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A clinical trial assessing the safety, tolerability and anti-tumour activity of the ITOP1 vaccination in patients with surgically resectable oesophageal adenocarcinoma

Submission date 04/12/2024	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 13/02/2025	**Overall study status** Ongoing	
Last Edited 08/10/2025	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims

Unfortunately, it is very common for patients with oesophageal cancer for their cancer to return at a later date. The VISTA trial aims at reducing this risk for those patients with oesophageal cancer who have received an initial course of chemotherapy and then had their main tumour removed by surgery. VISTA will investigate a new cancer vaccine called ITOP1, which uses virus-based technology. A cancer vaccine is similar to those given for seasonal flu and is made up of dead/weakened germs to train the immune system to protect against future infection. ITOP1 aims to help the immune system ‘mop up’ any cancer cells still in the body after treatment and prevent them from developing into new cancers. ITOP1 has not been used on patients before, and VISTA is designed to look at its safety, any side effects the vaccine may cause, and early signs of the vaccine’s potential to prevent cancer from coming back. The current UK standard of care for newly diagnosed treatment of oesophageal cancer is based on a course of chemotherapy given before the primary tumour is removed by surgery, followed by further chemotherapy once the patient has fully recovered from surgery. The first (prime) injection of the ITOP1 dose will be given 4 weeks after the first course of chemotherapy and before the surgery. A second (boost) dose injection would be given before the second course of chemotherapy. This ensures that it would not harm the standard of care that the patients can expect to receive. The aim of ITOP1 is that once the main tumour is removed, the body's immune response will be triggered by the vaccine and prevent the cancer from returning or spreading, which is the cause of the majority of oesophageal cancer deaths.

Who can participate?

Patients with a histological diagnosis of oesophageal or gastroesophageal junctional (types 1, 2 or 3) adenocarcinoma, deemed suitable for surgery with curative intent

What does the study involve?
In Phase I of the trial, 8 participants will receive ITOP1 and then a review of these patients' side effects to ITOP1 will be carried out before Phase II opens. Phase II will recruit 52 participants, to receive either ITOP1 or saline, which will be randomly assigned.

What are the possible benefits and risks of participating?
Whether or not participants would benefit from the treatment in the main phase of this research trial is unknown. By entering this trial, participants will be making a significant contribution to increasing the knowledge of oesophageal adenocarcinoma, which may help us to improve the future treatment of patients with these cancer types and others, based on their response to the trial treatment.

Risk: ITOP1 has not been given to human subjects before
Minimisation of risk: ITOP1 uses a replication deficient virus as a carrier or 'vector' as a way of delivering the cancer antigens; Ad5 is the adenovirus vector used. The use of Ad5 represents a mitigation, in that this is a well-established system that has been used clinically previously. The Phase I Safety Lead-in will give ITOP1 to 8x patients, with safety to be reviewed by a safety review committee before Phase II opening. Should participants report or display such signs or symptoms in keeping with a clinically significant viral infection at 5 days following ITOP1 administration, the investigator should investigate and treat accordingly and perform an adenovirus polymerase chain reaction (PCR) blood test. This PCR test will look to see if the ITOP1 virus has been able to make copies of itself. If this is positive, an additional blood sample may be requested by Infinitopes to perform custom PCR testing.

Risk: Administering ITOP1
Minimisation of risk: Assessment of full blood count, liver, renal and endocrine function will be made before each administration

Management of anticipated adverse reactions from ITOP1 is outlined in the guidelines in the protocol. To date, no subject has received ITOP1. There is currently no known antidote with ITOP1. Should an overdose occur, patients should be admitted for careful monitoring, and management should be supportive and tailored to symptoms as they arise. Any patient who inadvertently receives a higher dose than intended should be monitored closely, managed with appropriate supportive care until recovery and followed up expectantly.
Risk: There is a risk associated with additional research sample collection; Blood samples could cause pain, bruising or bleeding.
Risk minimisation: The trial will only be conducted at hospitals with expertise in the treatment and diagnosis of OAC to ensure the highest standard of care for the patients.

