Clinical trial results:
Therapeutic HPV vaccine (BNT113) trial in HPV16 driven carcinoma.

Summary

EudraCT number	2014-002061-30
Trial protocol	GB
Global end of trial date	24 January 2024

Results information

Result version number	v1 (current)
This version publication date	24 January 2025
First version publication date	24 January 2025

Trial information

Trial identification

Sponsor protocol code	RHMCAN0983

Additional study identifiers

ISRCTN number	ISRCTN51789191
ClinicalTrials.gov id (NCT number)	NCT03418480
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Hospital Southampton NHS Foundation Trust
Sponsor organisation address	MP138, R&D Department, Level E, Southampton General Hospital, Tremona Road, Southampton, United Kingdom, SO16 6YD
Public contact	Karen Martin, Southampton Clinical Trials Unit, 44 2381205154, ctu@soton.ac.uk
Scientific contact	Karen Martin, Southampton Clinical Trials Unit, 44 2381205154, ctu@soton.ac.uk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 July 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 January 2024
Global end of trial reached?	Yes
Global end of trial date	24 January 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Phase I objective: To establish a safe and tolerable dose of BNT113 [Arms 1A and 1B].

Phase II objectives: To assess if there is evidence of clinical effect (according to irRECIST 1.1 criteria) [Arm 1B] at 3 months after the last vaccination; to assess if there is evidence of clinical effect in terms of a significant increase of immune cells following BNT113 administration [Arm 1B].

Protection of trial subjects:

None

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 May 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 30
Worldwide total number of subjects	30
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	19
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between 16 May 2017, and 17 Jan 2023, 30 patients were recruited (Arm 1A Cohort 1 n=6, Arm 1A Cohort 2 n=11, Arm 1B n=13) to receive treatment.

Pre-assignment

Screening details:

A total of 69 patients were screened, 10 were excluded due to non-HPV16+ cancer, 6 were excluded due to clinician's choice, and 23 were excluded due to other reasons.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm 1A

Arm description:

Arm 1A included patients with previously treated HPV16+ head and neck squamous cell carcinoma.

Arm type	Experimental
Investigational medicinal product name	BNT113
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Injection

Dosage and administration details:

q1w x 4 then q2w x 4 with intrapatient dose escalation from 7.2 µg to 29 µg (Cohort 1, first 6 patients) or to 72.8µg (Cohort 2, last 11 patients)

Arm title	Arm 1B

Arm description:

Arm 1B included patients with HPV16+ advanced disease.

Arm type	Experimental
Investigational medicinal product name	BNT113
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Injection

Dosage and administration details:

q1w x 4 then q2w x 4 with intrapatient dose escalation from 7.2 µg to 72.8 µg

Number of subjects in period 1	Arm 1A	Arm 1B
Started	17	13
Completed	12	7
Not completed	5	6
Consent withdrawn by subject	-	1
Lost to follow-up	5	5

Baseline characteristics

Reporting groups	
Reporting group title	Arm 1A
Reporting group description:	
Arm 1A included patients with previously treated HPV16+ head and neck squamous cell carcinoma.	
Reporting group title	Arm 1B
Reporting group description:	
Arm 1B included patients with HPV16+ advanced disease.	

Reporting group values	Arm 1A	Arm 1B	Total
Number of subjects	17	13	30
Age categorical Units: Subjects			
Adults (18-64 years)	10	9	19
From 65-84 years	7	4	11
Age continuous Units: years			
median	63	58	
full range (min-max)	37 to 78	49 to 72	-
Gender categorical Units: Subjects			
Female	4	10	14
Male	13	3	16
Primary site of cancer			
Primary site of cancer			
Units: Subjects			
Anal	0	5	5
Cervix	0	2	2
Neck	2	1	3
Oropharynx	3	1	4
Pelvis	0	1	1
Penis	0	1	1
Tongue	5	1	6
Tonsil	7	0	7
Missing	0	1	1

End points

End points reporting groups

Reporting group title	Arm 1A
Reporting group description:	
Arm 1A included patients with previously treated HPV16+ head and neck squamous cell carcinoma.	
Reporting group title	Arm 1B
Reporting group description:	
Arm 1B included patients with HPV16+ advanced disease.	
Subject analysis set title	Safety population
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants received at least 1 dose or underwent DTH control reaction assessment.	
Subject analysis set title	Per protocol population
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received at least 1 maximum dose or their individual maximum tolerated dose.	

