

# A study to test the effectiveness of a vaccine targeting a protein that hides cancer cells from the body's immune system in operable colorectal cancer that has defective mismatch repair

<b>Submission date</b> 13/07/2024	<b>Recruitment status</b> Recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 21/03/2025	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 21/03/2025	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Early colon cancer is normally treated with surgery and chemotherapy for high-risk patients with cancer that has spread to the local lymph nodes. Despite these treatments, up to 50% of patients have cancer that comes back. There needs to be more understanding of the disease biology to improve treatments. About 15% of early colon cancer patients have, something called defective mismatch repair. This means that in the cancer more mutations or errors in the DNA are present than in a 'normal' bowel cancer patient. This is significant because the new generation of drugs which stimulate the immune system to attack cancer works very well in this subgroup. In fact, in trials, these drugs can make colon cancers disappear completely. The vaccine in this study works by stimulating the immune system to produce antibodies to attack this subtype of colon cancer. The study aims to give the vaccine before surgery and then see how much cancer killing has happened in the surgical specimen. It will also explore from the tumour specimen, blood tests and stool samples, what makes people become responders to treatment or not. If the study is successful, a larger phase study will be undertaken.

### Who can participate?

Adult patients aged 18 years old and over with adenocarcinoma cancer of the colon and high rectum

### What does the study involve?

Recruited patients will receive 3 doses of the vaccine, 2 weeks apart, before having their standard-of-care surgery. They will be monitored throughout the vaccine period and during follow-up through blood tests, physical exams and CT scans. Following surgery, patients may have further chemotherapy if residual disease is present. All patients will be followed up for a minimum of 2 years from surgery.

What are the possible benefits and risks of participating?

Benefits – the vaccine may activate the immune system to destroy cancer cells in the tumour.

Risks – patients may have inflammation around the injection site of the vaccine. Patients will be monitored closely during the vaccine and up to 1 hr after injection and any reactions will be treated locally by site staff.

Where is the study run from?

Royal Surrey County Hospital, UK

When is the study starting and how long is it expected to run for?

July 2024 to March 2029

Who is funding the study?

Imugene Limited, Australia

Who is the main contact?

Dr Tony Dhillon, Tony.dhillon@nhs.net

Plain English summary under review with external organisation

## Contact information

### Type(s)

Public, Scientific, Principal Investigator

### Contact name

Dr Tony Dhillon

### Contact details

Royal Surrey County Hospital, Egerton Road

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None provided

Tony.dhillon@nhs.net

### Type(s)

Public, Scientific

### Contact name

Dr Trial team -

### Contact details

University of Southampton

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# Additional identifiers

## EudraCT/CTIS number

Nil known

## IRAS number

1008650

## ClinicalTrials.gov number

Nil known

## Secondary identifying numbers

79361, IRAS 1008650

# Study information

## Scientific Title

A phase II trial of neoadjuvant PD-1 vaccine PD1-Vaxx in operable MSI high colorectal cancer

## Acronym

Neo-POLEM

## Study objectives

To determine major pathological response rates after administering neoadjuvant PD-1 vaccine IMU-201 (PD1-Vaxx) in operable MSI high CRC patients

To assess the safety of PD-1 vaccine IMU-201 (PD1-Vaxx) in the neo-adjuvant setting.

Rate of complete response (defined as no viable tumour cells) after receiving PD1-Vaxx

To report the objective response rate (ORR) of PD-1 vaccine IMU-201 (PD1-Vaxx) in the neo-adjuvant setting

To assess disease free survival (post-surgery) and overall survival

Clavien-Dindo assessment of complications of surgery

To assess health-related quality of life

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Pending approval; ref: 24/LO/0584

## Study design

Phase II trial

## Primary study design

Interventional

## Secondary study design

Non randomised study

## Study setting(s)

Hospital

**Study type(s)**

Safety, Efficacy

**Participant information sheet**

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

Operable microsatellite instability-high (MSI-high) colorectal cancer

**Interventions**

Arm 1, patients will be given PD-1 Vaxx which consists of 100ug/dose of IMU-201 and administered as a 0.5ml intramuscular injection. Administration takes place on Day 1, 15 and 29. Patients will then undergo surgery between 21-42 days after completing trial treatment. Follow-up will begin once the patient has been discharged from surgery and/or adjuvant chemotherapy. Patients will remain in active follow-up for up to 2 years. Once the last patient has completed their last visit, a check will be made on all patients to confirm their recurrence and survival status.

