ISRCTN51789191 https://doi.org/10.1186/ISRCTN51789191

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

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|---|---|---|
| **Submission date**<br>02/11/2016 | **Recruitment status**<br>No longer recruiting | [X] Prospectively registered<br>[_] Protocol<br>[_] Statistical analysis plan<br>[_] Results<br>[_] Individual participant data<br>[X] Record updated in last year |
| **Registration date**<br>15/12/2016 | **Overall study status**<br>Completed | |
| **Last Edited**<br>27/01/2025 | **Condition category**<br>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

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

**ClinicalTrials.gov (NCT)**
NCT03418480

**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

### Study design
Non-randomized interventional study

### Primary study design
Interventional

### Study type(s)
Treatment

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

### Interventions
-

### Intervention Type
Biological/Vaccine

### Phase
Not Applicable

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

### Primary outcome(s)
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))
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)
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

### Completion date
24/01/2024

## Eligibility

## Key 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
Adult

## Lower age limit
18 years

## Sex
All

## Total final enrolment
15

## Key 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
01/01/2017

### Date of final enrolment
19/07/2023

## Locations

### Countries of recruitment
United Kingdom

England

### Study participating centre
**University Hospital Southampton**
Southampton University Hospital
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### Study participating centre
**The Christie NHS Foundation Trust**
550 Wilmslow Road
Withington
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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**

# Results and Publications

**Individual participant data (IPD) sharing plan**
The current data sharing plans for the current study are unknown and will be made available at a later date.

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

**Study outputs**

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| HRA research summary | | | 28/06/2023 | No | No |
| Participant information sheet | Participant information sheet | 11/11/2025 | 11/11/2025 | No | Yes |
| Study website | Study website | 11/11/2025 | 11/11/2025 | No | Yes |