The trial has undergone a risk assessment involving the operational team, oncology consultants and nursing team, along with pharmacists and statisticians. The trial set-up has also involved patient involvement, with 3 members from a PPI group who have lived experience of oesophageal cancer. Meetings have been held to review the patient pathway through the trial, and also discuss the sampling schedule and visit burden, in addition to patient-facing documentation and their input has tailored how the trial is presented to potential patients. These PPI members will also sit on the TMG and DSMC.
Risk: Additional exposure to radiation due to additional CT Scans
Risk minimisation: A radiation risk assessment has been conducted on the trial, which determined that the additional risk of developing cancer as a consequence of taking part in this study is negligible due to the poor prognosis of this study group.

Where is the study run from?
University of Oxford, UK

When is the study starting and how long is it expected to run for?
December 2024 to October 2028

Who is funding the study?
Infinitopes

Who is the main contact?
OCTO-VISTA@oncology.ox.ac.uk

Plain English summary under review with external organisation

Contact information

Type(s)
Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1008088

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
OCTRU429

Study information

Scientific Title
A phase I/IIa, double-blinded, randomised controlled trial to assess the safety, tolerability, and early signs of anti-tumour activity of ITOP1 – a prime/boost viral vector vaccine targeting tumour-specific antigens in subjects with surgically resectable oesophageal adenocarcinoma

Acronym
VISTA

Study objectives
Characterisation of the safety and tolerability of ITOP1

Immunogenicity of ITOP1; Preliminary clinical efficacy of ITOP1

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 05/02/2025, South Central - Berkshire B Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, UK; +44 (0)2071048276; berkshireb.rec@hra.nhs.uk), ref: 25/SC/0004

Study design
Phase I/IIa double-blind randomized placebo-controlled trial

Primary study design
Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Surgically resectable oesophageal adenocarcinoma deemed suitable for surgery and neoadjuvant /adjuvant chemotherapy

Interventions
The trial design will piggyback onto the participant's regular standard of care (SoC) treatment such as surgery and chemotherapy (i.e., the vaccine will be given without any changes or disturbances to the standard of care treatment). The vaccine will be given to participants in two doses, the first dose (priming dose) will be given approximately four weeks after the first round of chemotherapy and before surgery. The second dose (booster) will be given before the second

round of chemotherapy. Once the main tumour is surgically removed, the vaccine is hoped to stimulate the immune system to prevent the development of new and spreading tumours, which is the main cause of death in patients with OAC.

The trial will be conducted in two phases and a total of 60 participants will be enrolled. In Phase I, 8 patients will receive the ITOP1 vaccine, and a safety review will be conducted before moving to Phase II. In Phase II, 52 patients will be randomly assigned on a 3:1 basis via the secure online database to receive either the ITOP1 vaccine or a placebo (sterile normal saline).

Intravenous bolus injection of ITOP1 will be achieved via peripheral venous cannulation on the day of treatment. In the Phase I Safety Lead-in of 8 participants, participants will receive $6x10^{10}$ viral particles of ITOP1A/B. For Phase II participants, between $2x10^{10}$ and $6x10^{10}$ viral particles will be administered per dose depending on the eligible participant's HLA genotype.

Treatment will be given in a prime/boost regimen following neoadjuvant and before adjuvant FLOT (fluorouracil, leucovorin, oxaliplatin, and docetaxel) chemotherapy. ITOP1/placebo prime dose should take place 4 weeks after their final cycle of neoadjuvant chemotherapy. ITOP1 boost dose/placebo visit is expected to take place 10 weeks (within a window of 8 -16 weeks) after surgery, however, can be delayed in accordance with post-surgery standard of care.

Participants will be followed up for 2 years from when they receive their first dose of ITOP1 /Placebo (with the possibility to extend with the optional survival follow-up period).

For Phase II, participants will be randomly allocated to the treatment options (3:1 to receive ITOP1 or placebo) via the automated, secure (encrypted), web-based database provided by the Oxford Clinical Trials Research Unit (OCTRU) using the REDCap platform randomisation function.

