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NHS Cancer Vaccine Launch Pad (CVLP) Technical Requirements Version 2

10-Oct-2025

BioNTech BNT113-01 (AHEAD-MERIT) HNSCC HPV16+ Trial

Document authorised by:

Name:	Professor Peter Johnson	**Role:**	Chief Investigator
Signature:		**Date:**	14-Oct-2025
Name:	Gillian Rosenberg	**Role:**	On behalf of CVLP Sponsor
Signature:	Gillian Rosenberg (Oct 14, 2025 17:07:33 GMT+1)	**Date:**	14-Oct-2025
Name:	Nicole Keyworth	**Role:**	Senior Trial Manager at SCTU
Signature:	Nicole Keyworth (Oct 14, 2025 17:08:04 GMT+1)	**Date:**	14-Oct-2025

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MAIN CVLP CONTACT

Chief Investigator and Medical Expert for the CVLP: Professor Peter Johnson
NHS England London
Wellington House
133-135 Waterloo Road
London
SE1 8UG

CVLP COORDINATION CENTRE

For general CVLP and clinical queries e.g. CVLP participant queries, CVLP supplies, data collection, please contact in the first instance:

CVLP SCTU Team
Tel: 023 8120 5154
Email: cvlp@soton.ac.uk

Address: Southampton Clinical Trials Unit
Southampton General Hospital
Tremona Road
SOUTHAMPTON
SO16 6YD

Tel: 023 8120 5154
Fax: 0844 774 0621
Email: ctu@soton.ac.uk
Web: www.southampton.ac.uk/ctu

SPONSOR

NHS England is the research sponsor for the CVLP. For further information regarding sponsorship conditions, please contact Gillian Rosenberg at:

Address: NHS England London
Wellington House
133-135 Waterloo Road
London
SE1 8UG

Email: england.cancervaccinelaunchpad@nhs.net

FUNDER

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

Technical Requirements Information

This Technical Requirements document describes the CVLP and provides information about procedures for entering participants to the CVLP with the aim of referring them to the BNT113-01 (AHEAD-MERIT) vaccine trial. Every care was taken in the drafting of this Technical Requirements document, but corrections or amendments may be necessary. These will be circulated to investigators in the CVLP, but CVLP sites consenting participants for the first time to the CVLP are advised to contact Southampton Clinical Trials Unit to confirm they have the most recent version.

Compliance

This CVLP will be conducted in compliance with the approved CVLP 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.

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1.0 Table of Contents

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2.0 Document Purpose

This document provides technical guidance for NHS Trusts utilising the Cancer Vaccine Launch Pad (CVLP), including referring NHS Trusts, herein referred to as CVLP sites, research trial sites, and the Cellular Pathology Genomic Centres (CPGCs) involved in preparing and shipping tissue samples to BioNTech's central laboratory, LabCorp, for central testing.

This document is relevant only to the BioNTech's head and neck cancer vaccine trial (BNT113-01, AHEAD-MERIT).

It should be read and utilised by the following individuals and teams:

- Clinical teams and the research delivery team at the CVLP sites, including the RN/healthcare practitioner that will be responsible for consenting and referring patients.
- Lead pathologist and any members of the pathology team at the CVLP site involved in sampling.
- Lead pathologist and any members of the pathology team at the CPGC involved in sampling.
- Principal Investigator, Co- Investigator, and relevant members of the R&D team at trial sites.

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3.0 Introduction & background to the Cancer Vaccine Launch Pad

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. We are investigating the optimum process for patients to receive cancer vaccines by enrolment in the CVLP.

Patients will be asked to consent to be put forward for clinical trials of cancer vaccines. 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 take part in the relevant trial.

If they would like to take part in the trial, surplus tissue samples obtained through standard care pathways, and potentially other biological samples depending on the cancer vaccine trial, will then be used to assess their eligibility against specific molecular or tumour inclusion criteria for the relevant trial.

A Clinical Liaison team (CL), managed by Southampton Clinical Trials Unit (SCTU), will coordinate the CVLP by supporting the CVLP referral and tissue pathways, connecting CVLP sites with designated trial sites, and making sure information is shared appropriately to enable the pre-screening and screening, recruitment and ongoing care of participants during the trial. An electronic CVLP referral tool will be utilised by sites to support the secure transfer of data between parties. If the CVLP Referral Tool is unavailable, data can be transferred between parties using the password protected CVLP-BNT113-01 data return template and the CVLP-BNT113-01 Referral Forms (see appendix 4).

The CVLP is agnostic to the commercial company and clinical trials. The research protocol sets out the full details of the CVLP.

The aims of the CVLP are to:

1. Accelerate the development of cancer vaccines and increase the opportunity for patients to take part in cancer vaccine trials.

2. Support recruitment into cancer vaccine trials and transfer tissue samples to industry partners for genomic analysis.

3. Continue to undertake a feasibility assessment of the CVLP with the aim to continue scaling it up in the future to support more trials of cancer vaccines.

The SCTU CVLP webpage contains all the CVLP study documents for CVLP sites including the research protocol, patient information sheet, consent form and GP letter. The webpage can be found here: https://www.southampton.ac.uk/ctu/trialportfolio/listoftrials/cvlp.page

Any queries about the CVLP should be directed to cvlp@soton.ac.uk.

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4.0 The BNT113-01 (AHEAD-MERIT) trial

The CVLP continues to support BioNTech with a second cancer vaccine trial, BNT113-01 (AHEAD-MERIT). This trial is an open label phase II/III randomised controlled trial to compare the efficacy of BNT113 in combination with pembrolizumab versus pembrolizumab monotherapy as a first line therapy in patients with unresectable recurrent or metastatic Head and Neck Squamous Cell Carcinoma (HNSCC) which is positive for human papilloma virus 16 (HPV16+) and expresses PD-L1.

BNT113 is an HPV16 ribonucleic acid-lipoplex (RNA-LPX) cancer vaccine which encodes for two tumour-associated antigens (TAAs): HPV16 viral proteins E6 and E7. BNT113 is designed to induce *de novo* anti-tumour immune responses and to enhance pre-existing immune responses directed against HPV16+ cancer cells. Patients will receive treatment with BNT113 in combination with pembrolizumab, the current standard of care for HNSCC whose tumours express PD-L1.

The BNT113-01 trial has two parts. Part A, an initial non-randomised safety run-in phase to confirm the safety and tolerability at the selected dose range level of BNT113 in combination with pembrolizumab. Recruitment to this phase has completed and the trial has moved to part B. Part B is the randomised phase of BNT113 in combination with pembrolizumab versus pembrolizumab monotherapy to generate pivotal efficacy and safety data.

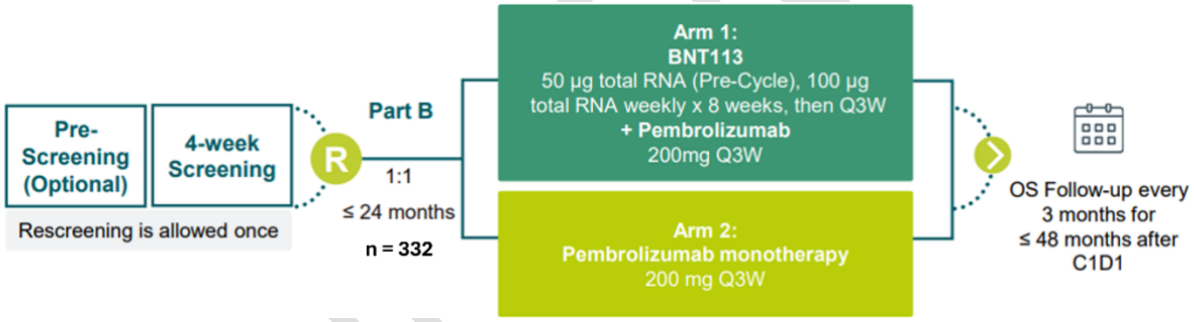

Figure 1 – Trial schema for Part B of the BNT113-01 trial.

More information on the clinical trial can be found here.

4.1 Screening patients for eligibility

4.1.1 Pre-screening

For Part B, an optional pre-screening phase is available for investigators to pre-screen patients who might be candidates for the trial in the near future to perform central HPV16 DNA testing and central PD-L1 expression testing. Results available from the pre-screening phase will not need to be repeated in the main screening phase if patients eventually develop confirmed relapse or metastatic disease.

Patients eligible for pre-screening are those at high risk of relapse after treatment of locoregional disease or patients with clinical or imaging abnormalities that may indicate recurrent or metastatic disease that is not yet confirmed, pending further investigation or follow-up.

The BNT113-01 trial protocol includes broad criteria for pre-screening so for the purposes of CVLP, the eligibility criteria have been narrowed to improve efficiency of screening at CVLP sites. Therefore, the CVLP pre-screening eligibility criteria will focus on identifying patients who have:

a.) clinical or radiological findings suggestive of recurrent or metastatic HNSCC pending confirmatory studies that is not expected to be curable with surgery or radiation, or
b.) those that have been treated for oligometastatic disease.
c.) Since initial diagnosis (maximum 5 years ago), have been deemed high risk of developing recurrent or metastatic disease in the near future (e.g. before the end of trial recruitment) as per consultant clinical judgement (e.g. including but not limited to; previous treatment for T4 or N3 HNSCC).

Please see Section 7.2 for the full eligibility criteria to consider when identifying patients suitable for BNT113-01 pre-screening.

It is expected that CVLP sites will predominantly identify patients suitable for BNT113-01 pre-screening.

4.1.2 Main Trial Screening

If a patient is a suitable candidate for immediate enrolment in the main trial, pre-screening should be skipped and the patient offered the possibility to proceed directly with main screening. Testing for HPV16 DNA and PD-L1 testing is possible within the main screening phase.

4.2 Randomisation into trial

If the patient is eligible after completing the main trial screening assessments, they will be randomised to the experimental group (BNT113 + Pembrolizumab) or the control group (Pembrolizumab monotherapy). Randomisation should occur no later than 28 days from informed consent and within 3 days before administration of trial treatment.

4.2.1 Treatment schedule post randomisation

Trial treatment is administered in 21-day cycles as shown in Figure 2.

Patients in the experimental group (Arm 1) will receive the first BNT113 dose (“pre-cycle”) of 50µg total RNA 7 days before the first pembrolizumab treatment (cycle 1 day 1) and subsequently 100µg total RNA will be given on a weekly basis for 8 weeks during the first 2 cycles, followed by 100µg total RNA administration every 3 weeks from cycle 3 onwards. The first administration of Pembrolizumab will be on cycle 1 day 1 and will be administered according to standard of care every 3 weeks.

