NHS Cancer Vaccine Launch Pad

NHS Cancer Vaccine Launch Pad Protocol

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The NHS Cancer Vaccine Launch Pad (CVLP) is coordinated by the Southampton Clinical Trials Unit (SCTU).

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FUNDER

This trial is primarily funded by NHS England with additional financial support from CVLP industry partners.

Protocol Information

This protocol describes the CVLP trial and provides information about procedures for entering participants. The protocol should not be used as a guide for the treatment of other non-trial participants; every care was taken in its drafting, but corrections or amendments may be necessary. These will be circulated to investigators in the trial, but sites entering participants for the first time are advised to contact Southampton Clinical Trials Unit to confirm they have the most recent version.

Compliance

This trial will be conducted in compliance with the approved protocol and will adhere to the principles of GCP guidelines, the current Data Protection Regulations, the Sponsor's (and any other relevant) SOPs, and other regulatory requirements as appropriate.

Contents

1. Introduction

The NHS Cancer Vaccine Launch Pad (CVLP) is a project to establish the feasibility of pathways to enable NHS patients with cancer to access cancer vaccine trials.

From August 2025, the scope of the CVLP will broaden to also support clinical trials of immunotherapies that may benefit from the CVLP pathway as detailed in this protocol. The CVLP will support clinical trials that fall within the scope detailed below:

- Personalised cancer vaccine trials requiring biological samples for vaccine manufacture
- Immunotherapy trials, including non-personalised / “off-the-shelf” cancer vaccine trials, with an element of molecular profiling using biological samples for trial eligibility and/or treatment stratification*.

*NB - The requirement for the trial to have molecular or genetic profiling is not limited to the investigational therapy but can be for any part of the decision-making process for eligibility or treatment stratification.

Therefore, the CVLP aims to investigate the optimum process for patients, across multiple cancer types, to receive cancer vaccines and novel immunotherapies by enrolment in the CVLP.

The CVLP will support delivery of key UK ambitions, including Genome UK, The Life Sciences Vision, the NHS Genomics Strategy, and the NHS 10 Year Health Plan for England. It includes these shared ambitions:

- To give patients an opportunity to participate in research for their potential benefit and to inform future care for other patients.
- To accelerate the development of cancer vaccines, as well as other immunotherapies, from being an innovation to representing 'business-as-usual'.
- To create the most advanced and integrated genomic research healthcare ecosystem in the world.
- To use genomic research assets to drive the next generation of Life Sciences discoveries.

The CVLP is a collaborative project including NHS England (NHSE), Genomics England, the Department of Health and Social Care, the Office for Life Sciences, and the National Institute for Health and Care Research with involvement of the Cancer Research UK Southampton Clinical Trials Unit (SCTU).

NHS England is the research sponsor for the NHS Cancer Vaccine Launch Pad. The day-to-day management of the CVLP will be coordinated through the Southampton Clinical Trials Unit (SCTU). This protocol sets out guidance to support cancer care providers, vaccine and immunotherapy manufacturers, and clinicians wishing to participate in the Cancer Vaccine Launch Pad. Please email cvlp@soton.ac.uk with any questions regarding this document.

Professor Peter Johnson
National Clinical Director for Cancer
NHS England

Dame Sue Hill
Chief Scientific Officer for England
SRO for Genomics in NHS England
NHS England

2. Background

2.1. Cancer Vaccines

Cancer vaccines are a type of cancer treatment designed to target an individual's unique cancer cells and are split into two types - personalised and non-personalised. Personalised cancer vaccines are created by analysing a patient's tumour and identifying specific mutations that are unique to that cancer, then using that information to create a vaccine tailored to that patient. Non-personalised or “off-the-shelf” cancer vaccines use mutations which are common in the same cancer type in many patients. The intention of both types is that the vaccine will stimulate the immune system to specifically recognise and destroy the cancer cells. Cancer vaccines are considered a type of targeted immunotherapy.

Newer cancer vaccines are based on messenger RNA (mRNA) technology. Unlike traditional vaccines, which contain dead or weakened forms of disease-causing agents, mRNA vaccines contain instructions for the body's own cells to produce a protein that is found in a patient's cancer cells.

Cancer vaccines are in the experimental stages, with phase 2 and 3 studies required to determine their safety and efficacy.

2.2. Immunotherapies

Targeted immunotherapies are a type of cancer treatment designed to help the immune system identify and attack cancer cells. These therapies work by focusing on particular features found on, or within, cancer cells that distinguish them from healthy cells.

There are different types of targeted immunotherapies. One approach uses antibodies that bind to specific targets on cancer cells, blocking signals that help the cancer grow or marking the cells for destruction by the immune system. Another approach involves immune checkpoint inhibitors, which block proteins that would normally restrain immune responses, thereby allowing T cells to better attack cancer.

Targeted immunotherapies may not be appropriate for all patients and all cancer types. Additional diagnostic testing, from patients’ biological samples such as blood and/or tumour tissue, may be required to determine if a targeted immunotherapy is likely to be beneficial for an individual patient and their specific cancer.

