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Therapeutic HPV vaccine trial +/- anti-CD40 in HPV-driven squamous cell carcinoma

Submission date 02/11/2016	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 15/12/2016	**Overall study status** Completed	
Last Edited 30/09/2026	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-a-vaccine-for-cancers-who-tested-positive-to-the-human-papilloma-virus-hare-40

Contact information

Type(s)
Public

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT03418480

Clinical Trials Information System (CTIS)
2014-002061-30

Protocol serial number

30900

Study information

Scientific Title
Therapeutic HPV vaccine (BNT113) trial in HPV16 driven carcinoma

Acronym
HARE-40

Study objectives
The overall aim of this study is to establish a safe and tolerable dose of HPV mRNA vaccine and assess if there is evidence of clinical effect according to irRECIST 1.1.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 18/07/2016, London - West London & GTAC Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8098; westlondon.rec@hra.nhs.uk), ref: 16/LO/0567

Primary study design
Interventional

Study design
Non-randomized interventional study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
HPV-driven squamous cell carcinoma

Interventions
Added 18/09/2026:
HARE-40 is a Phase I/II vaccine dose escalation trial with two different arms. The vaccine (BNT113) will be intravenously administered.

Arm 1A (Phase I) will perform intrapatient dose escalation in patients with previously treated HPV16+ Head & Neck Cancer using two dose cohorts to establish a safe, tolerable and recommended dose of BNT113. Arm 1A will consist of 6 patients in Cohort 1 and 9 patients in Cohort 2.

Arm 1B (Phase I/II) will begin by performing intrapatient dose escalation in 15 patients with advanced HPV16+ cancer (head and neck, anogenital, penile, cervical or unknown primary) using a single cohort to establish a safe, tolerable and recommended dose of BNT113.

Following DMEC review with input from SRC Arm 1B will be expanded to a second cohort of 14 patients to assess the Phase II clinical endpoints of activity and safety.

Intervention Type
Biological/Vaccine

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
BNT113

Primary outcome(s)
Current primary outcomes as of 18/09/2026:
Arms 1A and 1B:
Determination of a suitable dose of BNT113 based on defined criteria for DLTs (dose limiting toxicities) according to CTCAE version 4.03. This is measured by evaluation of DLTs until 28 days after last study treatment.

Arm 1B:
Disease control rate, defined as the rate of complete response, partial response or stable disease, is measured according to irRECIST 1.1 at the end of treatment CT scan at Day 85.

Previous primary outcomes:
Arm 1A:
The suitable dose of HPV mRNA vaccine is based on defined criteria for DLTs (dose limiting toxicities). This is measured by evaluation of DLTs until 28 days after last study treatment.

Arm 1B:
Disease control rate, defined as the rate of complete response, partial response or stable disease, is measured according to irRECIST 1.1 at the end of treatment CT scan at Day 85.

Key secondary outcome(s)
Current secondary outcomes as of 18/09/2026:
Arm 1A:
1. Adverse event rate is measured according to CTCAE v4.03 at the end of the trial until 28 days after last study treatment
2. Systemic levels of induced HPV-16 specific T-cell and B-cell immune responses are measured using specific biomarker tests at the end of study treatment
3. Duration of detectable vaccine-induced immune response is measured using specifically designed immune-assays at the end of study treatment
4. The clinical and immunological evaluation of DTH sites is assessed prior to vaccination and after the vaccination course, by clinical assessment and tissue biopsy, 48 hours post DTH injection in patients who had DTH control reaction assessments.

Arm 1B:
1. Adverse event rate is measured according to CTCAE v4.03 at the end of the trial until 28 days after last study treatment
2. Systemic levels of induced HPV-16 specific T-cell and B-cell immune responses are measured using specific biomarker tests during the course of trial at the end of study treatment
3. Duration of detectable vaccine-induced immune response is measured using specifically designed immune-assays, such as PBMCs during the course of the trial at the end of study treatment
4. The clinical and immunological evaluation of DTH sites is assessed prior to vaccination and

after the vaccination course, by clinical assessment and tissue biopsy 48 hours post DTH injection in patients who had DTH control reaction assessment.
5. Percentage change in densities of immune cells in tumour tissue (where paired samples can be collected) is assessed using tumour tissue biopsies at baseline and follow-up (Day 85)
6. Numbers of immune cells is assessed by immunohistochemistry or flow cytometry at baseline and follow-up (Day 85)
7. Clinical response is measured according to irRECIST 1.1 at 85 days and 6 and 9 months
8. Disease control rate is measured according to irRECIST 1.1 at 6 and 9 months
9. Best overall response is measured according to irRECIST 1.1 at 9 months
10. Intra-tumoural levels of HPV16specific immune responses (where paired tumour samples can be collected) is measured using tumour tissue biopsies at baseline and follow-up (Day 85)
11. Safety/tolerability of HPV mRNA vaccine in terms of the adverse event rate is measured according to CTCAE v4.03 at 36 and 85 days
12. Grade 3 or above vaccine- or combination administration-related toxicity is measured within 90 days after the last administration of study drugs
13. Progression-Free Survival (PFS) is measured from baseline to date of disease progression or death, from any cause
14. Overall Survival (OS) is measured from baseline to date of disease progression or death, from any cause
15. Disease Specific Interval (DSI) is measured from baseline to date of disease progression or death, from any cause