Patients in the control group (Arm 2) will receive their first dose of Pembrolizumab on cycle 1 day 1 and will be administered according to standard of care every 3 weeks.

Patients in both arms will complete trial treatment after 24 months or until unacceptable toxicity, withdrawal of consent, discontinuation due to investigator's decision, or disease progression.

Arm 1

Cycle	Pre-cycle	1			2			3			4			5...		
Day	1	1	8	15	1	8	15	1	8	15	1	8	15	1	8	15
BNT113	X	X	X	X	X	X	X	X			X			X		
Pembrolizumab (Q3W)		X			X			X			X			X		

Q3W = every 3 weeks.

Arm 2

Cycle	Pre-cycle	1			2			3			4			5...		
Day	1	1	8	15	1	8	15	1	8	15	1	8	15	1	8	15
Pembrolizumab (Q3W)		X			X			X			X			X		

Q3W = every 3 weeks.

Figure 2 – Treatment schedule for Part B of the BNT113-01 trial.

4.2.2 Tumour assessments

Patients receive imaging investigations at set time points during the trial performed by the trial sites.

All patients will undergo tumour assessments (CT and/or MRI) at screening, every 9+/-1 weeks for the first 6 months after randomisation, and every 12+/-2 weeks thereafter regardless of dose delays until disease progression or until the start of next-line anti-cancer therapy (whichever occurs earlier).

5. Roles within the CVLP Pathway

Roles within the CVLP pathway:

- **CVLP site** – a site that will identify potentially eligible patients and refer them to a trial site that is delivering a cancer vaccine trial for the BNT113-01 trial.
- **CPGC** - a site that will receive an FFPE tissue block from a CVLP site's local cellular pathology department and prepare tissue samples for a cancer vaccine trial according to the CVLP technical requirements document.
- **Trial site** – a site that is delivering the BioNTech recurrent/metastatic Head & Neck cancer trial (BNT113-01) and will receive CVLP referrals from a CVLP site.
- **CVLP Clinical Liaison (CL)** – a role carried out by Southampton Clinical Trials Unit (SCTU)
    - to support across all sites in managing communications and patient journey within the protocol timeframes and work with all sites.
    - to troubleshoot any issues; and
    - to support training and monitor CVLP patient recruitment.

6 CVLP pathway for BioNTech's BNT113-01 (AHEAD-MERIT) trial

Figure 3 shows the pathway map of patients recruited into the CVLP for the BNT113-01 clinical trial. Each step is outlined in further detail in the table on pages 10-14.

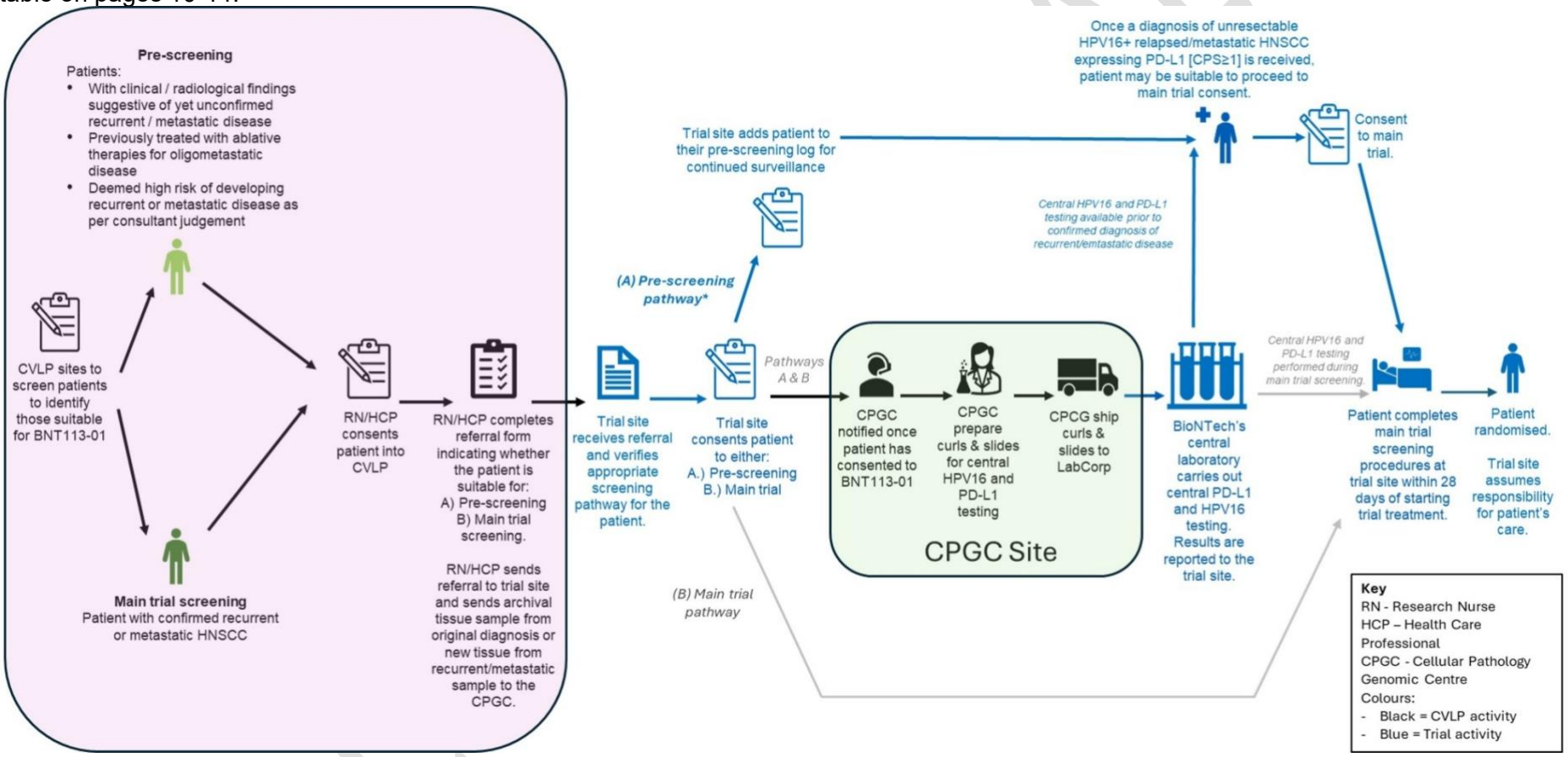

Figure 3 – CVLP pathway map for the BNT113-01 (AHEAD-MERIT) trial

Activity		Responsible
Identification and consent into the CVLP		
Step 1	• Patients should be identified for the CVLP following the referral criteria outlined in section 7.2.	CVLP site – clinical/research team
Step 2	• An adequately trained health care practitioner from the clinical care team/research team should take the patient's consent for the CVLP using the CVLP patient information sheet and consent form provided. Consent can be taken in person, remotely or via e-consent, please refer to the CVLP protocol for details. • Once a patient consents, the patient must be registered using the 'Process Consent' function in the CVLP Referral Tool (please see CVLP – BNT113-01 eCRF Completion Guidance document for more information) which will assign the patient a CVLP participant ID. Their name and details must be entered into the Referral Tool and a copy of their consent form uploaded to the CVLP Referral Tool in PDF or JPEG format. • At the same time, the research delivery team are to inform the local pathology department immediately about the recruited patient. • Local SOPs should be followed by the CVLP site research team for requesting the release of an FFPE tissue block to the CPGC, with the block being sent by a **tracked delivery method**. • The CVLP site research team (or local pathology team – see step 3) must enter the tumour block details, date of shipment and tracking information into the CVLP Referral Tool. A copy of the pathology report should also be uploaded to the CVLP Referral Tool in PDF, JPEG or DOCX formats. On completion, the CVLP Referral Tool will send an automatic notification to the CPGC to alert them to expect a FFPE block from the CVLP site. • The CVLP site research team should send the CVLP GP letter (Word template provided) including a copy of the CVLP patient information sheet to inform the patient's GP that they are participating into the CVLP.	CVLP site – clinical/research team
Tissue sample for the CVLP		
Step 3	• The CVLP site's local pathology department will identify an archival FFPE tissue block that was taken as part of the standard of care pathway for diagnosis of HNSCC. The sample should preferably be derived from a current site of	CVLP site – local pathology

	metastatic or recurrent disease. Otherwise, a sample from the primary tumour is an acceptable alternative.	
Step 4	• Once the tissue block is identified, it should be sent to the relevant Cellular Pathology Genomic Centre (CPGC) as soon as possible using **tracked delivery**, following standard packaging, and transport protocols. • The tumour block details, date of shipment and tracking information must be recorded into the CVLP Referral Tool. A copy of the pathology report should also be uploaded to the CVLP Referral Tool in PDF, JPEG or DOCX formats.	CVLP site – local pathology
Patient referral to the BNT113-01 trial		
Step 5	• Following confirmation that the patient is suitable for either BNT113-01 pre-screening or main trial screening (see Section 7.2 for pre-screening and main trial screening eligibility criteria), the CVLP site will complete the required eCRFs and report upload for either pre-screening or main trial referral in CVLP Referral Tool. For pre-screening the pathology report will need to be uploaded, and for main trial screening the pathology report, radiology report and last clinic letter will need to be uploaded. Once completed, the CVLP site will submit the referral via the Referral Tool to the appropriate trial site. Upon submission of the referral, the CVLP Referral Tool will send an automatic notification to the appropriate trial site to alert them to review the referral in the Referral Tool.	CVLP site – clinical/research team
Step 6	• On receipt of the referral, the trial site will access the CVLP Referral Tool to review the information provided by CVLP sites and confirm whether the patient is a suitable candidate for BNT113-01 pre-screening or main trial screening. • The trial site will contact the patient and arrange for them to be consented into the BNT113-01 trial. • Dependent on adoption, trial sites may have the option to utilise remote consent or in person consent for pre-screening depending on the patient's preference. • Trial sites must arrange to consent those who are suitable candidates for the main trial screening in person. **If the patient consents to pre-screening (see steps 7-9 and 11-12):** • the trial site will record the patient on their BNT113-01 pre-screening log held at their site. The trial site will also issue a unique pre-screening number (pre-screening ID). The trial site will update the CVLP Referral Tool with the pre-screening ID and confirm the date of consent. **If the patient consents to main trial screening (see steps 7-9, 11-14):**	Trial site

