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Understanding why cancer immunotherapy helps some people but causes side effects in others

Submission date 12/03/2026	**Recruitment status** Recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 24/04/2026	**Overall study status** Ongoing	
Last Edited 24/04/2026	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims

Immunotherapy (also called immune oncology treatment) is a type of cancer treatment that works by helping the body's immune system recognise and attack cancer cells. In recent years, immunotherapy has improved outcomes for many patients with different types of cancer. Some patients respond very well, while others may have little or no benefit. Currently, doctors cannot reliably predict which patients will respond well to immunotherapy and which patients may develop side effects.

The MANIFEST study (Multiomic ANalysis of Immunotherapy Features Evidencing Success and Toxicity) aims to improve our understanding of how cancers respond to immunotherapy and why some patients develop treatment-related side effects. Researchers will study biological samples and clinical information from patients receiving immunotherapy to identify patterns that may explain these differences.

By analysing blood, tumour tissue, and other samples collected during routine hospital visits, researchers hope to learn more about the biological features of cancer and how the immune system interacts with it during treatment. The study will also look at genetic and molecular information from cancer cells and immune cells.

The knowledge gained from this research may help doctors predict how different patients will respond to immunotherapy and identify those who may be at higher risk of side effects. In the future, this could help doctors choose the most appropriate treatments for patients and develop new ways to treat cancer.

This study is part of the wider MANIFEST consortium, a national research initiative in the UK designed to improve how immunotherapy treatments are used and to support more personalised cancer care.

Who can participate?

Adults (aged 18 years or older) who have been diagnosed with cancer and are due to receive immunotherapy treatment may be invited to take part in the study.

Participants will be recruited from participating hospitals across the United Kingdom. Patients may be approached about the study if their clinical team believes they meet the eligibility criteria.

Taking part in the study is completely voluntary. Patients can decide whether or not to participate, and choosing not to take part will not affect their treatment or care in any way. Participants can also withdraw from the study at any time without giving a reason.

What does the study involve?
This is an observational research study, which means that taking part will not change the treatment that patients receive as part of their usual care. Participants will continue to attend their normal hospital appointments and receive the treatment recommended by their clinical team.
If a patient agrees to take part, researchers will collect additional samples and information during routine clinic visits, including;
Blood samples:
Extra blood samples may be taken during routine blood tests. These samples help researchers study how the immune system and cancer cells change during treatment.
Tumour tissue samples:
Researchers may request access to leftover tumour tissue from biopsies or surgery that were already performed as part of routine care. In some cases, patients undergoing a biopsy whilst enrolled may be asked if they are willing to provide additional tissue sample specifically for research. This is optional, and patients can decline without affecting their treatment.
Stool samples:
Participants may be asked to provide stool (poo) samples. Researchers are interested in understanding how gut bacteria may influence how patients respond to immunotherapy or develop side effects.
Urine samples:
Some patients may also be asked to provide urine samples, particularly if their type of cancer commonly involves urine testing as part of routine care.
Samples may be collected at several time points, such as before starting treatment, during treatment, and if side effects occur. Researchers will also collect information from medical records, including details about cancer diagnosis, treatments received, scan results, blood tests, and any side effects experienced.
In some hospitals, patient-reported outcome questionnaires that are already used in routine care may also be included in the research analysis to better understand patients' symptoms and quality of life during treatment.
Researchers will analyse the samples in laboratories to study the biological and genetic characteristics of cancer and immune cells. This information will be used to understand how cancer changes during treatment and why responses and side effects vary between patients.

What are the possible benefits and risks of participating?
Participants are unlikely to benefit directly from taking part in the study. The purpose of the research is to increase scientific understanding of cancer and immunotherapy, which may benefit future patients.
There are some minor risks associated with taking part in the study. These mainly relate to the collection of research samples.
Blood tests may occasionally cause minor discomfort, bruising, dizziness, or infection at the site where the needle enters the skin.
Providing stool or urine samples does not pose any medical risk.
Participation in the study will not delay or change the medical treatment patients receive.

Where is the study run from?
The study is coordinated by The Christie NHS Foundation Trust in the United Kingdom.
Patients will take part through participating hospitals across the UK that are part of the MANIFEST research platform.

Biological samples and research data may be analysed by collaborating laboratories and research institutions within the MANIFEST consortium. These may include universities, academic research centres, and approved research partners.

When is the study starting and how long is it expected to run for?
The study is expected to begin recruitment in 2026.
Researchers plan to recruit approximately 3,000 patients across the UK.
Participants will be followed during their immunotherapy treatment and afterwards, and samples and clinical information may be analysed for several years to achieve the study objectives.
Overall, the study is expected to run for several years in order to collect and analyse sufficient data.

Who is funding the study?
The study is funded by the UK Office for Life Sciences (OLS) and the Medical Research Council (MRC).
The research is organised and sponsored by The Christie NHS Foundation Trust.