**Intervention Type**

Biological/Vaccine

**Pharmaceutical study type(s)**

Not Applicable

**Phase**

Phase II

**Drug/device/biological/vaccine name(s)**

IMU-201 (PD1-Vaxx)

**Primary outcome measure**

The proportion of major pathological response (MPR), defined by  $\leq 10\%$  viable tumour cells after receiving PD-1 vaccine IMU-201 (PD1-Vaxx), measured using the Pataer system at surgery

**Secondary outcome measures**

1. Proportion with complete response, defined as no viable tumour cells after receiving PD1-Vaxx. The proportion of patients with complete response after receiving at least 1 vaccine at surgery measured using patient data
2. Objective response rate (ORR), defined by RECIST v1.1, measured using patient data before surgery before surgery
3. Disease-free survival (DFS) following surgery measured using patient data from surgery to any recurrence at 12 months
4. Overall Survival (OS) measured using patient data from the time of registration to death from any cause at 12 months
5. Adverse events, as assessed by the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) v5.0. and graded according to CTCAE v5.0 from the time of initiation of the vaccine
6. Health-related quality of life measures using the EORTC QLQ-C30 and EQ-5D-5L at screening, pre-op and post-op
7. Grading of surgical complications measured using the Clavien-Dindo classification at screening, pre-op and post-op

**Overall study start date**

10/07/2024

**Completion date**

31/03/2029

## Eligibility

**Key inclusion criteria**

1. Patients must have a signed and dated written informed consent form. This must be performed before the performance of any protocol-related procedures that are not part of the normal care
2. Patients must be willing and able to comply with the scheduled visits, treatment schedules, laboratory tests and other requirements of the study
3. Histologically confirmed adenocarcinoma cancer of the colon and high rectum
4. ECOG Performance Status 0 or 1
5. Measurable disease per RECIST 1.1 criteria
6. Tumour tissue from a colonoscopy must be provided for biomarker analysis. If an insufficient amount of tumour tissue from a colonoscopy is available before the start of the screening phase patients will be required to consent to allow the acquisition of additional tumour tissue for the performance of biomarker analyses
7. To be entered into the study, patients must be classified as MSI-high (confirmation of MMR deficiency or MSI-H)
8. Stage II (T3-T4 N0) III (any T, N1 or N2, M0) CRC
9. Radiological evidence of operable CRC, determined by local MDT, usually a CT scan
10. Treatment naïve patients (no prior anti-CRC therapy)
11. Screening laboratory values must meet the following criteria:
  - 11.1. Neutrophils  $\geq 1.5 \times 10^9/L$
  - 11.2. Platelets  $\geq 100 \times 10^9/L$
  - 11.3. Haemoglobin  $\geq 9.0$  g/dl
  - 11.4. Serum creatinine  $\leq 1.5 \times$  upper limit of normal (ULN) or calculated creatinine clearance  $> 50$  mL/min (using the Cockcroft Gault formula)
  - 11.5. Total bilirubin  $\leq 1.5 \times$  ULN; for patients with documented/suspected Gilbert's disease, bilirubin  $\leq 3 \times$  ULN
  - 11.6. AST  $\leq 1.5 \times$  ULN
  - 11.7. ALT  $\leq 1.5 \times$  ULN
12. Aged  $\geq 18$  years
13. Women of childbearing potential (WOCBP) must have a negative serum or urine pregnancy test (minimum sensitivity 25 IU/L or equivalent units of HCG) within 72 hours before the start of the study drug
14. WOCBP must agree to follow instructions for method(s) of contraception, as indicated in the informed consent form. Contraception must be used for the duration of treatment and a period of 180 days after the last dose of the study drug
15. Males who are sexually active with WOCBP must agree to follow instructions for method(s) of contraception, as indicated in the informed consent form for 180 days. Men who are sexually active with WOCBP must continue contraception for 180 days after the last dose of the investigational drug (combination or monotherapy). In addition, male patients must be willing to refrain from sperm donation during this time.