	• The trial site will issue a unique participant number (patient ID) by registering the patient on the BNT113-01 IxRS system. The trial site will update the CVLP Referral Tool with the patient ID and confirm the date of consent.	
Tissue preparation for BNT113-01		
Step 7	• On entry of the date of consent to BNT113-01 pre-screening or main trial screening by trial sites, the CVLP Referral Tool will send an automatic notification to the relevant CPGC via email to alert sample preparation is required. • The CPGC will access the CVLP Referral Tool to obtain the patient's pre-screening ID or patient ID.	CPGC
Step 8	• The CPGC will prepare the curls and slides for central HPV16 DNA and PD-L1 expression testing following the instructions and cutting scheme provided in appendix 1. • For participants who have been consented to BNT113-01 pre-screening and main trial screening, the CPGC will prepare the curls and slides within 3 working days of being notified a sample is required.	CPGC
Step 9	• The standard turnaround time for HPV16 DNA and PD-L1 central testing is up to 30 calendar days for pre-screening from receipt of the sample by LabCorp. • Expedited central testing is required for pre-screening participants who have clinical or radiological findings suggestive of recurrent or metastatic HNSCC pending confirmatory studies that is not expected to be curable with surgery or radiation. CPGCs must indicate on the sample requisition form that results are required within 10-12 calendar days from sample receipt at LabCorp for these participants.	CPGC
Step 10	• The standard turnaround time for HPV16 DNA and PD-L1 central testing is 10-12 calendar days for main trial screening from receipt of the sample by LabCorp.	CPGC
Step 11	• The CPGC will send the curls and slides to BioNTech's central laboratory, LabCorp, using the DHL courier. • The CPGC will update the CVLP Referral Tool with the date of shipment and tracking information including the sample kit accession number and airway bill (AWB) number. The CPGC will also upload a copy of the completed sample requisition form and airway bill to the CVLP Referral Tool.	CPGC

Step 12	• BioNTech's central laboratory, LabCorp, will use the curls and slides prepared by the CPGC to undergo central testing as follows:
	  ○ Pre-screening (up to 30 calendar days turnaround time): PD-L1 expression followed by HPV16 DNA testing for those expressing PD-L1.
	  ○ Expedited pre-screening samples and main trial screening samples (10-12 calendar days turnaround time): PD-L1 and HPV16 DNA testing completed simultaneously.
	• The trial site will be informed of the results of the central HPV16 and PD-L1 testing directly as per trial protocol.
	• The trial site will inform the patient directly of the results of the central testing. Dissemination of central PD-L1 results, and HPV16 results if tested, to participants must be performed by trial sites under trial site PI oversight.
	• The trial site must update the CVLP Referral Tool with the outcome of central testing within 1 working day after receipt of the report.
		LabCorp / trial site

Pre-screening for BNT113-01		
Step 13	• Following notification of consent to BNT113-01 pre-screening, the CVLP site must ensure the CVLP Referral Tool is updated with a date that the CVLP expects a diagnosis of recurrent/metastatic HNSCC to be confirmed. As an example, this may be the date the patient is due to be discussed in MDT post imaging or biopsy, or the date the CVLP expects to receive the imaging or biopsy report. • When the CVLP site confirms a diagnosis of recurrent/metastatic HNSCC during pre-screening for BNT113-01, a main trial referral eCRF will require submission via the CVLP Referral Tool (please see CVLP – BNT113-01 eCRF Completion Guidance document for more information).	CVLP site – clinical/research team
Step 14	• On notification of a main trial referral, trial sites will review the patient's details and consider them for consent and inclusion in BNT113-01 main trial screening. • Trial sites will confirm the date of consent to main trial screening in the CVLP Referral Tool. Consent for main trial screening must be given in person. • As the central HPV16 and PD-L1 central testing will already have been completed as part of pre-screening, there will be	Trial site

	no requirement for trial sites to handle tissue for patients proceeding from pre-screening to main trial screening. There will also be no requirement for any further tissue preparation or shipment by the CPGC to BioNTech's central laboratory, LabCorp.	
Main Trial Screening and Randomisation for BNT113-01		
Step 15	• The trial site will perform the required investigations per the BNT113-01 trial protocol prior to the start of trial treatment.	Trial site
Step 16	• Patients that meet all eligibility criteria for inclusion in BNT113-01 are randomised to the experimental or control group. The trial site will update the CVLP Referral Tool with only the date of randomisation. The treatment arm will not be captured in the CVLP Referral Tool. • At this point, the trial site will take over responsibility for the patients care and ongoing cancer treatment and monitoring.	Trial site

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7.0 Guidance for CVLP sites on selection and enrolment of patients

7.1 Consent into the CVLP

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 surplus diagnostic tumour material and link it with routine healthcare data for potential recruitment into clinical trials. Please note, the CVLP does not cover consent into the BNT113-01 trial, consent for this trial will be taken at the trial site.

Informed consent should be obtained by a trained health care practitioner using the patient information sheet and consent form provided by NHSE.

The original consent form should be retained by the CVLP site for the hospital notes, and an additional copy should be provided to the patient.

If a patient wishes to withdraw their consent from the CVLP at any time, the CVLP site is responsible for informing the Clinical Liaison to ensure their data is not used any further and any identifiable data is anonymised. If the patient has been recruited into the trial and would also like to withdraw from that, they will need to follow up with the trial site directly to ensure patient is withdrawn from the trial participation.

7.2 Referral Criteria for BNT113-01

Patients who fulfil the following criteria are suitable candidates to be consented into the CVLP and referred to BNT113-01:

- Be over the age of 18.
- Have the capacity to consent to involvement in the CVLP.
- Have sufficient tumour available from either the original diagnosis or new tissue from recurrence/metastatic diagnosis for central HPV16 and PD-L1 testing (to be assessed by local pathology once tissue sample is collected).

Pre-screening:

Key inclusion criteria:

1. Previous diagnosis of histologically confirmed Head and Neck Squamous Cell Carcinoma (HNSCC) with no prior systemic anticancer therapy administered in the recurrent or metastatic setting.
2. Patients who either:
    a. Have clinical or radiological findings suggestive of recurrent or metastatic HNSCC pending confirmatory studies that is not expected to be curable with surgery or radiation, or
    b. Have been treated for oligometastatic disease with ablative therapies, or
    c. Since initial diagnosis (maximum 5 years ago), have been deemed high risk of developing recurrent or metastatic disease in the near future (e.g. before the end of trial recruitment) as per consultant clinical judgement (e.g. including but not limited to; previous treatment for T4 or N3 HNSCC).
3. Primary tumour location of the oropharynx.
    a. Those with a p16 positive status are eligible for pre-screening (irrespective of HPV16 DNA result, if this test has been performed locally).

   b. Those with a p16 negative status but positive HPV16 DNA status (on local assay) are also eligible for pre-screening.
   c. Those with an unknown p16 status are eligible for pre-screening.
   d. Primary tumour location of the oral cavity, hypopharynx and larynx can be enrolled if HPV16 driven disease is strongly suspected.

Key exclusion criteria:

1. Primary tumour site of nasopharynx (any histology).
2. Those with a p16 negative status and HPV16 DNA negative status (on local assay) are not eligible for inclusion in pre-screening.

Main trial screening:

Key inclusion criteria:

1. Patients with histologically confirmed HNSCC that is confirmed as recurrent or metastatic considered incurable by local therapies. HPV16 status and PD-L1 is centrally tested during screening and those confirmed CPS≥1 and HPV16+ are eligible.
2. Primary tumour location of the oropharynx.
   a. Primary tumour location of the oral cavity, hypopharynx and larynx can be enrolled if HPV16 driven disease is strongly suspected.
3. Measurable disease on imaging -
   a. At least one lesion measuring a minimum of 10mm on imaging.
   b. For some specific types of lesions (e.g. malignant lymph nodes, bone lesions & previously irradiated lesions) there are slightly different parameters. Please contact Clinical Liaison Team (cvlp@soton.ac.uk) for any queries.
4. ECOG Performance Status ≤1.

Key exclusion criteria:

1. Primary tumour site of nasopharynx (any histology).
2. Patients who have received prior systemic anticancer therapy administered in the recurrent or metastatic setting for HNSCC.
   a. Systemic therapy which was completed more than 180 days prior to randomisation, if given as part of multimodal treatment for locally advanced disease, is allowed.
3. Treatment with non-systemic anti-cancer therapy (e.g., surgery or radiotherapy) within 2 weeks prior to randomisation.
4. Patients that have disease suitable for local therapy administered with curative intent.
5. Known primary immunodeficiencies.
6. Prior splenectomy.
7. Patients with another primary malignancy that has not been in complete remission for at least 2 years, with the exception of those with a negligible risk of metastasis or death. For example:
   a. Adequately treated carcinoma *in situ* of the cervix
   b. Non-invasive basal or non-invasive squamous cell skin cancer
   c. Localised prostate cancer
   d. Non-invasive superficial bladder cancer
   e. Breast ductal carcinoma *in situ*
8. Current evidence of new or growing brain or spinal metastases during screening. Patients with known brain or spinal metastases may be eligible if they:
   a. Had radiotherapy or another appropriate therapy for the brain or spinal metastases,

   b. Have no neurological symptoms (excluding Grade ≤2 neuropathy).
   c. Have no evidence of clinical or radiological progression within 4 weeks prior to signing informed consent,
   d. Do not require steroid therapy within 7 days before randomisation or are undergoing slow steroid tapering, currently at doses ≤10mg and neurologically stable.
   e. Spinal bone metastases are allowed unless imminent fracture or cord compression is anticipated.
9. Life expectancy of less than 3 months and/or have rapidly progressive disease, as assessed by the treating investigator.

8.0 Guidance for CVLP and trial sites for referral and ongoing management of patients

8.1 Patient referral to the BNT113-01 trial

The CVLP site will complete the eCRFs and upload reports required for referral to the CVLP Referral Tool and submit to the trial site. For pre-screening the pathology report will need to be uploaded, and for main trial screening the pathology report, radiology report and last clinic letter will need to be uploaded. Trial site will be notified of the referral through an automatic notification. The data provided within and alongside the referral is required by the trial site to review eligibility, contact the patient and consent them to either pre-screening or main trial screening. The trial site may, as necessary, request additional source documentation from the CVLP site to confirm eligibility and/or meet monitoring requirements.

The referral form includes:

- Cancer classification and staging
- Tumour characteristics
- Relevant medical history
- Prior cancer therapies for underlying disease

The data provided for referral should be reviewed by a qualified health care practitioner from within the CVLP site team to confirm the integrity of the information prior to submission of the referral to the trial site. The ‘Submit Referral’ form should be completed in the CVLP Referral Tool with the details of the health care practitioner who has authorised submission of the referral.