Targeted immunotherapies represent a growing area of cancer research and are at varying stages of clinical development, with some already approved for use in certain cancers and others undergoing phase 2 and 3 clinical trials to assess safety and efficacy.

2.3. Aim of the CVLP

The aim of the CVLP is to investigate the basis for accelerated development of cancer vaccine and novel immunotherapy treatments.

The CVLP aims to investigate this by primarily testing a national formalised and standardised patient referral pathway and, when required, parallel testing of a high quality,

expanded pathway for tumour molecular analysis and sequencing, incorporating elements of the NHS Genomic Medicine Service, or equivalent service within devolved nations.

The CVLP will incrementally undertake feasibility assessments to determine the requirements and contributing factors for the development of the below, in preparation for cancer vaccines and other immunotherapies being adopted as part of standard of care:

- a national patient referral network,
- a streamlined tissue preparation pathway, and
- a successful large-scale sequencing pathway.

The primary objective of the CVLP is to determine whether it is feasible to recruit cancer patients to a platform for cancer vaccine and immunotherapy trials, whether there is capacity for tissue samples to be prepared within a suitable time frame (where required) and if this results in acceptable participation in cancer vaccine and immunotherapy clinical trials.

No specific therapeutic intervention will be carried out in this Launch Pad.

Patients who consent may be put forward for clinical trials and where required, surplus tissue samples or other biological samples, obtained through standard of care pathways may be used to assess their molecular eligibility or for treatment stratification. Their clinical data and molecular data (where required) may also be used for hypothesis generation for future trials.

The details of any suitable clinical trials will be made available to the participant and their treating clinical team to see if they would like to consent to take part in the relevant trial.

To achieve this the CVLP will:

1. Identify patients with cancer in the NHS against agreed eligibility criteria.
2. Request consent to the CVLP to access a patient's routinely collected personal, demographic and clinical details, to facilitate their entry in to a clinical trial of a cancer vaccine or immunotherapy that is available through the CVLP.
3. Dependent on the supported clinical trial, arrange for the selection of an appropriate tumour sample, collected during standard of care, for molecular analysis by the CVLP and/or onward clinical trial sponsor.
4. Dependent on the supported clinical trial, arrange for the collection and transfer of a blood sample (or other biological sample), for molecular analysis by the CVLP and/or onward clinical trial sponsor.
5. Collate personal and clinical details along with molecular information (if required) to refer potentially suitable patients into cancer vaccine and immunotherapy trials available through the CVLP, including referral to NIHR-led trials.
6. Coordinate the continued progression of those meeting the required clinical and, if required genetic/molecular, eligibility criteria through clinical trial screening to trial entry and treatment.
7. Annual follow up for all consented to CVLP for disease status and subsequent treatments.
8. Collate molecular information and clinical details from the CVLP to support hypothesis generation for future trials.

The CVLP will be run as a feasibility study, facilitating patient access to cancer vaccine and immunotherapy clinical trials. Patients will be identified across our network of CVLP sites. The programme will be of sufficient scale to allow thousands of patients to be recruited across the UK each year.

2.4. Set up of the CVLP

The CVLP has been set up in a phased approach as detailed in Table 1.

The first phase was designed as a pilot, supporting one commercial partner with identification of participants potentially suitable for one clinical trial of a personalised cancer vaccine.

The second phase expands on the pilot to investigate the CVLP pathways when identifying participants potentially suitable for multiple clinical trials of personalised and non-personalised / "off-the-shelf" cancer vaccines. In this phase, the CVLP will partner with multiple industry partners.

The third phase will investigate the CVLP pathways following a further expansion to the scope to also support clinical trials of novel immunotherapies. In this phase, the CVLP will continue to partner with multiple industry partners.

Table 1 – the phases of the CVLP.

Phase of CVLP	Number of clinical trials supported	Number of commercial partners	Number of cancer subtypes supported	Experimental cancer therapy supported
1	1	1	1	Personalised cancer vaccines
2	>1	>1	>1	Personalised cancer vaccines Non-personalised / "off-the-shelf" cancer vaccines
3	>1	>1	>1	Personalised cancer vaccines Non-personalised / "off-the-shelf" cancer vaccines Immunotherapies

3. Study Design

This is a multicentre prospective observational cohort study for the recruitment and referral of NHS cancer patients to clinical trials of cancer vaccines and immunotherapies available through the CVLP.

Dependent on the requirement of the cancer vaccine or immunotherapy trial, patients will be asked whether they agree to surplus tumour material, collected as part of standard of care, to be sent for DNA analysis and sequencing. Patients may also have blood samples, along with other biological samples (e.g. urine) collected which will also be sent for analysis.