Primary: Dose limiting toxicities

End point title	Dose limiting toxicities[1]
End point description:	
End point type	Primary
End point timeframe:	
During or within one week after the vaccination cycle	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics

End point values	Arm 1A	Arm 1B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	12		
Units: Subject				
Yes	0	0		
No	17	12		

Statistical analyses

No statistical analyses for this end point

Primary: Immune response: T cell response at any time

End point title	Immune response: T cell response at any time[2]
End point description:	
End point type	Primary
End point timeframe:	
Post-vaccination	

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics

End point values	Arm 1A	Arm 1B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Subject				
E6 and E7 Positive	2	2		
E6 Positive, E7 Negative	3	1		
E6 Negative, E7 Positive	0	0		
E6 and E7 Negative	4	3		
Missing	1	3		

Statistical analyses

No statistical analyses for this end point

Primary: Immune response: Antibody response at any time

End point title	Immune response: Antibody response at any time[3]

End point description:

End point type	Primary

End point timeframe:

Post-vaccination

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics

End point values	Arm 1A	Arm 1B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	9		
Units: Subject				
E2 and E7 Positive	0	2		
E2 Positive, E7 Negative	0	0		
E2 Negative, E7 Positive	8	3		
E2 and E7 Negative	6	4		
Missing	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: Disease control rate

End point title	Disease control rate[4][5]

End point description:

End point type	Primary

End point timeframe:

Post-treatment

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only descriptive statistics

End point values	Arm 1B	Per protocol population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9	9		
Units: Subject				
Stable disease	5	5		
Progression	2	2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
During the trial	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26

Reporting groups	
Reporting group title	Arm 1A
Reporting group description:	
Arm 1A included patients with previously treated HPV16+ head and neck squamous cell carcinoma.	
Reporting group title	Arm 1B
Reporting group description:	
Arm 1B included patients with HPV16+ advanced disease.	

Serious adverse events	Arm 1A	Arm 1B	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 17 (11.76%)	8 / 13 (61.54%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 17 (5.88%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 17 (5.88%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	1 / 1	1 / 1	
Nervous system disorders			
Cauda equina syndrome			
subjects affected / exposed	0 / 17 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			

subjects affected / exposed	0 / 17 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
General disorders and administration site conditions			
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 17 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 17 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute kidney injury			
subjects affected / exposed	0 / 17 (0.00%)	2 / 13 (15.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 17 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stridor			
subjects affected / exposed	0 / 17 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Urinary tract infection			

subjects affected / exposed	0 / 17 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Arm 1A	Arm 1B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 17 (100.00%)	12 / 13 (92.31%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	2 / 17 (11.76%)	1 / 13 (7.69%)	
occurrences (all)	2	1	
General disorders and administration site conditions			
Chills			
subjects affected / exposed	5 / 17 (29.41%)	2 / 13 (15.38%)	
occurrences (all)	12	2	
Fatigue			
subjects affected / exposed	10 / 17 (58.82%)	3 / 13 (23.08%)	
occurrences (all)	32	6	
Influenza like illness			
subjects affected / exposed	2 / 17 (11.76%)	1 / 13 (7.69%)	
occurrences (all)	3	2	
Pain			
subjects affected / exposed	1 / 17 (5.88%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Pyrexia			
subjects affected / exposed	2 / 17 (11.76%)	3 / 13 (23.08%)	
occurrences (all)	3	3	
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 17 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	3 / 17 (17.65%)	3 / 13 (23.08%)	
occurrences (all)	3	3	
Dyspnoea			
subjects affected / exposed	1 / 17 (5.88%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Nasal congestion			
subjects affected / exposed	5 / 17 (29.41%)	0 / 13 (0.00%)	
occurrences (all)	6	0	
Oropharyngeal pain			
subjects affected / exposed	4 / 17 (23.53%)	1 / 13 (7.69%)	
occurrences (all)	4	2	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 17 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Investigations			
Blood bilirubin increased			
subjects affected / exposed	2 / 17 (11.76%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Body temperature increased			
subjects affected / exposed	2 / 17 (11.76%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 17 (5.88%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	2 / 17 (11.76%)	2 / 13 (15.38%)	
occurrences (all)	2	2	
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 17 (17.65%)	0 / 13 (0.00%)	
occurrences (all)	6	0	
Headache			