NOTE: If the CVLP Referral Tool is unavailable, patient referrals will be submitted using the password protected CVLP-BNT113-01 Referral Forms. These forms should be sent directly to the trial site team by secure NHS email, with the CVLP Clinical Liaison copied in. The CVLP site should also attach the patients required reports - for pre-screening the pathology report will need to be uploaded, and for main trial screening the pathology report, radiology report and last clinic letter will need to be uploaded. Data provided by referral forms in periods of downtime will be entered into the CVLP Referral Tool by the SCTU Data Management team.

8.2 Patient management and communication between CVLP and trial sites

Following randomisation, the trial site will take overall responsibility for the patients care and ongoing cancer treatment and monitoring. However, dependent on proximity to the trial site, the patient may visit the CVLP site in relation to unplanned clinical care requirements, an adverse event following trial treatment, or an unrelated clinical event that may impact

treatment and ability to participate in the trial. The CVLP site should inform the trial site over email if this occurs, copying in the Clinical Liaison.

Patients will be given a Clinical Trial Card to present in any instances of attendance at GP or A&E or admission. If the patient informs the trial team of any attendance or admission that warrants further clinical information, the trial site may contact the referring CVLP site for further details.

9.0 Monitoring and performance

9.1 Risk escalation policy

CVLP sites should follow standard governance and incident reporting procedures to capture any patient safety issues or deviations. It is the responsibility of the CVLP site to take appropriate action and inform the Southampton Clinical Trials Unit if at any point patient safety is compromised. The Southampton Clinical Trials Unit will support CVLP sites to carry out a root cause analysis on any major patient safety issues or deviations. The CVLP Delivery Group will be responsible for reviewing any safety issues or deviations that constitute a Corrective and Preventative Action (CAPA) and the corresponding root cause analysis. If any safety issues or deviations occur at the trial site, they will be managed as per the trial protocol and reported back to the CVLP site where necessary in relation to ongoing patient care.

9.2 Reporting

SCTU will work with CVLP sites during the set-up phase to estimate their delivery trajectories for the number of patients recruited into the CVLP. This will be reviewed on a continual basis.

SCTU will work with CVLP sites, CPGCs, trial sites, BioNTech and LabCorp to collate and regularly review an issue log to address operational issues and ensure learning from sites informs ongoing development of the CVLP platform.

9.3 CVLP sites reimbursement

The tables below show the activities that are required at the CVLP site and the per patient cost allocated to complete them.

Activity	Time allocated	Cost
Identification of patients	Research nurse or health care practitioner – 60mins	£44
Approach potential patients	Research nurse/HCP – 20mins	£15
Informed consent	Research nurse/HCP - 20 mins	£15
Eligibility check	Research nurse/HCP – 15mins Clinician – 10mins	£28
GP letter	Research nurse/HCP - 15 mins	£11
Tissue block retrieval	Research nurse/HCP – 30mins	£22
Organising specimen dispatch	Research nurse/HCP - 30 mins	£22
Specimen postage	N/A	£3
Liaison with CPGC	Research nurse/HCP – 15 mins	£11
Data entry	Research nurse/HCP – 30mins Clinician – 30mins	£73
Dissemination of eligibility results to patients	Clinician – 10 mins	£17

Total time/cost allocated	**Research nurse/HCP – 265 mins** **Clinician – 40 mins**	**£261**

All new sites will also receive a one-off cost for set up and existing CVLP sites will receive a re-training cost for each supported trial.

Activity	Time allocated	Cost
SIV/Training Session	Research nurse or health care practitioner – 60mins Clinician – 60mins	£146

Funding will also be provided to the CPGC to process the tissue. This will be a set cost and will be communicated directly with each CPGC.

Travel reimbursement will be available to patients travelling to trial sites for pre-screening or main trial screening assessments who consent to the BNT113-01 study. Reasonable expenses for CVLP patients (covering transportation, meals, parking fees and carer costs, as well as accommodation if necessary) will be covered by the trial Sponsor, BioNTech. Reimbursement for patients will continue to be managed by trial sites through their standard processes, as agreed in individual trial site agreements, and all expenses claimed will need to be supported by valid receipts.

10.0 Data sharing

NHSE has completed a Data Protection Impact Assessment that has been signed off by NHSE Information Governance to ensure the correct agreements are in place to enable data sharing between CVLP sites, SCTU Clinical Liaison, trial sites and BioNTech. This is available on request from the SCTU (cvlp@soton.ac.uk).

NHSE will have a Data Agreement in place with BioNTech to enable CVLP sites to send pseudonymised tissue samples and accompanying data.

CVLP sites, CPGCs and trial sites will be required to sign the Research IRAS agreement titled ‘Organisation Information Document’ which will outline the activity required, funding received and data sharing and processing.

CVLP sites and CPGCs will also be required to sign a confidentiality agreement (CDA) with BioNTech.

Any patient data shared by the CVLP site, trial site or CPGC will be securely stored in the CVLP Referral Tool. Only the relevant staff will have access to datasets within the CVLP Referral Tool.

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Appendix 1 – Guidance for CVLP and CPGCs on tissue sample collection and shipping

CVLP site

The tissue sample is taken during processing of the tissue specimen as part of standard of care either at initial diagnosis or at suspicion of recurrence or metastasis.

Tissue processing and the preparation of FFPE blocks by local pathology departments should be performed according to the local histopathology laboratory manual. However, local pathology departments at the CVLP site must process the tissue into formalin fixed, paraffin embedded (FFPE) blocks using 10% neutral buffered formalin. Any other fixative used will result in cancellation of testing and the central HPV16 and PD-L1 assays will not be performed. Decalcified tissue is also not acceptable and will result in cancellation of testing and the central HPV16 and PD-L1 assays will not be performed.

Cell blocks made from fine needle aspirations (FNA) are not acceptable sample material for central HPV16 and PD-L1 testing. Resection material and core needle biopsies or other routine sample collection material is acceptable. For queries regarding acceptable sample material, please contact cvlp@soton.ac.uk for review on a case-by-case basis.

A recent tissue block used to confirm recurrence or metastasis is preferable, however an archival tissue block from initial diagnosis is an acceptable alternative. FFPE tissue blocks must be less than 5 years old and have tumour present to be suitable for BNT113-01.

The FFPE tissue block should be sent to the relevant CPGC following local biological specimen transportation guidance but must be via a **tracked shipping method**. The pathology report should be sent with the tissue block.

Local pathology department or the CVLP research delivery team will record the date of shipment in the CVLP Referral Tool and must have a process in place to track the sample until it is received by the CPGC. If the CVLP Referral Tool is unavailable, sample tracking information must be recorded on the CVLP-BNT113-01 Data Return.

CPGCs

Once the CPGC receives the sample from the CVLP site's local pathology department, the FFPE tissue block(s) should be stored by the CPGC until an automatic notification is received via email from the CVLP Referral Tool or from the Clinical Liaison team to notify that the patient has consented into pre-screening or main trial screening for BNT113-01.

Once the CPGC has been informed that the patient has consented into pre-screening or main trial screening via the automatic notification, the CPGC should prepare curls and slides following the instructions and cutting scheme outlined below. It is mandatory to include a redacted copy of the pathology report when submitting samples to BioNTech's central laboratory, LabCorp. All personal identifiable information must be removed from the report (including full name, date of birth, address, telephone number and email address).

For participants who have consented to BNT113-01 pre-screening and main trial screening, CPGCs will be required to prepare the curls and slides within 3 working days of being notified to prepare the sample.

A total of five slides and three curls (1 curl per tube) will be used for central PD-L1 and HPV16 DNA testing to see if the patient is potentially eligible for inclusion in the trial. Once HPV16 and PD-L1 results have been obtained, no further tumour material will be required.

LabCorp will provide kits and bulk supplies for both pre-screening and main trial screening.

For participants consented to pre-screening, the kits named "**Part B Pre-Screening V3.0 CPGC**" should be used.

For participants consented to main screening, the kits named "**Part B Tissue biopsy CPGC**" should be used.

LabCorp will supply the CPGCs with the following bulk supplies as part of the initial supply:

- 1 Microscope slides (72/box)
- 3 Empty microscope slide box (25 capacity)

Each individual kit includes:

- 1 Label for slide box
- 3 Eppendorf tubes
- 3 Labels for Eppendorf tubes
- 1 Envelope
- 1 Requisition Form (pre-screening or main screening)

LabCorp will also supply the following:

- 1 Airway Bill (AWB)
- 1 Shipping box, each also including a refrigerant pack

CPGC sites will need to use the LabCorp Web Resupply Form to order re-supplies of BNT113-01 sample kits. Alternatively, as a back-up ordering method, re-supplies can be ordered by contacting LabCorp by phone, however the web form is the preferred method for ordering. Please note upon re-supply, the airway bill and shipping box is not part of the lab kit so need to be added to the resupply order manually.

LabCorp Web Resupply Form: http://www.drugdevelopment.labcorp.com/kitordering

Guidance for completing the web resupply form is provided in Appendix 4.

To call LabCorp Central Laboratory Services in Geneva from:
Monday – Friday 08:00-19:00 (Geneva time = GMT +1)
Saturday: 10:00-17:00 (Geneva time = GMT +1)
Telephone number (toll free contact number): +800 88 77 44 11

The initial supplies will take up to 8-12 working days to be delivered from the time the order is placed. Re-supplies will take 11-15 working days to be delivered from the time the order is placed. Supplies can be expedited for delivery within 8 working days if required, please contact cvlp@uhs.nhs.uk if expedited delivery is needed. All supply orders need to be ordered by 11:00am UK time in order to be processed the same day. Orders received after 11:00am will be processed the following business day (Monday-Friday).

Please note, for any CPGCs located in an extended delivery area, deliveries may take longer than the standard turnaround time.

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The SCTU will supply the CPGCs with the following bulk supplies in addition to the supplies provided by LabCorp:

- Disposable forceps
- PCR clean

To order resupplies of these items, CPGC sites will need to request re-supplies via SCTU by emailing cvlp@soton.ac.uk with the quantity required.

Preparation of slides and curls for BNT113-01

5 slides and 3 curls (1 curl per tube) should be provided, following the cutting scheme and precautions described below.

In line with NHS routine standard genomic sample handling and processing, to avoid contaminations of sample material with DNases/RNases or foreign DNA/RNA, the following measures must be taken:

Note: Extreme care must be taken during sectioning the FFPE blocks for BNT113-01 as HPV16+ FFPE tissue samples are particularly prone to contaminating other samples due to potentially high copy numbers of HPV DNA.