Intervention Type
Drug

Phase
Phase I/II

Drug/device/biological/vaccine name(s)
ITOP1A/B [ITOP1] , ITOP1C/D [ITOP1] , ITOP1E/F [ITOP1]

Primary outcome(s)
The safety and tolerability of ITOP1 measured using data collected in the Case Report Form (CRF) and medical notes of the incidence of serious adverse events (SAEs), the incidence of Grade 3 or higher AEs (graded according to CTCAE v5.0), the incidence of immune-related adverse events (irAE) and participant progression to surgical resection during the treatment period (week 12-26) and follow-up period (week 40-116)

Key secondary outcome(s))
1. Immunogenicity of ITOP1 will be measured using the tumoral and peripheral immune responses to ITOP1, and kinetics of the ITOP1 induced specific T cell response through sample analysis of the tumour sample from surgery resection in addition to the translational blood samples taken at various visits from Baseline to Week 116
2. Preliminary clinical efficacy of ITOP1 will be measured by recurrence-free survival (recurrence

at any site by RECIST v1.1) at follow-up CT/MRI scans (Week 40-116), and overall survival measured from the time of surgery (Week 14 through to Week 116, and optional long-term Follow-up period)

Completion date
31/10/2028

Eligibility

Key inclusion criteria
1. Histological diagnosis of oesophageal or gastroesophageal junctional (types 1, 2 or 3) adenocarcinoma, deemed suitable for surgery with curative intent
2. Deemed suitable for oesophagectomy with curative intent by the relevant multidisciplinary team
3. Planned neoadjuvant and adjuvant treatment with FLOT chemotherapy
4. ECOG performance status of 0 or 1
5. Written informed consent obtained for Phase I/Phase II.
6. Age 18 years and above
7. Willing and able to comply with the protocol for the duration of the study including undergoing treatment, scheduled visits, examinations, biopsies and follow-up.
8. Adequate normal organ and marrow function as defined below.
8.1. Laboratory parameters for vital functions should be in the normal range. Laboratory abnormalities that are not clinically significant are generally permitted, except for the following laboratory parameters, which must be within the ranges specified, regardless of clinical significance:
8.2. Lab Test Value required: Haemoglobin (Hb): ≥ 90 g/L
8.3. Neutrophil count: ≥ 1.5 x 10^9/L
8.4. Platelet count: ≥ 100 x 10^9/L
8.5. Serum creatinine, or Creatinine Clearance: ≤ 1.5x Institutional Upper Limit of Normal (ULN), or ≥ 40 mL/min (by Cockcroft-Gault formula)
8.6. AST or ALT, AST (SGOT)/ALT (SGPT): ≤ 2.5 x institutional upper limit of normal
8.7. Alkaline phosphatase: ≤ 2.5 x ULN
8.8. Serum bilirubin: ≤ 1.5 x institutional ULN. This will not apply to subjects with documented Gilbert's syndrome as evidenced by persistent or recurrent hyperbilirubinemia that is predominantly unconjugated in the absence of haemolysis or hepatic pathology, who are excluded if total bilirubin > 3.0 x ULN or direct bilirubin > 1.5 x ULN

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
Current exclusion criteria as of 21/02/2025:

1. Prior treatment in another clinical study with an investigational product within 4 weeks prior to Day 1 of the study; any respective adverse events must have resolved to Grade 1 or lower to be eligible.
2. Any contraindications to the FLOT chemotherapy or planned surgery
3. Active or prior documented autoimmune disease within the past 2 years NOTE: Subjects with coeliac disease vitiligo or psoriasis not requiring systemic treatment (within the past 2 years) are not excluded
4. Active or prior documented inflammatory bowel disease (e.g., Crohn's disease, ulcerative colitis)
5. History of allogeneic organ transplant
6. Mean QT interval corrected for heart rate (QTc) ≥470 ms calculated from 3 electrocardiograms (ECGs) using Fredericia's Correction
7. Uncontrolled intercurrent 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, active bleeding diatheses including any subject known to have evidence of acute or chronic hepatitis B, hepatitis C, known immunodeficiency or human immunodeficiency virus (HIV), or psychiatric illness/social situations that would limit compliance with study requirements or compromise the ability of the subject to give written informed consent
8. Known history of previous clinical diagnosis of tuberculosis
9. History of severe allergic reactions to any unknown allergens or any components of the study drugs.
10. Known dihydropyrimidine dehydrogenase (DPD) deficiency
11. Peripheral sensory neuropathy with functional impairment.
12. History of sarcoidosis/sarcoidosis syndrome.
13. Major surgical procedure (as defined by the Investigator) within 30 days prior to Day 1 or still recovering from prior surgery.
14. SARS-CoV2 vaccine (mRNA, subunit/viral vector or other) within 6 weeks of administration of first dose of study drug(s); or any live attenuated vaccine within 28 days of first dose of study drug(s).
15. Women who are breastfeeding or pregnant as evidenced by positive serum pregnancy test (minimum sensitivity 25 IU/L or equivalent units of HCG).
16. Patients of reproductive potential who are not willing to use adequate contraceptive measures for the duration of the trial and for 6 months after the last dose of trial IMP (both male and female patients). Male participants must use condoms for the duration of the trial and for 6 months after the last dose of trial IMP.
17. Patients unable to commit to avoiding contact with young children or the severely immunocompromised for 5 days after each IMP dose*
18. Any condition that, in the clinical judgment of the treating physician, is likely to interfere with the evaluation of trial treatment, interpretation of subject safety or trial results, prevent the subject from complying with any aspect of the protocol or that may put the subject at unacceptable risk.

