeks 0, 3, 6, 8, 12 and the safety follow-up visit

Part 1: One or more RDE(s) for mRNA-4194 will be determined via the incidence and severity of DLTs, AEs, AESIs, and SAEs at screening, weeks 0, 3, 6, 8, 12 and the safety follow-up visit

Part 2: Safety and tolerability of mRNA-4194 is assessed via the incidence and severity of DLTs, AEs, AESIs, and SAEs at screening, weeks 0, 3, 6, 8, 12, 16, 24, 28, 52 and the safety follow-up visit

Key secondary outcome(s)
The effect of mRNA-4194 on MSI-H adenomatous colorectal polyp burden after priming treatment will be assessed using the percent change in the sum of MSI-H adenomatous polyp diameter(s) pre- and post-treatment by colonoscopy per central read, at the initial (screening) colonoscopy and follow-up colonoscopy (week 28)

Completion date
01/09/2029

Eligibility

Key inclusion criteria
1. ≥18 years of age (inclusive) at the time of signing the informed consent.
2. Known LS, i.e., previously confirmed to be a carrier of a germline pathogenic variant in MLH1, MSH2, MSH6, PMS2, or EPCAM by genetic testing through a UKAS-accredited (or equivalent international agency) laboratory setting.
3. For Part 2 only: Participants must have at least one colorectal polyp with an adenomatous appearance measuring ≥2 mm and <10 mm in diameter identified on the screening colonoscopy

(i.e., within 28 days prior to the planned first dose of study intervention).
3.1. Polyp size will be based on measurements taken during the screening colonoscopy by the gastroenterologist performing the procedure. Polyp measurements will be performed in one dimension (transverse plane) under standard conditions as outlined in the Laboratory Manual using endoscopic tools as a reference (e.g., closed biopsy forceps [2.5 mm], open biopsy forceps [7 mm], and standard cold snare [9 mm]).
3.2. The participant must agree to allow adenomatous polyps ≥2 mm and <10 mm to be left in situ for longitudinal evaluation. The participant must agree to an additional colonoscopy at 28 weeks for resection of all polyps identified, including those identified at baseline and left in situ and any new polyps.
3.3. The retained polyp(s) must be absent of features suspicious for advanced neoplasia, as determined by internationally validated endoscopic methods (see Appendix 2). Participants with adenomatous polyps meeting the following morphological endoscopic criteria are eligible:
3.3.1. Kudo pit pattern type III-IV
3.3.2. JNET (Japan Expert NBI Team) classification type 2A
3.3.3. Paris polyp type 0-Ip, 0-Isp, 0-Is, 0-IIa, or 0-IIb, provided there is no visible depression within the polyp (0-IIc or mixed 0-IIa+IIc)
3.4. All adenomatous polyps <2 mm or ≥10 mm will be resected at the time of the screening colonoscopy, as will all polyps with non-adenomatous morphology.
4. For Part 2 Only: Predicted to be fit and eligible to undergo repeat colonoscopy at 28 weeks and 2 years after trial entry
5. Healthy adults or adults with pre-existing medical conditions who are in stable condition. A stable medical condition is defined as disease not requiring significant change in therapy or hospitalisation due to worsening disease for 3 months before enrolment.
6. Participants who have adequate haematologic and physiologic function, confirmed by the following laboratory values:
6.1. Bone marrow function:
6.1.1. Neutrophil count ≥1.5 × 10^9/l
6.1.2. Haemoglobin ≥90 g/L or ≥6.2 mmol/l
6.1.3. Platelets ≥100 × 10^9/l
6.2. Hepatic function:
6.2.1. Alanine aminotransferase (ALT) ≤2.5 × upper limit of normal (ULN). If ALT is above normal (>1 × ULN) at baseline, AST must also be measured and must be ≤2.5 × ULN.
6.2.2. Total bilirubin ≤1.5 × ULN (<3.0 × ULN if the participant has Gilbert's disease).
6.3. Renal function:
6.3.3. Creatinine clearance of ≥30 ml/min (using the CockcroftGault formula).
6.4. Coagulation function:
6.4.1. Prothrombin time/international normalised ratio and activated partial thromboplastin time ≤1.5 × ULN.
7. Participants who are assigned male at birth or can produce sperm must agree to the following during the study intervention administration period and for at least 30 days after the last dose of study intervention:
7.1. Refrain from donating sperm
PLUS either:
7.2. Be abstinent from reproductive sexual intercourse as their preferred and usual lifestyle (abstinent on a long term and persistent basis) and agree to remain abstinent
OR
7.3. Must agree to use a highly effective contraception/barrier as detailed below:
7.4. Agree to use an external condom (with a person of childbearing potential [POCBP] partner use of an additional highly effective contraceptive method with a failure rate of <1% per year and should also be advised of the benefit for a POCBP partner to use a highly effective method of contraception as a condom may break or leak when having sexual intercourse with a POCBP

who is not currently pregnant.
8. Participants who are assigned female at birth or could become pregnant:
8.1. A participant who could become pregnant is eligible to participate if they are not pregnant or breastfeeding and one of the following conditions applies:
Agree to use an external condom (with a person of childbearing potential [POCBP] partner use of an additional highly effective contraceptive method with a failure rate of <1% per year and should also be strongly advised of the benefit for a POCBP partner to use a highly effective method of contraception as a condom may break or leak when having sexual intercourse with a POCBP who is not currently pregnant.
8.2. A POCBP must have a negative highly sensitive pregnancy test (urine or serum, Human Chorionic Gonadotropin (HCG) test as required by local regulations) within 24 hours before the first dose of study intervention
9. The participant is willing and able to give signed informed consent which includes compliance with the requirements and restrictions listed in the informed consent form & protocol