- Appropriate PPE for genomic sample handling is mandatory for all procedure steps with gloves being changed between handling different samples.
- Process only one sample at a time.
- Sample handling must be performed in a dedicated area for processing of genomic samples.
- Decontaminate/clean workspace and instruments that are not single-use with DNA-/RNA-/DNases-/RNases- Remover (e.g. PCR clean, according to the instructions) before processing of each individual FFPE block: e.g. cutting surface board, blade guard, tissue block holder, microtome handle, forceps, cooling plate etc.
- **Please use single-use disposable forceps (provided by SCTU) and single-use blades for each sample. Microtome blade must be changed between tissue blocks.**
- Ensure the sample kits used are within their expiry dates.

Preparation of slides and tubes for BNT113-01:

- Slides
  - Sections should be mounted on the SuperFrost slides provided.
  - Label each slide (5 in total) with BNT113-01 Subject ID, FFPE block ID and cutting sequence number using an indelible histology marker pen (water and solvent-resistant). This is to make sure that the sequence of cutting is known as for some analysis consecutive sections are chosen.
- Tubes
  - Each curl should be collected in separate 1.5 ml Eppendorf PP Biopur Safe-Lock Microcentrifuge Tube provided (Product # 02260028 in US or # 0030123328 in EU)
  - Label the tubes (3 in total) with BNT113-01 Subject ID, FFPE block ID and cutting sequence number using an indelible histology marker pen (water and solvent-resistant) using the tube labels provided. This is to make sure that the

sequence of cutting is known as for some analysis consecutive sections are chosen.
    - 1 curl should be collected per tube.
- Packaging
    - Slide mailer
    - Label the slide mailer with the BNT113-01 Subject ID

Preparation of tissue samples for BNT113-01:

- Please use one side of the blade for removing air-exposed, potentially contaminated tissue, and prepare sections using the opposite end of the microtome blade.
- Prepare sections following the cutting scheme and instructions below (cool FFPE block in between if needed):

Cutting sequencing number	Sample type	Thickness [µm]	Purpose	Shipment temperature (Site to Labcorp)
1	Slide	4-5	H&E	Refrigerated
2*	Curl (**1 curl per tube**)	10	HPV16 DNA	Refrigerated
3*	Curl (**1 curl per tube**)	10	Retention HPV16 DNA	Refrigerated
4*	Curl (**1 curl per tube**)	10	Retention HPV16 DNA	Refrigerated
5	Slide	4-5	PD-L1 testing	Refrigerated
6	Slide	4-5	PD-L1 testing	Refrigerated
7	Slide	4-5	Retention PD-L1 testing	Refrigerated
8	Slide	4-5	Retention PD-L1 testing	Refrigerated

*1 curl per tube (1.5ml eppendorf safe lock)

1. Cut 1 unstained tumour slide of 4-5 micron thickness for H&E staining which will be performed by LabCorp.
2. Cut 3 consecutive curls of 10 micron thickness. Cut 1 curl at a time and transfer to individual tubes (**1 curl per tube**) using single-use forceps. Do not use a brush for handling curls.
3. Store curls immediately at +2 to +8 °C until shipment.
4. Cut 4 consecutive unstained tumour slides of 4-5 micron thickness.

- Air-dry slides following local processes.
- Transfer the slides into the slide mailer (provided in bulk).
- Place the appropriate label provided in the LabCorp kit on to the slide mailer.
- Please write the correct pre-screening or patient ID on the label of the slide mailer.
- Complete the LabCorp requisition form fully.
- Slides and curls should be stored at refrigerated temperature until shipment to LabCorp.

Shipping the tissue samples

The CPGC will then need to send the prepared curls and slides refrigerated to BioNTech's central laboratory, LabCorp, on the same day or the next day at the latest. AWBs will be pre-

populated with LabCorp's correct shipment address so the following is provided for reference:

LabCorp Central Laboratory Services S.à.r.l
Rue Moïse-Marcinhes 7
1217 Meyrin Geneva Switzerland

Please refer to available LabCorp resources online for further information about kits, re-supply, packing and shipping videos, courier information:
https://www.labcorp.com/biopharma/central-labs/trial-management/resources

Initial set-up with DHL:
LabCorp will be responsible for setting up CPGCs as pick up locations with DHL on the EKAS system. During this process, each CPGC will be assigned a CPGC LabCorp site ID and this will be provided to CPGCs prior to activation by the SCTU.

Prior to CPGC activation for BNT113-01, CPGCs should telephone DLH using the number provided below at least 1 week prior to the first sample will be scheduled for collection to ensure set-up in the EKAS system has been completed correctly. The protocol number (BNT113-01) and CPGC LabCorp site ID will need to be provided to complete this step. CPGCs should discuss with DHL whether they fall under an extended delivery area as collections from these areas may take longer than the standard turnaround time.

Booking shipments with DHL:
To book a shipment pick up by DHL, please use the contact information below.

Contact phone number: 0800 279 8067
Email: LabcorpCLS.ekas@dhl.com

Ideally, sample collection will need to be arranged over the phone or by email the day prior to shipment and a two-hour window is to be agreed with the courier for collection. If the sample collection is postponed or cancelled, the courier service needs to be informed directly to postpone or cancel collection.

In the event urgent same day shipment is required, a collection needs to be ordered before the cut off of 11am.

Completing LabCorp requisition forms

A paper copy of the requisition form provided by BioNTech's central laboratory, LabCorp, (see appendix 2) should be completed and included with the tissue sample. The requisition form must be **fully** completed to include the following:

- Pre-screening ID (for patients consented to pre-screening) or Patient ID (for patients consented to main trial screening) – This is the unique ID number that the BNT113-01 trial site produces once the patient consents into the trial. The CVLP Referral Tool will hold this information for CPGC's to access. If the CVLP Referral Tool is unavailable, this information will be provided by the Clinical Liaison (cvlp@uhs.nhs.uk) to the CPGC by NHS email.
- Subject year of birth – Example 1999. The day and month of birth should always be 01 JAN as BioNTech only collect the year of birth.

- Gender – Select male or female.
- Requisition completion date
- Please indicate using the tick box whether HPV16 testing is required within 10-12 calendar days (this will be required for all main trial screening patients and pre-screening patients with clinical or radiological findings suggestive of recurrent / metastatic disease.

Packaging samples

Prior to packaging, please ensure the requisition form is filled out completely, and a copy taken of the completed requisition form and airway bill for upload to the CVLP Referral Tool. If the CVLP Referral Tool is unavailable, the requisition form and airway bill should be emailed to the CVLP Clinical Liaison (cvlp@uhs.nhs.uk) Please also ensure all samples are labelled correctly.

Sample shipments can be consolidated. The shipping box can hold 2-4 lab kits.

Freeze two refrigerant packs (provided with the refrigerated box) for 72 hours in -20˚ freezer and leave at room temperature for 1 hour prior to use.

1. Insert the tube(s) into the Specimen Collection Bag containing an absorbent pack. Place bag on flat surface to minimize wrinkles, especially at adhesive sealing area. Remove tape liner to expose adhesive. Fold along bag opening so star is inside of box shape. Press from center to edge to seal.

2. Place one frozen refrigerant pack into the Styrofoam container

3. Place a layer of paper towels on top of the refrigerant pack. Place the Specimen Collection Bag containing refrigerated specimens into the styrofoam. Place a second layer of paper towels on top of the specimen collection bag followed by a second refrigerant pack. Fill excess space with filler paper

4. Replace the styrofoam lid

5. Place the cardboard spacer or top of the Styrofoam. Place the pathology report in the ambient section

6. Insert the shipping documentation into the transparent pouch ensuring that the waybill remains visible. Affix the pouch to the cardboard box on the “Place waybill here” section

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Appendix 2 – Example Requisition Forms

Pre-screening:

labcorp

Labcorp Central Laboratory Services S.à.r.l
Rue Moïse-Marcinhes 7
1217 Meyrin Geneva Switzerland
Tel: 0041 58 822 7901
Fax: 0041 58 822 7521

Accession No.
«Requisition_n»

THE ACCESSION NUMBER IS THE REFERENCE NUMBER FOR COMMUNICATION WITH LABCORP.
Page 1 of 5

«Bar_req»

2-part

Laboratory Requisition Form
BioNTech SE
Protocol: BNT113-01
Investigator: «Inv_n»

VISIT: PART B PRE-SCREENING V3.0 CPGC

DO NOT RETURN THIS PAGE

Testing For This Visit

Please refer to the Laboratory Manual for detailed sample collection, preparation, and handling instructions.

Associated Test Groups(s)	Draw Container	Return Container	Shipment Condition
SM PATH REPORT	1 x envelope		Ambient
DIGITAL SLIDES 40X-SLIDE * SM FFPE SLIDES PARTB-PRESCREEN * TARGET LESION CONF-SLIDE *	1 x super frost microscope slide, 1 x label, 1 x microscope slide box, 3 x eppendorf tubes, 3 x labels		Refrigerated
BATCH HPV PANEL HPV-16 - CURL ** HPV PANEL HPV-16 - CURL ** SM EXTRACTED DNA-PART B ** SM FFPE CURLS PART B-PRESCREEN * TESTING REQUIRED-CURLS *	1 x super frost microscope slide, 1 x label, 1 x microscope slide box, 3 x eppendorf tubes, 3 x labels		Refrigerated

* Conditional
** Reflex

This kit should be used for Sites under protocol version 3.0 and above.

Please remember to send the Pathology Report along with the tissue biopsy.

Please note that for tissue submission: requirement is 10% NBF (10% Neutral Buffered Formalin), any other fixative used will result in cancellation of testing and HPV16 and PDL1 assays will not be performed.

Please follow Part B specimen collection instructions in the lab manual.

Provide **both slides and curls** as per below:
- 5 slides of 4-5 µm thickness: one for H&E and four for PD-L1.
- 3 curls of 10 µm thickness (each curl in its own tube) for HPV16 DNA.

Slides stability is 6 months when stored at 2-8 °C (preferred) or 4 months when stored at 25 °C.
Curls stability is 18 months for ambient and refrigerated storage.

Pre-screening number indicated on this requisition form must match the Pre-screening number indicated on your site pre-screening log.
Please consider whether the expedited turnaround time of 10-12 days is required, or the standard ~30 days is adequate.