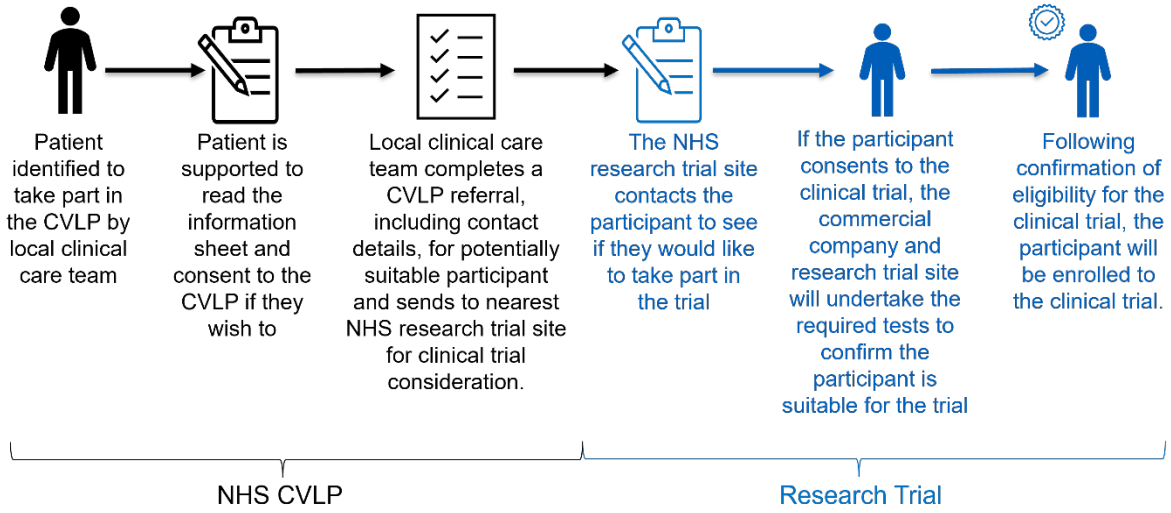
Patients will also be asked to allow access to their relevant medical records and to the storage of routine clinical data. Access to this data will be strictly controlled by NHS England as the

Data Controller, in compliance with applicable Data Protection Legislation. The clinical data will be linked to any molecular information generated as part of the CVLP.

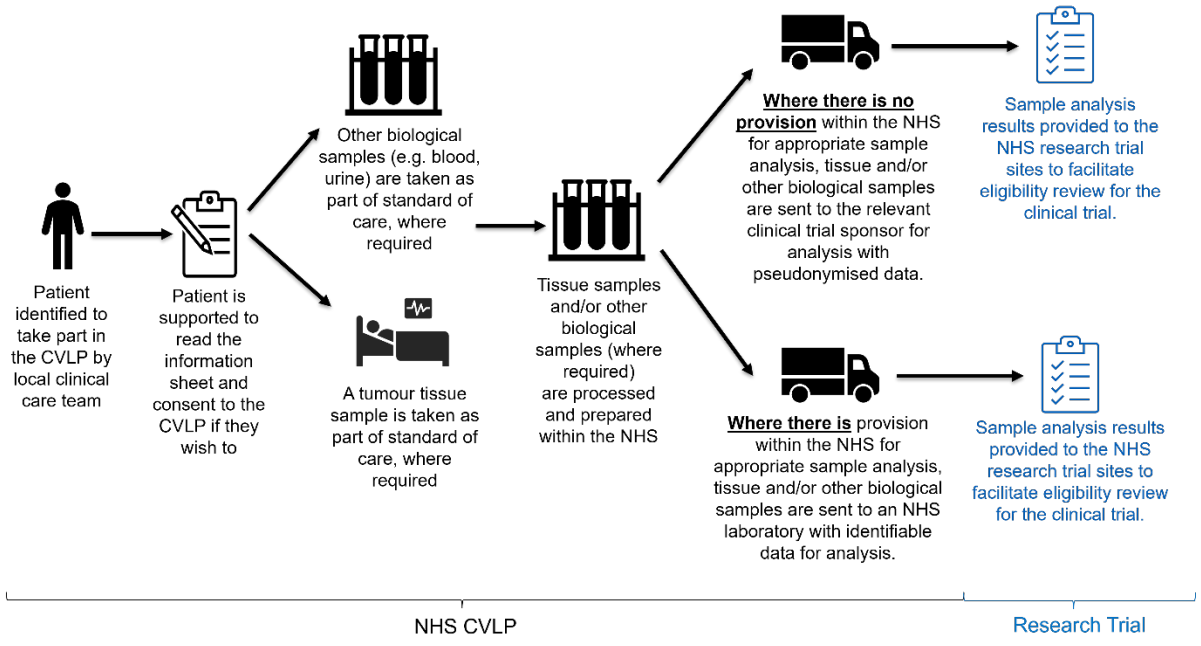
Clinical data will be recorded in the CVLP referral tool at baseline and following any participation in a cancer vaccine or immunotherapy trial. These will include diagnosis, date of diagnosis, month and year of birth, sex, ethnicity, participation in a clinical trial, histopathology date and tumour staging. Outcomes following participation in a clinical trial and yearly survival data will also be collected and stored in the CVLP referral tool.

One or a combination of the referral, tissue, or other biological sample and sequencing pathways will be utilised dependent on the requirements of the supported clinical trials.