*Defined as follows:
'Young children' are individuals aged 0 to 12 years old who do not otherwise meet the criteria for 'severely immunocompromised'.
'Severely immunocompromised' are those who meet any of the following criteria:
1. Active haematological malignancy (excluding monoclonal gammopathy of undetermined significance (MGUS), or those currently receiving treatment for a haematological malignancy and /or those within 1 year of bone marrow or stem cell transplant
2. Solid organ transplant(s) requiring immunosuppression

3. Advanced or untreated HIV/AIDs
4. Congenital or primary immunodeficiencies
5. Immunosuppressive therapy (equivalent to ≥20 mg/day of prednisone for ≥2 weeks)
6. End-stage renal disease
7. Other condition(s) which, in the opinion of the Principal Investigator, would put close contacts of participants receiving ITOP1 at unreasonable risk should ITOP1 result in clinically significant viral shedding in the 5 days following dosing

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Previous exclusion criteria:

1. Prior treatment in another clinical study with an investigational product within 4 weeks prior to Day 1 of the study; any respective adverse events must have resolved to Grade 1 or lower to be eligible.
2. Any contraindications to the FLOT chemotherapy or planned surgery
3. Active or prior documented autoimmune disease within the past 2 years NOTE: Subjects with coeliac disease vitiligo or psoriasis not requiring systemic treatment (within the past 2 years) are not excluded
4. Active or prior documented inflammatory bowel disease (e.g., Crohn's disease, ulcerative colitis)
5. History of allogeneic organ transplant
6. Mean QT interval corrected for heart rate (QTc) ≥470 ms calculated from 3 electrocardiograms (ECGs) using Fredericia's Correction
7. Uncontrolled intercurrent 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, active bleeding diatheses including any subject known to have evidence of acute or chronic hepatitis B, hepatitis C, known immunodeficiency or human immunodeficiency virus (HIV), or psychiatric illness/social situations that would limit compliance with study requirements or compromise the ability of the subject to give written informed consent
8. Known history of previous clinical diagnosis of tuberculosis
9. History of severe allergic reactions to any unknown allergens or any components of the study drugs.
10. Known dihydropyrimidine dehydrogenase (DPD) deficiency
11. Peripheral sensory neuropathy with functional impairment.
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15. Women who are breastfeeding or pregnant as evidenced by positive serum pregnancy test (minimum sensitivity 25 IU/L or equivalent units of HCG).
16. Patients of reproductive potential who are not willing to use adequate contraceptive measures for the duration of the trial and for 6 months after the last dose of trial IMP (both male and female patients)
17. Any condition that, in the clinical judgment of the treating physician, is likely to interfere with the evaluation of study treatment, interpretation of subject safety or study results, prevent the subject from complying with any aspect of the protocol or that may put the subject at unacceptable risk.

Date of first enrolment
30/05/2025

Date of final enrolment
31/10/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Churchill Hospital
Churchill Hospital
Old Road
Headington
Oxford
United Kingdom
OX3 7LE

Study participating centre
St James's University Hospital
Beckett Street
Leeds
United Kingdom
LS9 7TF

Study participating centre
Southampton General Hospital
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Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Industry

Funder Name
Infinitopes

Results and Publications

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

IPD sharing plan summary
Data sharing statement to be made available at a later date

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