No NCR	«Label_6»		«Bar_req»
49	210445	Keep on file for your records. DO NOT return to Labcorp.	JSR 250317

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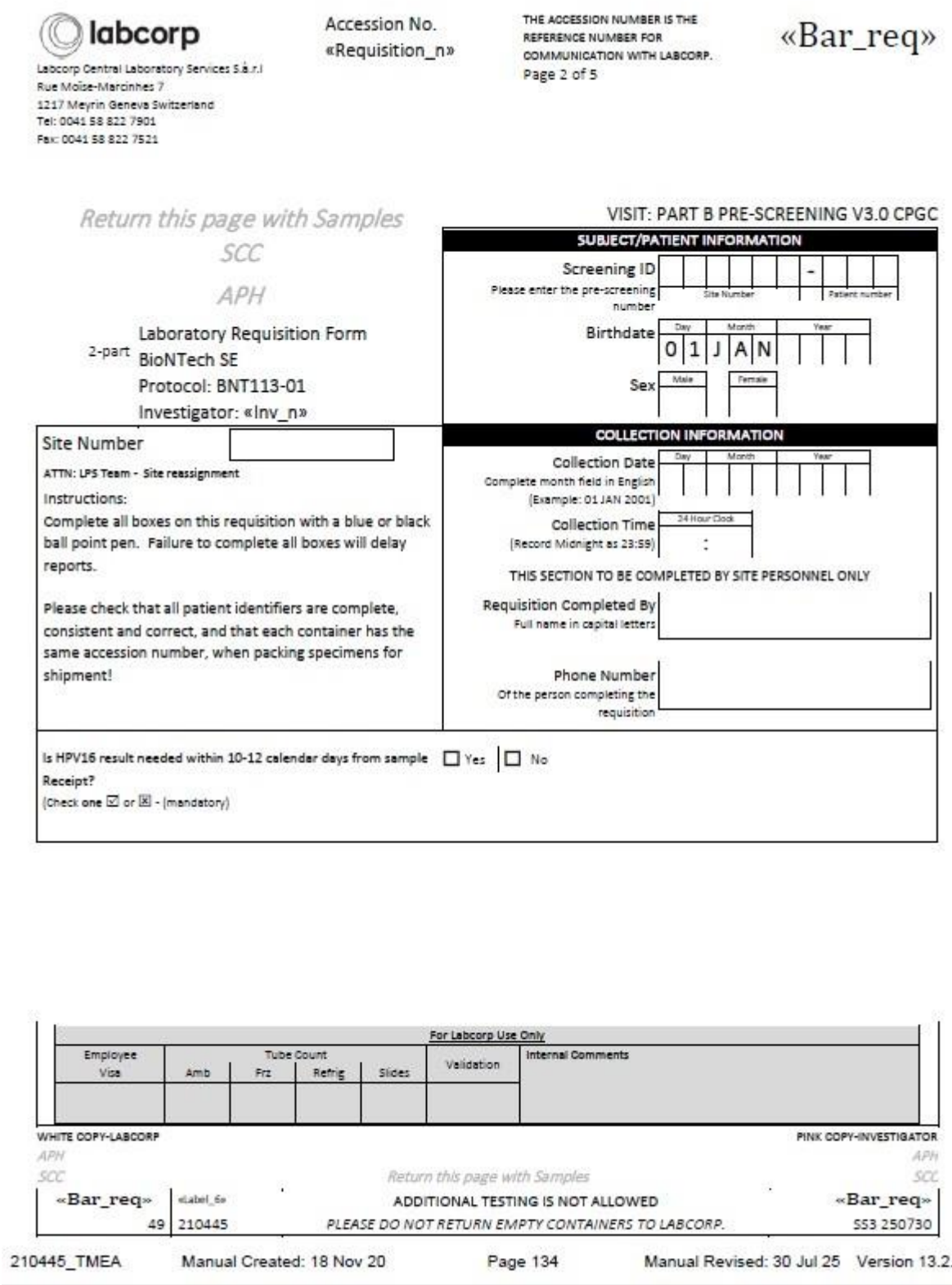

labcorp

Labcorp Central Laboratory Services S.à.r.l
Rue Moïse-Marcinhes 7
1217 Meyrin Geneva Switzerland
Tel: 0041 58 822 7901
Fax: 0041 58 822 7521

Accession No.
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THE ACCESSION NUMBER IS THE REFERENCE NUMBER FOR COMMUNICATION WITH LABCORP.
Page 2 of 5

«Bar_req»

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2-part Laboratory Requisition Form
BioNTech SE
Protocol: BNT113-01
Investigator: «Inv_n»

VISIT: PART B PRE-SCREENING V3.0 CPGC

SUBJECT/PATIENT INFORMATION

Screening ID
Please enter the pre-screening number
Site Number | Patient number

Birthdate: Day 01 | Month JAN | Year

Sex: Male | Female

Site Number

ATTN: LPS Team - Site reassignment

Instructions:
Complete all boxes on this requisition with a blue or black ball point pen. Failure to complete all boxes will delay reports.

Please check that all patient identifiers are complete, consistent and correct, and that each container has the same accession number, when packing specimens for shipment!

COLLECTION INFORMATION

Collection Date
Complete month field in English (Example: 01 JAN 2001)
Day | Month | Year

Collection Time
(Record Midnight as 23:59)
24 Hour Clock

THIS SECTION TO BE COMPLETED BY SITE PERSONNEL ONLY

Requisition Completed By
Full name in capital letters

Phone Number
Of the person completing the requisition

Is HPV16 result needed within 10-12 calendar days from sample Receipt?
(Check one ☑ or ☒ - (mandatory) ☐ Yes ☐ No

For Labcorp Use Only

Employee Visa	Tube Count: Amb	Frz	Refrig	Slides	Validation	Internal Comments

WHITE COPY-LABCORP — PINK COPY-INVESTIGATOR

APH *SCC* *Return this page with Samples* *APH* *SCC*

«Bar_req» | «Label_6» | ADDITIONAL TESTING IS NOT ALLOWED | «Bar_req»
49 | 210445 | *PLEASE DO NOT RETURN EMPTY CONTAINERS TO LABCORP.* | 553 250730

210445_TMEA Manual Created: 18 Nov 20 Page 134 Manual Revised: 30 Jul 25 Version 13.2.0

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1217 Meyrin Geneva Switzerland
Tel: 0041 58 822 7901
Fax: 0041 58 822 7521

Accession No.
«Requisition_n»

THE ACCESSION NUMBER IS THE REFERENCE NUMBER FOR COMMUNICATION WITH LABCORP.

«Bar_req»

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VISIT: PART B PRE-SCREENING V3.0 CPGC

Laboratory Requisition Form
2-part BioNTech SE
Protocol: BNT113-01
Investigator: «Inv_n»

Screening ID
Please enter the pre-screening number
Site Number | Patient number

Collection Date
Complete month field in English (Example: 01 JAN 2001)
Day | Month | Year

Mandatory for all Tissue Specimens Submitted	
Biopsy / Surgical Resection Date	Date (DD-MMM-YYYY) _____
Block ID (Sample ID from Pathology Report Form)	☐ _____ ☐ Wet Tissue Submitted, Block ID not applicable
Pathological Diagnosis of Samples Submitted or Historical Diagnosis (if wet tissue submitted)	☐ HNSCC ☐ Other (specify): _____
Anatomical site *Note: Bone lesions cannot be decalcified.* *Note: Site refers to the location of the tissue sent for testing (e.g., lymph node metastasis, lung metastasis, primary or relapsed tumor in the oropharynx), and not the primary origin of the tumor.*	☐ Oropharynx ☐ Hypopharynx ☐ larynx ☐ oral cavity ☐ Lung ☐ Liver ☐ lymph node ☐ bone ☐ Other (specify):_____
Origin of submitted tissue *Note: only select "Primary Tumor" if "Anatomical site" above is a lymph node OR primary tumor (e.g. oropharynx) AND the sample is from the time of initial diagnosis - for samples from relapses select the other option.*	☐ Primary tumor ☐ Metastatic Tumor Location
Fixative used *Note: 10% Neutral Buffered Formalin is required*	☐ 10% Neutral Buffered Formalin ☐ Other (specify): _____
Tissue decalcified? *Note: Decalcified tissue is NOT acceptable and it will result in cancellation*	☐ Yes ☐ No

(continued to next page)

For Labcorp Use Only						
Employee Visa	Tube Count				Validation	Internal Comments
	Amb	Frz	Refrig	Slides		

WHITE COPY-LABCORP
PINK COPY-INVESTIGATOR

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«Bar_req»	«Label_6»	ADDITIONAL TESTING IS NOT ALLOWED	«Bar_req»
49	210445	*PLEASE DO NOT RETURN EMPTY CONTAINERS TO LABCORP.*	JSR 250317

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1217 Meyrin Geneva Switzerland
Tel: 0041 58 822 7901
Fax: 0041 58 822 7521

Accession No.
«Requisition_n»

THE ACCESSION NUMBER IS THE REFERENCE NUMBER FOR COMMUNICATION WITH LABCORP.

«Bar_req»

Return this page with Samples
SCC
APH

VISIT: PART B PRE-SCREENING V3.0 CPGC

Laboratory Requisition Form
2-part BioNTech SE
Protocol: BNT113-01
Investigator: «Inv_n»

Screening ID
Please enter the pre-screening number
Site Number | Patient number

Collection Date
Complete month field in English (Example: 01 JAN 2001)
Day | Month | Year

(Continued from previous page)

SM FFPE SLIDES PARTB-PRESCREEN	
Fixation Duration in 10% Neutral Buffered Formalin *Note: this information is recommended for blocks and slides*	☐ Not applicable (wet tissue submitted) ☐ 0<6 hr ☐ 6<24 hr ☐ 24<48 hr ☐ 48<72 hr ☐ >72 hr ☐ Unknown

SM FFPE SLIDES PARTB-PRESCREEN, SM FFPE CURLS PART B-PRESCREEN	
Slide/curl sectioning date	☐ Date (DD-MMM-YYYY) _____ ☐ N/A (block or wet tissue submitted)

SM FFPE SLIDES PARTB-PRESCREEN	
Section Micron Thickness *Note: for slides only*	IHC / IHC-Genomics ☐ N/A (block or wet tissue submitted) ☐ 4 µm ☐ 5 µm

For Labcorp Use Only						
Employee Visa	Tube Count				Validation	Internal Comments
	Amb	Frz	Refrig	Slides		

WHITE COPY-LABCORP
PINK COPY-INVESTIGATOR

APH *APH*
SCC *SCC*

Return this page with Samples

«Bar_req»	«Label_6»	ADDITIONAL TESTING IS NOT ALLOWED	«Bar_req»
49	210445	*PLEASE DO NOT RETURN EMPTY CONTAINERS TO LABCORP.*	JSR 250317

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Rue Moise-Marcinhes 7
1217 Meyrin Geneva Switzerland
Tel: 0041 58 822 7901
Fax: 0041 58 822 7521

Accession No.
«Requisition_n»

THE ACCESSION NUMBER IS THE REFERENCE NUMBER FOR COMMUNICATION WITH LABCORP.