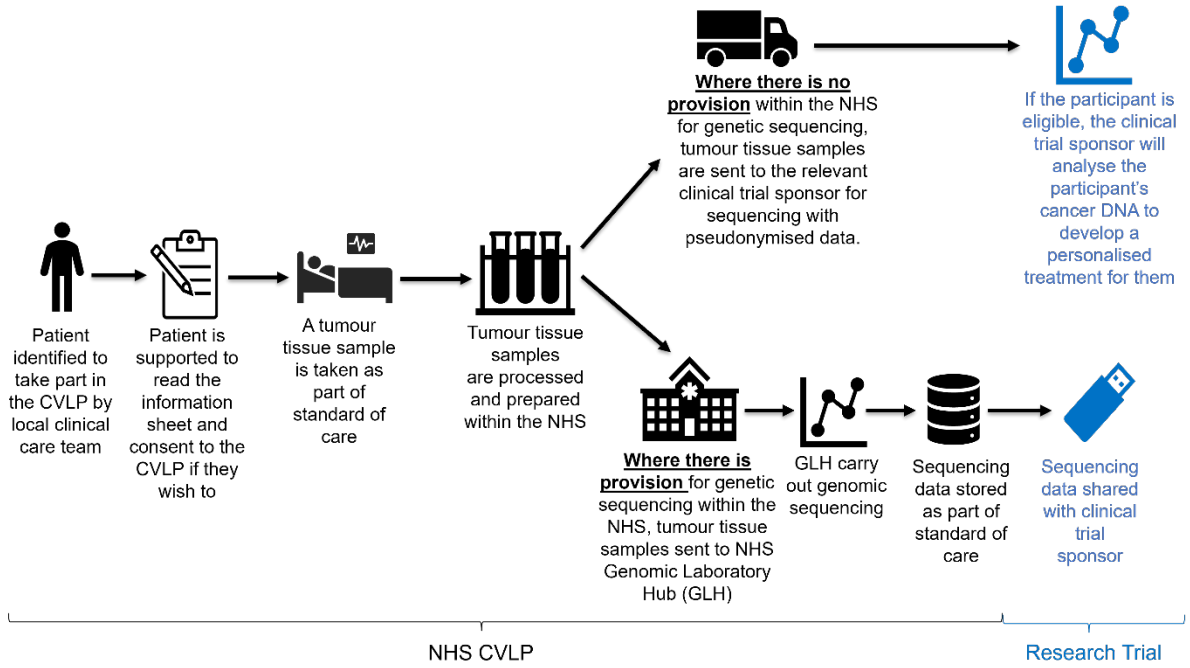
Referral pathway



Tumour tissue (and other biological samples) pathway



Sequencing pathway



In instances where the CVLP supports a clinical trial that requires genomic sequencing, tumour material will be transferred initially to the clinical trial sponsors for nucleic acid extraction, quality assessment and genomic sequencing.

The future ambition is for the samples to be processed and sequenced within the NHS with NHS Genomic Laboratory Hubs (GLHs) or equivalent in the devolved nations undertaking this through standard of care pathways. Prior to the transition, a validation process will be conducted to enable the NHS GLHs to carry out DNA/RNA extraction and then nucleic acid sequencing for "repatriation" into the NHS.

Therefore, where clinical trials requiring genomic sequencing are supported by the CVLP, the CVLP will take on the additional task of organising the sequencing and analysis of the tumour DNA to identify mutations that may be suitable for use in a personalised cancer treatment.

Tumour sequencing, conducted either by the commercial partners or by the NHS, will be delivered in an efficient, streamlined, and timely manner at no cost to the participant or the provider trust or Health Board.

The processes used will follow standard protocols established by the Genomic Medicine Service (GMS) or equivalent in the devolved nations.

3.1. Study research questions

No formal statistical analysis is planned, but the feasibility study will examine the following success criteria:

1. Is the CVLP model a feasible model for recruiting suitable patients to participate in cancer vaccine and immunotherapy trials?

The target number of patients across all cancers to make the CVLP feasible for the support of the planned clinical trials is:

- A total of 300 patients consented by end of November 2024
- A total of 600 patients consented by end of December 2025
- A minimum of 200 additional patients consented per year in following years.

Target numbers of patients is conditional on the size of the cancer vaccine and immunotherapy trials that will be linked to the CVLP and the agreements set within these collaborations.

2. What proportion of patient tumour samples will be prepared for analysis within two weeks (when required)?

When required, patient tumour samples need to be prepared for analysis within no more than two weeks of notification of potential trial suitability. This is the timescale required by clinical trial sponsors to ensure the data is available in accordance with the clinical trial protocols. The target is that this time is met in all cases.

3. What proportion of CVLP participants go on to participate in a cancer vaccine or immunotherapy clinical trials by end of study?

This is an exploratory endpoint to understand how many patients from the CVLP go on to take part in the cancer vaccine or immunotherapy clinical trials linked to the CVLP if eligible. This is expected to be around 10% but may depend upon the number and type of clinical trials supported at any time.

3.2. Secondary research questions

4. Can sequencing outputs from NHS laboratories be used for the manufacturing of therapeutic personalised cancer treatments? (Not applicable until provision is made for genetic sequencing to be completed within the NHS)

This is an exploratory endpoint to determine how the sequencing outputs from NHS laboratories can be used for the manufacturing of therapeutic personalised cancer vaccines.