Previous secondary outcomes:
Arm 1A:
1. Adverse event rate is measured according to CTCAE v4.03 at the end of the trial until 28 days after last study treatment
2. Systemic levels of induced HPV-16 specific T-cell and B-cell immune responses are measured using specific biomarker tests at the end of study treatment
3. Duration of detectable vaccine-induced immune response is measured using specifically designed immune-assays at the end of study treatment
4. The clinical and immunological evaluation of DTH sites is assessed prior to vaccination and after the vaccination course, by clinical assessment and tissue biopsy, 48 hours post DTH injection

Arm 1B:
1. Adverse event rate is measured according to CTCAE v4.03 at the end of the trial until 28 days after last study treatment
2. Systemic levels of induced HPV-16 specific T-cell and B-cell immune responses are measured using specific biomarker tests during the course of trial at the end of study treatment
3. Duration of detectable vaccine-induced immune response is measured using specifically designed immune-assays, such as PBMCs during the course of the trial at the end of study treatment
4. The clinical and immunological evaluation of DTH sites is assessed prior to vaccination and after the vaccination course, by clinical assessment and tissue biopsy 48 hours post DTH injection
5. Percentage change in densities of immune cells in tumour tissue (where paired samples can be collected) is assessed using tumour tissue biopsies at baseline and follow-up (Day 85)
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7. Clinical response is measured according to irRECIST 1.1 at 85 days and 6 and 9 months
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12. Grade 3 or above vaccine- or combination administration-related toxicity is measured within 90 days after the last administration of study drugs
13. Progression-Free Survival (PFS) is measured from baseline to date of disease progression or death, from any cause
14. Overall Survival (OS) is measured from baseline to date of disease progression or death, from any cause
15. Disease Specific Interval (DSI) is measured from baseline to date of disease progression or death, from any cause

Completion date
24/01/2024

Eligibility

Key inclusion criteria
Current inclusion criteria as of 18/09/2026:
Inclusion Criteria Arm 1A:
1. Previous HPV16+ head and neck squamous cell carcinoma
2. At least 12 months after completion of treatment
3. Within 5 years of treatment completion
4. Currently no clinical evidence of disease
5. ECOG performance status 0 or 1
6. Able to provide written informed consent
7. Patient has adequate venous access in order to obtain all required blood samples and to undergo Leukapheresis as per protocol

Inclusion Criteria Arm 1B:
1. HPV16+ head and neck, cervical, anogenital, penile and unknown primary carcinoma patients with recurrent disease.
2. Intention to treat is palliative
3. Tissue samples available confirming HPV16+ disease to send to Central Laboratory
4. Able to provide written informed consent
5. Patient has adequate venous access in order to obtain all required blood samples and to undergo Leukapheresis as per protocol

Previous inclusion criteria:
Inclusion Criteria Arm 1A:
1. Previous HPV16+ head and neck squamous cell carcinoma
2. At least 12 months after completion of treatment
3. Within 5 years of treatment completion
4. Currently no clinical evidence of disease
5. ECOG performance status 0 or 1
6. Able to provide written informed consent

Inclusion Criteria Arm 1B:
1. HPV16+ head and neck, cervical, anogenital and penile carcinoma patients with recurrent disease.
2. Intention to treat is palliative.

3. Patient willing to have repeated tumour biopsies and re-biopsy deemed safe and feasible clinically.
4. Tissue samples available confirming HPV16+ disease to send to Central Laboratory.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
110 Years