«Bar_req»

Return this page with Samples
SCC
APH

VISIT: PART B PRE-SCREENING V3.0 CPGC

Screening ID
Please enter the pre-screening number
Site Number | Patient number

Collection Date
Complete month field in English (Example: 01 JAN 2001)
Day | Month | Year

2-part Laboratory Requisition Form
BioNTech SE
Protocol: BNT113-01
Investigator: «Inv_n»

Anatomic Pathology Specimen - Part B Pre-Screening V3.0

Submit:
- Slides and Curls: SM FFPE SLIDES PART B and SM FFPE CURLS PART B

Mark the appropriate box below.

Condition	Sample
Tumor Slides are submitted for PD-L1 analysis. Tumor Slides and FFPE Curls are submitted for HPV16 analysis. Mark these two boxes if SM FFPE SLIDES PARTB-PRESCREEN and SM FFPE CURLS PART B-PRESCREEN samples are submitted.	☐ SLIDES ☐ CURLS

Comment

For Labcorp Use Only

Employee Visa	Tube Count				Validation	Internal Comments
	Amb	Frz	Refrig	Slides		

WHITE COPY-LABCORP

PINK COPY-INVESTIGATOR

APH
SCC

Return this page with Samples

APH
SCC

«Bar_req»	«Label_6»	ADDITIONAL TESTING IS NOT ALLOWED	«Bar_req»
49	210445	*PLEASE DO NOT RETURN EMPTY CONTAINERS TO LABCORP.*	JSR 250317

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Main Trial Screening:

labcorp
Labcorp Central Laboratory Services S.à.r.l
Rue Moïse-Marcinhes 7
1217 Meyrin Geneva Switzerland
Tel: 0041 58 822 7901
Fax: 0041 58 822 7521

Accession No.
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THE ACCESSION NUMBER IS THE REFERENCE NUMBER FOR COMMUNICATION WITH LABCORP.
Page 1 of 5

«Bar_req»

2-part Laboratory Requisition Form
BioNTech SE
Protocol: BNT113-01
Investigator: «Inv_n»

VISIT: PART B TISSUE BIOPSY CPGC

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Testing For This Visit

Please refer to the Laboratory Manual for detailed sample collection, preparation, and handling instructions.

Associated Test Groups(s)	Draw Container	Return Container	Shipment Condition
SM PATH REPORT	1 x envelope		Ambient
DIGITAL SLIDES 40X-SLIDE * SM FFPE SLIDES PART B * TARGET LESION CONF-SLIDE *	1 x super frost microscope slide, 1 x label, 1 x microscope slide box, 3 x eppendorf tubes, 3 x labels		Refrigerated
HPV PANEL HPV-16 - CURL * SM EXTRACTED DNA-PART B * SM FFPE CURLS PART B *	1 x super frost microscope slide, 1 x label, 1 x microscope slide box, 3 x eppendorf tubes, 3 x labels		Refrigerated

* Conditional

Please remember to send the Pathology Report along with the tissue biopsy.

Please note that for tissue submission: requirement is 10% NBF (10% Neutral Buffered Formalin), any other fixative used will result in cancellation of testing and HPV16 and PDL1 assays will not be performed.

Leave Patient ID field blank unless patient is being re-screened.

Please follow Part B specimen collection instructions in the lab manual.

Provide both slides and curls as per below:
- 5 slides of 4-5 µm thickness: one for H&E and four for PD-L1
- 3 curls of 10 µm thickness (each curl in its own tube) for HPV16 DNA.

Slides stability is 6 months when stored at 2-8 °C (preferred) or 4 months when stored at 25 °C.
Curls stability is 18 months for ambient and refrigerated storage.

No NCR	«Label_6»		«Bar_req»
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2-part Laboratory Requisition Form
BioNTech SE
Protocol: BNT113-01
Investigator: «Inv_n»

VISIT: PART B TISSUE BIOPSY CPGC

SUBJECT/PATIENT INFORMATION

Screening ID — Site Number | Patient number

Patient ID — Leave blank unless patient is being rescreened — Site Number | Patient number

Birthdate — Day | Month | Year: 0 1 J A N

Sex — Male | Female

Site Number

ATTN: LPS Team - Site reassignment

Instructions:
Complete all boxes on this requisition with a blue or black ball point pen. Failure to complete all boxes will delay reports.

Please check that all patient identifiers are complete, consistent and correct, and that each container has the same accession number, when packing specimens for shipment!

COLLECTION INFORMATION

Collection Date — Complete month field in English (Example: 01 JAN 2001) — Day | Month | Year

Collection Time — [Record Midnight as 23:59] — 24 Hour Clock

THIS SECTION TO BE COMPLETED BY SITE PERSONNEL ONLY

Requisition Completed By — Full name in capital letters

Phone Number — Of the person completing the requisition

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Employee Visa	Tube Count: Amb	Frz	Refrig	Slides	Validation	Internal Comments

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VISIT: PART B TISSUE BIOPSY CPGC

Screening ID ☐☐☐☐☐☐ - ☐☐☐☐ (Site Number / Patient number)

Patient ID ☐☐☐☐☐☐ - ☐☐☐☐ (Site Number / Patient number)
Leave blank unless patient is being rescreened

Collection Date ☐☐ Day ☐☐☐ Month ☐☐☐☐ Year
Complete month field in English (Example: 01 JAN 2001)

2-part Laboratory Requisition Form
BioNTech SE
Protocol: BNT113-01
Investigator: «Inv_n»

Mandatory for all Tissue Specimens Submitted	
Biopsy / Surgical Resection Date	Date (DD-MMM-YYYY) _____
Block ID (Sample ID from Pathology Report Form)	☐ _____ ☐ Wet Tissue Submitted, Block ID not applicable
Pathological Diagnosis of Samples Submitted or Historical Diagnosis (if wet tissue submitted)	☐ HNSCC ☐ Other (specify): _____
Anatomical site *Note: Bone lesions cannot be decalcified.* *Note: Site refers to the location of the tissue sent for testing (e.g., lymph node metastasis, lung metastasis, primary or relapsed tumor in the oropharynx), and not the primary origin of the tumor.*	☐ Oropharynx ☐ Hypopharynx ☐ larynx ☐ oral cavity ☐ Lung ☐ Liver ☐ lymph node ☐ bone ☐ Other (specify):_____
Origin of submitted tissue *Note: only select "Primary Tumor" if "Anatomical site" above is a lymph node OR primary tumor (e.g. oropharynx) AND the sample is from the time of initial diagnosis - for samples from relapses select the other option.*	☐ Primary tumor ☐ Metastatic Tumor Location
Fixative used *Note: 10% Neutral Buffered Formalin is required*	☐ 10%Neutral Buffered Formalin ☐ Other (specify): _____
Tissue decalcified? *Note: Decalcified tissue is NOT acceptable and it will result in cancellation*	☐ Yes ☐ No

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Employee Visa	Tube Count				Validation	Internal Comments
	Amb	Frz	Refrig	Slides		

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VISIT: PART B TISSUE BIOPSY CPGC

Screening ID ___ - ___ (Site Number / Patient number)

Patient ID ___ - ___ (Site Number / Patient number)
Leave blank unless patient is being rescreened

Collection Date (Day / Month / Year)
Complete month field in English (Example: 01 JAN 2001)

2-part Laboratory Requisition Form
BioNTech SE
Protocol: BNT113-01
Investigator: «Inv_n»

(Continued from previous page)

SM FFPE SLIDES PART B

Fixation Duration in 10% Neutral Buffered Formalin
Note: this information is recommended for blocks and slides

- ☐ Not applicable (wet tissue submitted)
- ☐ 0<6 hr
- ☐ 6<24 hr
- ☐ 24<48 hr
- ☐ 48<72 hr
- ☐ >72 hr
- ☐ Unknown

SM FFPE SLIDES PART B, SM FFPE CURLS PART B

Slide/curl sectioning date

- ☐ Date (DD-MMM-YYYY) _____
- ☐ N/A (block or wet tissue submitted)

SM FFPE SLIDES PARTB

IHC / IHC-Genomics

Section Micron Thickness
Note: for slides only

- ☐ N/A (block or wet tissue submitted)
- ☐ 4 µm
- ☐ 5 µm

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Employee Visa	Tube Count				Validation	Internal Comments
	Amb	Frz	Refrig	Slides		

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Laboratory Requisition Form
2-part BioNTech SE
Protocol: BNT113-01
Investigator: «Inv_n»

VISIT: PART B TISSUE BIOPSY CPGC

Screening ID | | | | | | - | | | | (Site Number / Patient number)

Patient ID (Leave blank unless patient is being rescreened) | | | | | | - | | | | (Site Number / Patient number)

Collection Date (Complete month field in English (Example: 01 JAN 2001)) Day | Month | Year

CONDITIONAL TESTING - Please mark the box(es) ☑ or ☒ to ensure proper ordering of test(s)!
If you fail to mark the checkbox, testing may be ordered per Covance policy without investigator notification.

Submit:
- Slides and Curls: SM FFPE SLIDES PART B and SM FFPE CURLS PART B

Mark the appropriate box below.

Condition	Sample
Tumor Slides are submitted for PD-L1 analysis. Tumor Slides and FFPE Curls are submitted for HPV16 analysis. Mark these two boxes if SM FFPE SLIDES PART B box SM FFPE CURLS PART B samples are submitted.	☐ SLIDES ☐ CURLS

Comment

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Employee Visa	Tube Count: Amb	Frz	Refrig	Slides	Validation	Internal Comments

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«Bar_req»	«Label_6»	ADDITIONAL TESTING IS NOT ALLOWED	«Bar_req»
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Appendix 3 – Web Re-supply

Please follow the following guidance when completing the LabCorp re-supply webform.

Section A:

- Pharmaceutical Sponsor: BioNTech
- Complete Protocol Number: BNT113-01
- LabCorp Project Number: 210445
- Principal Investigator Name: CPGC Lead details
- Site Number: CPGC LabCorp Site ID
- Country: UK
- Email address: main contact email address for requestor

Section B:

- Lab kit (Please note a critical minimum order quantity of 2 pre-screening kits **and** 1 main screening kit applies)
    - Part B Pre-Screening V3.0 CPGC (minimum order quantity 2)
    - Part B Tissue biopsy CPGC (minimum order quantity 1)
- Additional bulk supplies:
    - Microscope slides (Superfrost package)
    - Empty microscope slide box
- Shipping boxes
    - Refrigerated boxes (each box should include a refrigerant pack but please add wording in the form comments section to request refrigerant packs are included for completeness)
- Shipping documents
    - Airway Bill (AWB)

In the event expedited shipment is required, please indicate this on the form and notify the CVLP team at cvlp@soton.ac.uk.