4.1. Definition of end of study

Since the CVLP is intended as a feasibility study to establish the conditions for successful transition into standard of care pathways, the CVLP will be closed when it is deemed to no longer be feasible or if there is no demand from partner organisations for high volume patient identification and sample access to facilitate recruitment of suitable patients to cancer vaccine and immunotherapy clinical trials.

5. Selection and enrolment of patients

5.1. Eligibility

Inclusion criteria:

Participants who fulfil the following criteria will be eligible for the CVLP:

- Be over the age of 16
- Have a tumour which has been, or will be resected or biopsied

- Have the capacity to consent to involvement in the CVLP
- Have sufficient tumour available for genomic analyses for clinical trials which require it (to be assessed by local pathology once tissue sample is collected)

There are no exclusion criteria specifically for the CVLP.

There will be other eligibility criteria to be considered in addition to the above list. These additional eligibility criteria will be specific for each clinical trial that patients are considered for and referred to and will be outlined in the clinical trial specific - Technical Requirement document.

The CVLP will expand progressively based on cancer subtype. The initial focus was on patients with colorectal cancer, and from March 2025, the CVLP will expand to include other cancer types.

5.2. Consent process

The CVLP will require informed consent. This will enable participants to enter the CVLP freely, with full information about what it means to use their routinely collected personal and clinical information and where required, surplus diagnostic tumour material and other biological samples for potential recruitment into clinical trials of experimental cancer therapies.
Consent must be taken by a health care professional trained in receiving patient consent and well versed with the CVLP study protocol. Participants may decide to take part at the initial discussion, or they may require longer to consider whether they would like to take part. Consent will be obtained using e-consent or paper consent methods in-person or remotely.

E-consent
For e-consent, the Participant Information Sheet and Informed Consent Form will be emailed by the SCTU via Adobe Sign to the participant and the staff member taking informed consent in advance of or during the scheduled in person appointment to consent the patient, or telephone/video call appointment to remotely consent the patient. Site staff should ensure that the patient provides verbal consent for their email address to be sent to the SCTU and this verbal consent must be documented in the patient's medical notes. If the participant withdraws this verbal consent at any time, the SCTU must be notified immediately so the patient's details can be destroyed from SCTU records.

Staff receiving consent will go through the CVLP study information and informed consent process during the in-person appointment or telephone/video call. Once the patient has signed consent electronically, the staff member taking informed consent will also electronically sign the informed consent form. A record of the in-person consent or remote phone/video call should be documented in the patient's medical notes. When consent is completed, an automatic email providing a copy of the completed informed consent form will be sent to the participant for their records; the staff member who took informed consent for printing and filing in the patient's medical records; and the SCTU trial mailbox.

Potential participants can be supported by carers/family members/others to use the e-consent system as appropriate.

Remote paper consent
For remote paper consent, the Participant Information Sheet must be sent to the participant in advance before the scheduled telephone or video call appointment. Staff receiving consent will go through the CVLP study information and informed consent process on phone/video call. For consent, the patient will sign the consent form and return a copy of signed Informed Consent Form in the post/email. The staff receiving consent will sign the patient signed

consent form after receiving this from patient. For remote consent, there will be a discrepancy in dates between patient and staff signing the consent, but this will be explained in patient notes in the informed consent documentation. Site must hold a copy of the fully executed consent form before carrying out any trial activity.

Informed consent will be obtained before any participant personal and clinical information will be shared through the CVLP with suitable clinical trials and where required, before their tumour sample and other biological samples are made available for preparation and analysis.

Obtaining informed consent will be a two-stage process. Firstly, information about the CVLP will be shared using the Patient Information Sheet. Secondly, consent will be obtained using the Informed Consent Form.

Participants will consent for:

i) Access to surplus diagnostic tumour samples and collection of blood or other biological samples (as required),
ii) Collection of routine clinical data, including:
    I. Demographics including ethnicity
    II. staging
    III. diagnostic tests
    IV. treatments received as standard of care
iii) Collection of whether consent to participate in a supported cancer vaccine or immunotherapy trial is given and any reasons for clinical trial withdrawal or discontinuation as relevant to the CVLP
iv) Collection of yearly survival data
v) Collation and storage of this data in the electronic referral tool,
vi) Sending tissue and other biological samples to approved partner organisations in the programme to assess molecular eligibility, to determine treatment stratification, or for personalised treatment manufacture, for cancer vaccine or immunotherapy trials,
vii) Permission to be contacted and offered the choice to participate in trials sponsored by partner organisations,
viii) Permission for data relevant to participation in cancer vaccine or immunotherapy trials to be shared between CVLP sites and trial sites.

The original consent form will be retained by the recruiting NHS site for the hospital notes, and an additional copy will be provided for the patient.

A letter will be sent to the patient's GP informing that they have consented into the CVLP.

Where a participant is required to re-consent or new information is required to be provided to a participant, it is the responsibility of the CVLP sites to ensure this is done in a timely manner.