Healthy volunteers allowed
Yes

Age group
Mixed

Lower age limit
18 years

Upper age limit
100 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Active cancer or pre-malignant condition, other than superficial non-melanoma skin cancers (e. g., basal cell carcinoma and squamous cell carcinoma), at time of enrolment.
2. Received treatment, including surgical resection, for cancer within the preceding 3 years for LS-related cancers or within the preceding 5 years for non-LS-related cancer.
3. Toxicities from prior cancer therapy that have not recovered to Grade 1 or baseline with the exceptions of alopecia, vitiligo, and, if approved by the Chief Investigator or designated clinician , other toxicities not reasonably expected to recover.
4. For Part 2 only: A diagnosis of active inflammatory bowel disease which would compromise identification of polyps at baseline or week 28 colonoscopy
5. For Part 2 only: Prior total or subtotal resection of the colon or another prior surgical procedure preventing colonoscopy.
6. Regular use of non-steroidal anti-inflammatory drugs (NSAIDs) or cyclooxygenase-2 (COX-2) inhibitors (eg, ibuprofen, naproxen, celecoxib), defined as ≥3 doses per week for a duration of ≥4 weeks within the past 6 months, unless discontinued at least 4 weeks prior to Screening. Use of aspirin is permitted but must be documented (note that for subjects in Part 2 on anti-platelet and anticoagulant therapy, Exclusion Criterion #15 must be followed.
7. Immunosuppressive doses of systemic steroids or absorbed topical steroids (doses >10 mg

prednisolone (prednisone) daily equivalent) within 2 weeks before study intervention administration or currently requiring maintenance doses of >10 mg prednisolone (prednisone) or equivalent per day.
8. History of primary immunodeficiency or solid organ transplantation.
9. Any history of live or live attenuated vaccinations within 28 days prior to cycle 1 day 1 (C1D1), i. e., the first dose of study treatment. Recent non-live vaccines (including mRNA vaccines) are permitted but should not be administered within 14 days prior to study dose.
10. History of anaphylaxis or severe hypersensitivity reaction requiring medical intervention after receipt of any mRNA vaccine or therapeutic, or any components of an mRNA vaccine or therapeutic.
11. Major surgical procedures ≤28 days or nonstudyrelated minor procedures ≤7 days prior to C1D1. In all cases, the participant must be sufficiently recovered and stable before treatment administration.
12. Any of the following cardiac abnormalities:
12.1. Medically uncontrolled hypertension
12.2. New York Heart Association Class III or IV cardiac disease
12.3. Myocardial infarction within prior 6 months
12.4. Unstable angina pectoris
12.5. Unstable arrhythmias or prolonged corrected QT interval (QTc) >450 ms in males or >470 ms in females (unless a pacemaker is in place)
13. Has an active bacterial infection requiring use of systemic antibiotics or an active infection including tuberculosis (clinical evaluation that includes clinical history, physical examination and radiographic findings, and tuberculosis testing in line with local practice), hepatitis B (known positive HBsAg result), or hepatitis C. Participants with a past or resolved hepatitis B virus (HBV) infection (defined as the presence of anti HBc and absence of HBsAg) are eligible. Participants positive for hepatitis C virus (HCV) antibody are eligible only if polymerase chain reaction is negative for HCV RNA. Human immunodeficiency virus (HIV)-positive participants with CD4 count ≥350 cells/mm3 and an undetectable HIV viral load within the past year (low level variations from 50-500 viral copies which do not lead to changes in antiretroviral therapy) are eligible.
14. Active gastrointestinal bleeding or haemoptysis
15. For Part 2 only: Use of antiplatelet or anticoagulation therapy that cannot be safely stopped peri-colonoscopy for the durations specified in the BSG/ESG
16. Any unstable or clinically significant concurrent medical condition, psychiatric illness, substance abuse, or social situation that would limit compliance with study requirements or compromise the ability of the participant to provide written informed consent, per the discretion of the Investigator.
17. Previous exposure to an investigational preventative cancer vaccine.
18. Has concurrent enrolment in another clinical study (unless it is an observational /noninterventional clinical study).

Date of first enrolment
15/06/2026

Date of final enrolment
02/02/2029

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Churchill Hospital
Old Road
Headington
Oxford
England
OX3 7LJ

Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type

Funder Name
Moderna

Alternative Name(s)
Moderna Therapeutics, Moderna, Inc., Moderna, Inc

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Data sharing statement to be made available at a later date