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Appendix 4 – CVLP pathway for BioNTech's BNT113-01 (AHEAD-MERIT) trial (CVLP Referral Tool unavailable)

The below process is to be followed if the CVLP Referral Tool is either not in use at the CVLP site (pending transition) or temporarily unavailable for use.

Activity		Responsible
Identification and consent into the CVLP		
Step 1	• Patients should be identified for the CVLP following the referral criteria outlined in section 7.2.	CVLP site – clinical/research team
Step 2	• An adequately trained health care practitioner from the clinical care team/research team should take the patient's consent for the CVLP using the CVLP patient information sheet and consent form provided. Consent can be taken in person, remotely or via e-consent, please refer to the CVLP protocol for details. • Once a patient consents, their name and details should be added to the CVLP data return template, sending an updated version of this to the SCTU Clinical Liaison team (cvlp@uhs.nhs.uk) weekly on Friday (latest 2pm) using encrypted NHS mail. • At the same time, the research delivery team are to inform the local pathology department immediately about the recruited patient. • Local SOPs should be followed by the CVLP site research team for requesting the release of an FFPE tissue block to the CPGC, with the block being sent by a **tracked delivery method**. A copy of the participants pathology report should be included with the shipment. • The CVLP site research team will inform the CPGC by email that a patient has been recruited, and they can expect to receive an FFPE tissue block from the CVLP site, copying in the Clinical Liaison via cvlp@uhs.nhs.uk. When doing so, the CVLP research team will also attach a scanned copy of patient's signed informed consent for the CPGC to receive the FFPE tissue block. • The CVLP site research team (or local pathology team – see step 3) must enter the tumour block details, date of shipment and tracking information into the CVLP data return template. The CVLP site research team should send the CVLP GP letter (Word template provided) including a copy of the CVLP patient information sheet to inform the patient's GP that they are participating into the CVLP.	CVLP site – clinical/research team

Tissue sample for the CVLP		
Step 3	• The CVLP site's local pathology department will identify an archival FFPE tissue block that was taken as part of the standard of care pathway for diagnosis of HNSCC. The sample should preferably be derived from a current site of metastatic or recurrent disease. Otherwise, a sample from the primary tumour is an acceptable alternative.	CVLP site – local pathology
Step 4	• Once the tissue block is identified, it should be sent to the relevant Cellular Pathology Genomic Centre (CPGC) as soon as possible using **tracked delivery**, following standard packaging, and transport protocols. • The CVLP site research team (or local pathology team) must enter the tumour block details, date of shipment and tracking information into the CVLP data return template.	CVLP site – local pathology
Patient referral to the BNT113-01 trial		
Step 5	• Following confirmation that the patient is suitable for either BNT113-01 pre-screening or main trial screening (see Section 7.2 for pre-screening and main trial screening eligibility criteria), the CVLP site will complete and email the required password protected 'CVLP – BNT113-01 Pre-Screening Referral Form' or 'CVLP – BNT113-01 Main Trial Screening Referral Form'. The CVLP site should also attach the patients required reports - For pre-screening the pathology report will need to be uploaded, and for main trial screening the pathology report, radiology report and last clinic letter will need to be uploaded. The referral form can be sent directly to the trial site by secure NHS email, copying in the Clinical Liaison (cvlp@uhs.nhs.uk). The CVLP site should also update the data return template to confirm if a referral has been submitted.	CVLP site – clinical/research team
Step 6	• On receipt of the referral, the trial site reviews the information provided by CVLP sites and confirm whether the patient is a suitable candidate for BNT113-01 pre-screening or main trial screening. • The trial site will contact the patient and arrange for them to be consented into the BNT113-01 trial. • Dependent on adoption, trial sites may have the option to utilise remote consent or in person consent for pre-screening depending on the patient's preference. • Trial sites must arrange to consent those who are suitable candidates for the main trial screening in person. **If the patient consents to pre-screening (see steps 7-9 and 11-12):** • The trial site will record the patient on their BNT113-01 pre-screening log held at their site. The trial site will also issue a unique pre-screening number (pre-screening ID). The trial	Trial site

	site will confirm pre-screening consent and send the following information to the Clinical Liaison (cvlp@uhs.nhs.uk) by email: 1) BNT113-01 pre-screening ID 2) Date of pre-screening consent 3) Patient name 4) Patient NHS number **If the patient consents to main trial screening (see steps 7-9, 11-14):** • The trial site will issue a unique participant number (patient ID) by registering the patient on the BNT113-01 IxRS system. The trial site will confirm main trial screening consent and send the following information to the Clinical Liaison (cvlp@uhs.nhs.uk) by email: 1) BNT113-01 patient ID 2) Date of main trial screening consent 3) Patient name 4) Patient NHS number	
Tissue preparation for BNT113-01		
Step 7	• On confirmation of the date of consent to BNT113-01 pre-screening or main trial screening by trial sites, the Clinical Liaison team will send a notification to the relevant CPGC via email to alert that sample preparation is required. This email will include the BNT113-01 pre-screening/patient ID.	CPGC
Step 8	• The CPGC will prepare the curls and slides for central HPV16 DNA and PD-L1 expression testing following the instructions and cutting scheme provided in appendix 1. • For participants who have been consented to BNT113-01 pre-screening and main trial screening, the CPGC will prepare the curls and slides within 3 working days of being notified a sample is required.	CPGC
Step 9	• The standard turnaround time for HPV16 DNA and PD-L1 central testing is up to 30 calendar days for pre-screening from receipt of the sample by LabCorp. • Expedited central testing is required for pre-screening participants who have clinical or radiological findings suggestive of recurrent or metastatic HNSCC pending confirmatory studies that is not expected to be curable with surgery or radiation. CPGCs must indicate on the sample requisition form that results are required within 10-12 calendar days from sample receipt at LabCorp for these participants.	CPGC

Step 10	• The standard turnaround time for HPV16 DNA and PD-L1 central testing is 10-12 calendar days for main trial screening from receipt of the sample by LabCorp.	CPGC
Step 11	• The CPGC will send the curls and slides to BioNTech's central laboratory, LabCorp, using the DHL courier. • The CPGC will complete the CPGC data return template and return it to the Clinical Liaison (cvlp@uhs.nhs.uk), confirming the dates that samples were shipped, the sample kit accession number and airway bill (AWB) number. The CPGC will also send a copy of the completed sample requisition form and airway bill to the Clinical Liaison (cvlp@uhs.nhs.uk).	CPGC

Step 12	• BioNTech's central laboratory, LabCorp, will use the curls and slides prepared by the CPGC to undergo central testing as follows:
	  ○ Pre-screening (up to 30 calendar day turnaround time): PD-L1 expression followed by HPV16 DNA testing for those expressing PD-L1.
	  ○ Expedited pre-screening samples and main trial screening samples (10-12 calendar day turnaround time): PD-L1 and HPV16 DNA testing completed simultaneously.
	
	• The trial site will be informed of the results of the central HPV16 and PD-L1 testing directly as per trial protocol.
	
	• The trial site will inform the patient directly of the results of the central testing. Dissemination of central PD-L1 results, and HPV16 results if tested, to participants must be performed by trial sites under trial site PI oversight.
	
	• The trial site must email the outcome of central testing to the CVLP site and the Clinical Liaison (cvlp@uhs.nhs.uk) within 1 working day after receipt of the report.
		LabCorp / trial site

Pre-screening for BNT113-01		
Step 13	• Following notification of consent to BNT113-01 pre-screening, the CVLP site must ensure that the trial site team and the Clinical Liaison (cvlp@uhs.nhs.uk) are updated with the date that CVLP expects a diagnosis of recurrent/metastatic HNSCC to be confirmed. As an example, this may be the date the patient is due to be discussed in MDT post imaging or biopsy, or the date the CVLP expects to receive the imaging or biopsy report. • If the CVLP site confirms a diagnosis of recurrent/metastatic HNSCC during pre-screening for BNT113-01, then the	CVLP site – clinical/research team

	'CVLP – BNT113-01 Main Trial Referral Form' should be completed and sent to directly to the trial site, copying in the Clinical Liaison (cvlp@uhs.nhs.uk). The CVLP site should also update the data return template to confirm if a main trial referral has been submitted.	
Step 14	• On receipt of a confirmed recurrent/metastatic HNSCC diagnosis during pre-screening and main trial referral, trial sites will review the patient's details and consider them for consent and inclusion in BNT113-01 main trial screening. • Trial sites will confirm the date of consent to main trial screening by email to the Clinical Liaison (cvlp@uhs.nhs.uk), the email should also include the patients name, NHS number and BNT113-01 patient ID. Consent for main trial screening must be given in person. • As the central HPV16 and PD-L1 central testing will already have been completed as part of pre-screening, there will be no requirement for trial sites to handle tissue for patients proceeding from pre-screening to main trial screening. There will also be no requirement for any further tissue preparation or shipment by the CPGC to BioNTech's central laboratory, LabCorp.	Trial site
Main Trial Screening and Randomisation for BNT113-01		
Step 15	• The trial site will perform the required investigations per the BNT113-01 trial protocol prior to the start of trial treatment.	Trial site
Step 16	• Patients that meet all eligibility criteria for inclusion in BNT113-01 are randomised to the experimental or control group. The trial site will email the Clinical Liaison (cvlp@uhs.nhs.uk) with the date of randomisation along with the patient's name, NHS number and BNT113-01 patient ID. The treatment arm should not be sent to the Clinical Liaison. • At this point, the trial site will take over responsibility for the patients care and ongoing cancer treatment and monitoring.	Trial site

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Appendix 5 – Summary of significant changes to the Technical Requirements

Technical Requirements version and date		Summary of significant changes
V1	02-Apr-2025	First version
V2	10-Oct-2025	**1)** Inclusion of high-risk patients into pre-screening inclusion criteria. **2)** Updated CVLP/BNT113-01 Pathway image to reflect change 1. **3)** Clarification of patient reports to be uploaded / attached with referral. **4)** Clarification on meaning of measurable disease (inclusion criteria). **5)** Inclusion of disposable forceps and PCR clean supply. **6)** Clarification on requirement for unstained slide. **7)** Inclusion of HPV16 testing timeframe requirement onto requisition form. **8)** Updated requisition form image to reflect change 7.