5.3. Registration procedure

Once a patient is confirmed eligible and has consented into the CVLP, the recruiting NHS site will add the patient details including contact information and routine clinical data into a central electronic referral tool managed by the Southampton Clinical Trials Unit and NHS England. This will enable the patient to be contacted to offer research trials sponsored by partner organisations.

To register patients, CVLP sites will need to complete the required fields within the CVLP referral tool, after which the referral tool will automatically assign a unique subject ID. This ID

will consist of a 4-digit site number (for example 1001 for University Hospital Southampton NHS Foundation Trust) followed by a 4-digit participant number between 0001-9999, which will be assigned sequentially.

Patients who are screen failures will have their year of birth and reasons for failure recorded on a screening log. The screening log will be completed by CVLP sites, recording all patients considered for the study and these will be sent to Southampton Clinical Trials Unit on a regular basis.

5.4. Publicity

Resources may be provided to CVLP sites to aid in increasing public awareness of the CVLP. This may include but is not limited to distribution of study specific information via a short animation, posts published on social media and display of study specific posters at recruiting CVLP sites.

5.5. Withdrawal criteria

No withdrawal criteria are specified other than patient preference. Patients will be able to withdraw from the study at any time and in this event any stored tissue, blood and other biological samples, including nucleic acid, will be disposed of.

The level of withdrawal should be clarified with the patient:

- Withdrawal from CVLP follow-up data collection, but would like to still be contacted about future clinical trials that partner with the CVLP.
- Withdrawal from contact about future clinical trials that partner with the CVLP but continues to provide CVLP follow-up data.
- Withdrawal from CVLP follow-up data collection and does not want to be contacted about future clinical trials that partner with the CVLP.
- Withdrawal from all CVLP activities and requests deletion of personal identifiable data held.

5.6. Study discontinuation

Patients may be discontinued from the study at any time. Specific reasons for discontinuing a patient from this study are:

- Voluntary discontinuation by the patient who is at any time free to discontinue their participation in the study. It should be ascertained and documented as to whether the patient wishes to withdraw from the study completely or only from study procedures (i.e., is happy for information to be collected) according to the levels of withdrawal as detailed in section 5.5.

Patients within this study may have their records flagged with the NHS system to allow tracking through NHS sites and cancer registries and linkage to other health-related records.

5.7. End of study

The end of study for individual patients will occur when one of the following events takes place:

1. The patient reaches the final yearly survival check for the CVLP.
2. The patient is discovered to be ineligible for the CVLP over the course of the study.
3. The patient is lost to annual follow up.

4. The patient withdraws consent from the CVLP.
5. The patient dies.

6. Sample collection

6.1. Biological Samples

Dependent on the requirements of the cancer vaccine or immunotherapy trials supported by the CVLP, tissue samples, blood samples and other biological samples may be collected and used for molecular profiling and genetic sequencing.

Tissue samples accessed for the purposes of CVLP will be surplus diagnostic material collected during routine standard of care.

A unique feature of the CVLP is to test the effective integration with NHS pathology networks through existing NHS tissue pathways. This will involve interfacing with individual pathology units within existing NHS pathology networks.

The specification for tissue, blood or other biological samples may vary and will be dependent on individual cancer vaccine or immunotherapy clinical trial protocols. Details of the sample requirements for each supported clinical trial will be available in the Technical Requirements document specific for each clinical trial.

6.2. Decentralised Cancer Vaccine and Immunotherapy Trial Activity

One of the principles of the CVLP is to widen access to clinical trials of cancer vaccines. To improve participant recruitment with a meaningfully diverse patient population, some trial activities which are within usual care competence may be decentralised and carried out at CVLP sites. For example, collection of a screening or surveillance blood samples, urine or saliva samples. Although these samples may not be collected routinely as standard of care, they do not require staff to have any additional training and can be safely carried out by health care professionals not delegated by the PI. The list of decentralised trial related activities to occur at CVLP sites is not exhaustive and will be risk assessed on a supported trial-by-trial basis. Details of the decentralised trial activities for each cancer vaccine or immunotherapy trial will be available in the Technical Requirements document specific for each trial.

7. Safety

No specific therapeutic intervention is proposed: this programme consists only of collating clinical, and where needed deriving molecular and genetic, information to facilitate the entry of patients to cancer vaccine and immunotherapy trials.

8. Statistics and data analyses

8.1 Sample size

No formal sample size calculation has been performed as sample size targets will be based on recruitment rates over time required by the clinical trials linked to CVLP. In determining whether all patient tumour samples (when required) are prepared for analysis within two weeks, a sample size of 200 per associated clinical trial provides a lower 95% Wilson confidence interval[1] of 0.98 if the observed proportion is 1 (and above 0.9 if at least 189 are

processed in time). This provides evidence that a high proportion of patient samples can be prepared for analysis within two weeks. Sample sizes are anticipated to be at least this large in order to support the other clinical trials linked to CVLP.