Who is the main contact?
The Chief Investigator for the study is:
Professor Samra Turajlić
Consultant Medical Oncologist
Patients who have questions about the study can speak to their clinical team or local research staff at their hospital, or contact the study team via email: the-christie.manifest-study@nhs.net

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Central Portfolio Management System (CPMS)
70680

Grant code

MR/Z505158/1

Integrated Research Application System (IRAS)
361605

Study information

Scientific Title
MANIFEST: Multiomic ANalysis of Immunotherapy Features Evidencing Success and Toxicity

Acronym
MANIFEST

Study objectives
Primary objective:
To determine the proportion of patients who derive clinical benefit from treatment with anti-cancer immunotherapies

Secondary objectives:
1. To determine the proportion of patients who develop primary vs. secondary resistance in the peri-operative and advanced settings
2. To determine the proportion of patients who experience immune-related adverse events (irAEs) during treatment with anti-cancer immunotherapy
3. To profile biological and clinical characteristics at baseline and during treatment with immunotherapy to identify indicators of treatment response and resistance
4. To profile biological and clinical characteristics at baseline and during treatment with immunotherapy to decipher predictors of irAEs

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 21/01/2026, North West - Greater Manchester East Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; -; gmeast.rec@hra.nhs.uk), ref: 25/NW/0307

Primary study design
Observational

Secondary study design
Cohort study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Psychosocial oncology and survivorship

Interventions

MANIFEST is an observational research study. It will involve patients who are receiving immunotherapy as part of their planned cancer treatment at NHS hospitals - the study will not change or interfere with the care they receive. The aim is to collect and analyse samples and data that may help us better understand why some people benefit from immunotherapy, while others do not, and why some experience side effects.

We aim to recruit up to 3,000 adult patients with cancer who are about to start or are currently receiving immunotherapy. Patients will only take part if they give informed consent.

Participants will be invited to give samples and data at different time points over the course of their treatment.
Generally, these may include:
• Blood samples (up to 60 ml, about 4 tablespoons) at baseline (before treatment), early during treatment (usually around weeks 2 and 6), and at later timepoints (weeks 12, 24, and 52).
• Stool samples collected at up to 4 timepoints to study the gut microbiome.
• Tumour samples taken from leftover tissue from routine biopsies or surgeries. No additional procedures are required solely for the study.
• Clinical data collected from patient records, including test results, scans, and details of treatment and outcomes.

The exact schedule may vary depending on each patient's treatment timeline and the availability of clinical appointments. The samples will be analysed in research laboratories using a variety of methods to study the immune system, tumour DNA, and other biological factors.

All data and samples will be securely stored and handled with strict confidentiality. Participation is voluntary, and patients can withdraw at any time without affecting their care.

Intervention Type
Other

Primary outcome(s)
1. Proportion of patients who derive clinical benefit from treatment with anti-cancer immunotherapies measured using Review of clinical outcomes from patient medical records and routine clinical assessments, including radiological imaging and clinical response documentation recorded in the electronic case report form (eCRF) at Baseline and throughout treatment and follow-up during the study period (up to 36 months follow-up after recruitment)

Key secondary outcome(s))
1. Development of primary versus secondary resistance to immunotherapy measured using Review of clinical outcomes from patient medical records, including disease progression documented through routine clinical imaging and oncology assessments at Baseline and throughout treatment and follow-up during the study period

2. Occurrence and severity of immune-related adverse events (irAEs) during treatment with immunotherapy measured using Clinical assessment and review of patient medical records with adverse events graded using Common Terminology Criteria for Adverse Events (CTCAE) v5.0 at Throughout treatment and follow-up during the study period

3. Biological characteristics associated with treatment response or resistance to immunotherapy measured using Laboratory analysis of biological samples including tumour blood, stool and urine using molecular and immunological profiling techniques such as whole exome sequencing,

RNA sequencing, immune methylation profiling, and T-cell/B-cell receptor sequencing, as well as spatial biology profiling at Baseline and longitudinal sampling during treatment (multiple timepoints as defined in the study schedule)

4. Biological characteristics associated with development of immune-related adverse events measured using Laboratory analysis of biological samples (blood, tumour tissue, stool, urine) including genomic, immune and microbiome profiling, as well as spatial biology profiling at Baseline, longitudinal sampling during treatment, and additional sampling at the time of immune-related adverse events

Completion date
31/07/2029

Eligibility

Key inclusion criteria
1. Written or electronic informed consent
2. Age 18 years or older
3. Confirmed diagnosis of a solid organ malignancy with a clinical indication and appropriate treatment plan to commence an immunotherapy either as standard of care or as part of a clinical trial with/without the use of investigational agents

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
120 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Medical or psychological condition that would preclude informed consent
2. Subjects unable to comply with the study or sample schedule

Date of first enrolment
04/02/2026

Date of final enrolment
31/07/2028

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
-
-
-
England
-

Sponsor information

Organisation
The Christie NHS Foundation Trust

ROR
https://ror.org/03v9efr22

Funder(s)

Funder type
Government

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

Data collected will be stored in a custom-built Trusted Research Environment hosted by TRELLis software (the MANIFEST Database). This is a unique infrastructure developed at Crick with funding from DARE-UK from Health Data Research UK, allowing deployment of secure environments across AWS, Google and Azure clouds, using Snowflake data-fabric (ISO27001 and HIPAA compliant). Data can be loaded from multiple sources allowing both primary and meta-analysis against identifiable data. The data collected will include anonymised and pseudonymised clinical data collected from the study (patient outcomes, treatment regimens, adverse events etc) as well as data generated from the further downstream analysis of the patient samples provided under the MANIFEST platform (for description of the platform and current data paradigms, see Lim, Tippu et al. Cancer Discov 2025). The MANIFEST database will led by the MANIFEST Data Management Group (DMG) whose responsibilities will include review and approval of applications to access the data within the MANIFEST database. The DMG will assess applications against key criteria including scientific and strategic merit, applicant capability to deliver, ethical and legal compliance, data minimisation and justification, data security and access environment and operational feasibility. We expect that both academic and industry partners would find value in accessing the MANIFEST database in parts or entirety. Data sharing would be through secure means within the TRE environment or though other direct sharing permissions with explicit consent of the DMG. The MANIFEST ICF and PIS were written with this model in mind, and we have included key clauses on sharing data for further research uses including with commercial partners.

IPD sharing plan summary

Stored in publicly available repository