16. Azoospermic males are exempt from contraceptive requirements. WOCBP who are continuously not heterosexually active are also exempt from contraceptive requirements, and still must undergo pregnancy testing as described in this section

**Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

44

**Key exclusion criteria**

1. History of severe allergic reactions (i.e, Grade 4 allergy, anaphylactic reaction from which the patient did not recover within 6 hours of institution of supportive care) to any unknown allergens or any components of the PD-1 vaccine formulations
2. Distant metastases or peritoneal nodules (M1)
3. Active or prior documented autoimmune disease (including inflammatory bowel disease, coeliac disease and Wegener syndrome)
4. Any concurrent chemotherapy or biologic or hormonal therapy for CRC treatment. Concurrent use of hormones for non-cancer-related conditions (e.g. insulin for diabetes and hormone replacement therapy) is acceptable
5. History of primary immunodeficiency, solid organ transplantation, or previous clinical diagnosis of tuberculosis
6. If they are positive for hepatitis B virus surface antigen (HBVsAg) or hepatitis C virus ribonucleic acid (HCV antibody) indicating acute or chronic infection
7. If they have known history of testing positive for human immunodeficiency virus (HIV) or known acquired immunodeficiency syndrome (AIDS)
8. Receipt of live, attenuated vaccine within 28 days prior to the first dose of PD-1 vaccine IMU-201 (PD1-Vaxx) (patients, if enrolled, should not receive live vaccine during the study and 180 days after the last dose of Investigational Medicinal Product (IMP))
9. Other invasive malignancy within two years except for non-invasive malignancies such as cervical carcinoma in situ, non-melanomatous carcinoma of the skin or ductal carcinoma in situ of the breast that has/have been surgically cured. Cancer patients with incidental histological findings of prostate cancer (tumour/node/metastasis stage of T1a or T1b or prostate-specific antigen <10) who have not received hormonal treatment may be included.
10. Uncontrolled inter-current illness including, but not limited to, ongoing or active infection, symptomatic congestive heart failure, uncontrolled hypertension, unstable angina pectoris, cardiac arrhythmia, active peptic ulcer disease or gastritis, or psychiatric illness/social situations that would limit compliance with study requirement or compromise the ability of the patient to give written informed consent
11. Any condition that, in the opinion of the investigator or sponsor, would interfere with the evaluation of the investigational product or interpretation of patient safety or study results
12. Patients with a condition requiring systemic treatment with either corticosteroids (>10 mg

daily prednisolone equivalents) or other immunosuppressive medications within 14 days of study drug administration. Inhaled or topical steroids and adrenal replacement doses >10 mg daily prednisolone equivalents are permitted in the absence of active autoimmune disease

13. Systemic antibiotic treatment within 7 days prior to the start of trial treatment

**Date of first enrolment**

31/08/2024

**Date of final enrolment**

31/10/2025

## **Locations**

**Countries of recruitment**

Australia

England

United Kingdom

**Study participating centre**

**Royal Surrey County Hospital**

Egerton Road

Guildford

United Kingdom

GU2 7XX

**Study participating centre**

**The Christie**

550 Wilmslow Road

Withington

Manchester

United Kingdom

M20 4BX

## **Sponsor information**

**Organisation**

University of Southampton

**Sponsor details**

MP131, Southampton General Hospital

Southampton

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United Kingdom  
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**Sponsor type**

University/education

**Website**

<https://www.southampton.ac.uk/>

**ROR**

<https://ror.org/01ryk1543>

## **Funder(s)**

**Funder type**

Industry

**Funder Name**

Imugene Limited

## **Results and Publications**

**Publication and dissemination plan**

1. Peer reviewed scientific journals
2. Conference presentation
3. Publication on website
4. Submission to regulatory authorities

**Intention to publish date**

31/03/2030

**Individual participant data (IPD) sharing plan**

The data-sharing plans for the current study are unknown and will be made available at a later date

To meet our ethical obligation to share data generated by interventional clinical trials responsibly, SCTU operates a transparent data-sharing request process. At a minimum, anonymous data will be available for request from three months after the publication of an article, to researchers who provide a completed Data Sharing request form that describes a methodologically sound proposal, for the approved proposal and a signed Data Sharing Agreement if appropriate. Data will be shared once all parties have signed relevant data-sharing documentation.



Researchers interested in our data are asked to complete the Request for Data Sharing form (CTU/FORM/5219) [template located on the SCTU website, <https://www.southampton.ac.uk/ctu>] to provide a brief research proposal on how they wish to use the data. It will include; the objectives, what data are requested, timelines for use, intellectual property and publication rights, data release definition in the contract, participant informed consent, etc. If considered necessary, a Data Sharing Agreement from Sponsor may be required.

#### **IPD sharing plan summary**

Data sharing statement to be made available at a later date