8.2 Statistical analysis

No formal statistical testing will be performed. Baseline characteristics of participants (e.g., demographics, disease characteristics) will be described using appropriate summary statistics. Timelines for preparation of tumour samples for analysis (where required) will be summarised as median, quartiles, 5th and 95th percentiles and range (in days). The proportion of participants who subsequently participate in cancer vaccine or immunotherapy trials will also be calculated. Each proportion will be presented alongside its corresponding 95% Wilson score confidence interval [1]. Loss to follow-up, withdrawals and deaths will also be reported. Descriptive correlative analysis of the patients entering CVLP based on baseline variable, omics and clinical outcomes on standard of care treatment will be undertaken.

9. CVLP network

9.1. Overview

The CVLP will work within existing NHS structures within the UK, along with existing NHS pathology structures within the UK, to support clinical trial sponsors by ensuring timely access to biological samples, equity of access and throughput into the CVLP.

Partners will be kept informed of the number of sites that are active and the number of patients recruited and referred to their clinical trials via the CVLP.

9.2. NHS site activation

NHS providers wishing to take part in the CVLP will require activation. This is a three-stage process.

1. Stage 1 involves sites submitting an Expression of Interest and completing a feasibility assessment.
2. Stage 2 is a central check of the information provided and central prioritisation. Once selected to proceed with set-up, the Local Information Pack will be provided to begin set-up.
3. Stage 3 involves local R&D approval which includes local confirmation of capacity and capability (C&C) and execution of the Organisation Information Document (OID).

Once sites have obtained local approval in Stage 3, they will formally join the CVLP and will be able to offer CVLP participation to patients.

9.3. NHS site responsibilities

Each NHS site is required to have a nominated pathologist, senior clinician and clinical Research Nurse/Allied Health Professional supporting research activities.

The senior clinician will be responsible for teams that might identify eligible patients, and the Clinical Research Nurse will be responsible for teams who initiate consent for participation in the CVLP.

The nominated pathologists will be responsible for confirming tissue handling protocols and resources. At least one other person, or a shared mailbox, should be copied into emails, in order to minimise the likelihood of a single point of failure.

Support will be made available, by means of virtual training sessions, in order to help sites pass promptly from Stage 1 to Stage 3.

SCTU will provide templates for Organisation Information Document (OID) including the required Data Sharing Agreements and Material Transfer Agreements and will ensure these are in place prior to sites activating the CVLP.

9.4. Site Payments

CVLP sites will be reimbursed for CVLP activities. Specific payment details will be included in the Organisation Information Document.

This trial is adopted onto the NIHR portfolio. This enables CVLP sites to apply to their comprehensive local research network for service support costs, if required.

9.5. Onwards referral for participation in cancer vaccine or immunotherapy clinical trials

The primary objective of the CVLP is to establish the feasibility of recruiting cancer patients who might be suitable for cancer vaccines or novel immunotherapy treatments. As such, based on their healthcare records and diagnostic test results, many of the patients going through the CVLP may be eligible for interventional clinical trials of cancer vaccines or novel immunotherapies. These trials are sponsored by our supporting partners and are run separately from the CVLP. Patients will be contacted if they are potentially suitable for a supported clinical trial and a separate consent process will take place. Suitable patients that have been referred via the CVLP will be contacted by NHS research trial sites delivering the cancer vaccine or immunotherapy clinical trials.

All participants in the CVLP will receive communication about onward opportunities for participation in supported cancer vaccine or immunotherapy clinical trials. This “onward referral” will be by means of an email to the NHS research trial sites delivering the cancer vaccine or immunotherapy clinical trials. The referral will transition to be made via the CVLP referral tool.

9.6. Supporting partner information

The CVLP aspires to support multiple partner organisations, accommodating identification of patients suitable for multiple clinical trials of cancer vaccines or novel immunotherapies and parallel sample handling where required.

The CVLP will offer significant advantages in terms of patient and biological sample access, particularly tissue sample access, and in terms of better establishing onward opportunities.

The CVLP will support clinical trials of cancer vaccines and novel immunotherapies that may benefit from the CVLP pathway as detailed in this protocol. The CVLP will support clinical trials that fall within the scope detailed below:

- Personalised cancer vaccine trials requiring biological samples for vaccine manufacture

- Immunotherapy trials, including non-personalised / “off-the-shelf” cancer vaccine trials, **with** an element of molecular profiling using biological samples for trial eligibility and/or treatment stratification*.

*NB - The requirement for the trial to have molecular or genetic profiling is not limited to the investigational therapy but can be for any part of the decision-making process for eligibility or treatment stratification.

10. Regulatory

10.1 Ethics approval

The study protocol has received the favourable opinion of a Research Ethics Committee (REC).

The study will be conducted in accordance with the recommendations for physicians involved in research on human patients adopted by the 18th World Medical Assembly, Helsinki 1964 as revised and recognised by governing laws and EU Directives.

Each patient’s consent to participate in the study will be obtained after a full explanation has been given of treatment options, including the conventional and generally accepted methods of treatment. The right of the patient to refuse to participate in the study without giving reasons will be respected.

The patient remains free to withdraw at any time from study follow-up without giving reasons and without prejudicing their further treatment.