Sex
All

Total final enrolment
30

Key exclusion criteria
Current exclusion criteria as of 18/09/2026:
1. Patients unable to consent
2. Any patient who has been previously vaccinated with BNT113 in any Arm of the trial.
3. Under 18 years of age
4. Systemic steroids (>10 mg Prednisolone/day or equivalent) or other drugs with a likely effect on immune competence are forbidden during the trial. The predictable need of their use will preclude the patient from trial entry. Replacement steroids for adrenal insufficiency/failure are allowed.
5. Major surgery in the preceding three to four weeks, which the patient has not yet recovered from.
6. Patients who are of high medical risk because of non-malignant systemic disease, as well as those with active uncontrolled infection
7.Patients with clinically relevant autoimmune disease will be excluded.
8.Patients who are known to be allergic to any of the excipients or constituents of the vaccine
9. Patients with any other condition which in the Investigator’s opinion would not make the patient a good candidate for the clinical trial, such as concurrent congestive heart failure or prior history of New York Heart Association (NYHA) class III/IV cardiac disease
10. Current malignancies at other sites, with the exception of adequately treated basal or squamous cell carcinoma of the skin. For Arm 1A; cancer survivors, who have undergone potentially curative therapy for a prior malignancy, have no evidence of that disease for five years and are deemed at low risk for recurrence, are eligible for the trial. For Arm 1B; cancer survivors, who have undergone potentially curative therapy for a prior malignancy and have no evidence of that disease for one year, are eligible for the trial.
11. Patients who are serologically positive for or are known to suffer from Hepatitis B, C, Syphilis or HIV. Counselling will be offered to all patients prior to testing

12. Patients who have a positive pregnancy test or who are breast feeding.
13. Fertile males or females who are unable or unwilling to use a highly effective method of birth control (less than 1% per year, e.g. condom with spermicide, diaphragm with spermicide, birth control pills, injections, patches, intrauterine device, or intrauterine hormone-releasing system) during study treatment and until 28 days after patients finish the trial treatment.
14. Arm 1B patients with the presence of liver metastasis: Elevated Liver Function Tests – ALT >5.0 x ULN, AST >5.0 x ULN, ALP >5.0 x ULN. Patients who are likely to have rapid disease progression may not be good candidates for the trial. In such cases, please discuss with the Chief Investigator.
15. Elevated Liver Function Tests – ALT >3.0 x ULN, AST >3.0 x ULN, Bilirubin >3.0 x ULN.
16. Any other investigational drug within 28 days or 5 half-lives depending on what gives the longer range before the first treatment of this study; exceptions may be possible with discussion with the CI.

Previous exclusion criteria:
1. Patients unable to consent
2. Under 18 years of age
3. Systemic steroids or other drugs with a likely effect on immune competence are forbidden during the trial. The predictable need of their use will preclude the patient from trial entry. Replacement steroids for adrenal insufficiency/failure are allowed.
4. Major surgery in the preceding three to four weeks, which the patient has not yet recovered from
5. Patients who are of high medical risk because of non-malignant systemic disease, as well as those with active uncontrolled infection
6. Patients with any other condition which in the Investigator's opinion would not make the patient a good candidate for the clinical trial, such as concurrent congestive heart failure or prior history of New York Heart Association (NYHA) class III/IV cardiac disease
7. Current malignancies at other sites, with the exception of adequately treated basal or squamous cell carcinoma of the skin. Cancer survivors, who have undergone potentially curative therapy for a prior malignancy, have no evidence of that disease for five years and are deemed at low risk for recurrence, are eligible for the study
8. Patients who are serologically positive for or are known to suffer from Hepatitis B, C, Syphilis or HIV. Counselling will be offered to all patients prior to testing
9. Patients who have a positive pregnancy test
10. Fertile males or females who are unable or unwilling to use a highly effective method of birth control (less than 1% per year, e.g. condom with spermicide, diaphragm with spermicide, birth control pills, injections, patches, intrauterine device, or intrauterine hormone-releasing system) during study treatment and until end of treatment +28 days (day 113)
11. Elevated Liver Function Tests – ALT, AST, Bilirubin
12. Any other investigational drug within 28 days or 5 half-lives depending on what gives the longer range before the first treatment of this study

Date of first enrolment
18/05/2017

Date of final enrolment
19/07/2023

Locations

Countries of recruitment

United Kingdom

England

Study participating centre
University Hospital Southampton
Southampton University Hospital
Tremona Road
Southampton
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SO16 6YD

Study participating centre
The Christie NHS Foundation Trust
550 Wilmslow Road
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Sponsor information

Organisation
University Hospital Southampton NHS Foundation Trust

ROR
https://ror.org/0485axj58

Funder(s)

Funder type
Government

Funder Name
European Commission

Alternative Name(s)
European Union, Comisión Europea, Europäische Kommission, EU-Kommissionen, Euroopa Komisjoni, EC, EU

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Funder Name
BioNTech

Alternative Name(s)
BioNTech SE, Biopharmaceutical New Technologies

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
Germany

Results and Publications

Individual participant data (IPD) sharing plan

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Abstract results		01/09/2024	30/09/2026	No	No
Basic results			10/03/2026	No	No
HRA research summary			28/06/2023	No	No
Study website		11/11/2025	11/11/2025	No	Yes