The NHS hospitals and SCTU will ensure that patients’ anonymity will be maintained and that their identities are protected from unauthorised parties. On any data that leaves the NHS, patients will not be identified by their names, but by an identification code. SCTU will keep a patient enrolment log showing codes, names and addresses.

10.2 Confidentiality

Patients’ identification data will be required for the registration process. All parties, including NHS England as Sponsor, will preserve the confidentiality of patients taking part in the study.

10.3 Indemnity

The sponsor of the study is NHS England. For NHS sponsored research HSG 96/48 reference no.2 refers if there is negligent harm during the clinical study when the NHS body owes a duty of care to the person harmed, NHS Indemnity covers NHS staff, medical academic staff with honorary contracts, and those conducting the study. NHS Indemnity does not offer no-fault compensation and is unable to agree in advance to pay compensation for non-negligent harm. Ex-gratia payments may be considered in the case of a claim.

10.4 Clinical trial authorisation

This study does NOT involve the testing of any Investigational Medicinal Products (IMPs) therefore approval from the Medicines and Healthcare products Regulatory Agency is not required.

10.5 Sponsor

NHS England is acting as the sponsor for this study. The Southampton Clinical Trials Unit (SCTU), Chief Investigator and other appropriate organisations have been delegated specific duties by the Sponsor and this is documented in the trial Task Allocation Matrix.

The duties assigned to the participating sites (NHS hospitals or others taking part in this study) are detailed in the Organisation Information Document (OID).

10.6 Deviations and serious breaches

Any study protocol deviations/violations and breaches of Good Clinical Practice occurring at sites should be reported to SCTU and the local Trust's R&D Office immediately. SCTU will then advise of and/or undertake any corrective and preventative actions as required. All potential serious breaches will be reported to the REC to ensure adherence to the Research Governance Framework for Health and Social Care.

10.7 Audits and inspections

The study may be subject to inspection and audit by NHS England, under their remit as sponsor, the SCTU as Sponsor's delegate and other regulatory bodies to ensure adherence to the principles of GCP, Research Governance Framework for Health and Social Care, applicable contracts/agreements and national regulations.

11. Data management

Participant data will be entered remotely at the CVLP sites and retained in accordance with the current Data Protection Regulations. The CVLP sites are responsible for ensuring the accuracy, completeness, and timeliness of the data entered.

The participant data is pseudo anonymised by assigning each participant a participant identifier code which is used to identify the participant during the study and for any participant-specific clarification between SCTU, CVLP site, NHS pathology (or equivalent within devolved nations) and research trial sites. Only pseudonymised patient data will be shared outside of the NHS, including partner organisations. Identifiable data will be held by the SCTU as a delegate of the Sponsor in order to perform the Clinical Liaison role.

The Informed Consent Form will specify the participant data to be collected and how it will be managed or might be shared; including handling of all Personal Identifiable Data (PID) and sensitive PID adhering to relevant data protection law.

There will be a phased roll out of the new CVLP referral tool during which sites will continue to use the legacy data collection methods from NHS England and gradually move over to the new CVLP referral tool. This will be governed by a risk assessed change management process.

A Data Management Plan (DMP) has been developed to cover both the legacy and new data collection method, providing full details of the study specific data management strategy for the CVLP.

The new CVLP referral tool will be accessed via the URL bcinsight.cancervlp.nhs.uk and only trained personnel with specific roles assigned will be granted access. Completion guidelines will be provided to the investigator sites to aid data entry of participant information.

Data queries will either be automatically generated within the referral tool, or manually raised by the study team, if required.

At the end of the study, all queries will have been resolved and the referral tool frozen. The referral tool will be archived according to SCTU Standard Operating Procedures (SOPs) and NHS policy.

12. Archiving

Adequate and accurate records to enable the conduct of the study to be fully documented and the study data to be subsequently verified must be maintained. After study closure, all source documentation and study related documents must be maintained. All study documents will be retained for a period of at least 5 years following completion or discontinuation of the CVLP.

13. References

1. Edwin B. Wilson (1927) Probable Inference, the Law of Succession, and Statistical Inference, Journal of the American Statistical Association, 22:158, 209-212, DOI: 10.1080/01621459.1927.10502953

14. Summary of significant changes to the protocol

Protocol date and version	Summary of significant changes
V1.1	First version
V1.2	Appendices removed that were no longer required.
V1.3	Blood sample amended as not required for the first study the CVLP is supporting.
V1.4	Added option for remote consent
V2.0	Addition of a statistics section and research questions amended. Addition of option to use e-consent (Adobe Sign) when consenting patients. General clarifications made throughout and addition of Southampton Clinical Trials Unit (SCTU) as the coordinating centre.
V3.0	General clarifications made throughout and update to study end points. Addition of option to decentralised cancer vaccine trial activity and referral tool.
V4.0	Redesign of the CVLP to broaden scope to support clinical trials of novel immunotherapies that may benefit from a referral network +/- supporting tissue/biological sample handling pathway +/- supporting sequencing pathway.

CVLP Protocol v4 30-JUL-2025 - Clean

Final Audit Report 2025-07-30

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