subjects affected / exposed	9 / 17 (52.94%)	3 / 13 (23.08%)	
occurrences (all)	23	10	
Presyncope			
subjects affected / exposed	0 / 17 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	3	
Syncope			
subjects affected / exposed	1 / 17 (5.88%)	2 / 13 (15.38%)	
occurrences (all)	1	2	
Tremor			
subjects affected / exposed	1 / 17 (5.88%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 17 (5.88%)	4 / 13 (30.77%)	
occurrences (all)	2	5	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	2 / 17 (11.76%)	4 / 13 (30.77%)	
occurrences (all)	2	7	
Diarrhoea			
subjects affected / exposed	3 / 17 (17.65%)	2 / 13 (15.38%)	
occurrences (all)	7	3	
Dyspepsia			
subjects affected / exposed	2 / 17 (11.76%)	2 / 13 (15.38%)	
occurrences (all)	2	2	
Nausea			
subjects affected / exposed	8 / 17 (47.06%)	5 / 13 (38.46%)	
occurrences (all)	21	5	
Paraesthesia oral			
subjects affected / exposed	2 / 17 (11.76%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Vomiting			
subjects affected / exposed	1 / 17 (5.88%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			

Hyperhidrosis			
subjects affected / exposed	1 / 17 (5.88%)	3 / 13 (23.08%)	
occurrences (all)	1	4	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 17 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	2 / 17 (11.76%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 17 (11.76%)	1 / 13 (7.69%)	
occurrences (all)	2	1	
Back pain			
subjects affected / exposed	2 / 17 (11.76%)	4 / 13 (30.77%)	
occurrences (all)	3	4	
Limb discomfort			
subjects affected / exposed	1 / 17 (5.88%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Muscle spasms			
subjects affected / exposed	2 / 17 (11.76%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Myalgia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 13 (7.69%)	
occurrences (all)	2	4	
Pain in extremity			
subjects affected / exposed	0 / 17 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 17 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	4	
Metabolism and nutrition disorders			

Decreased appetite subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 3	1 / 13 (7.69%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 January 2017	Addition of 12 month continutation of treatment period for Arm 1B patients; Movement of secondary endpoints to tertiary endpoints, clarity and further information on the procedures of dose modification in the event of adverse drug reactions, clarity on the preventative management of adverse drug reactions, change to the information about the storage of the vaccine to fall in line with the changes in the IMPD
19 October 2017	Exclusion criteria has been updated to clarify the upper limits of patients with elevated Liver Function Tests; Consenting timeline for Arm 1A and 1B extended, as well as allowing routine treatment day bloods to be taken up to 1 working day prior to vaccination. Clarifications on continued treatment options and dose modifications also included.
11 July 2018	Clarification of blood requirements for standard pathology blood analysis, Change from C5a analysis to NHS complement function, HPV ISH changed to HPV typing, Cytokine blood withdrawal clarification, Clarification of tissue biopsy procedure, Removal of 7 day time-lag between dosing for both Arms, Clarification for vital sign monitoring, Change of name of IMP manufacturer, Clarification of reporting requirements.
19 December 2019	Removal of DTH and Complement function test; additional clarity regarding withdrawal of consent, storage temperatures for IMP updated, RNA (LIP) changed to RNA-LPX to harmonise with Investigator Brochure
24 February 2021	CI location and contact details updated; Updated drug name to BNT113. Change of manufacturing name to BioNTech Manufacturing GmbH. DTH analysis added back as tertiary endpoint to protocol
22 March 2022	Change in exclusion criteria, patients with history of anaphylactic reactions or severe allergies are no longer excluded from the trial. There are additional recommended actions for treatment of Adverse Drug Reactions (ADR) in appendix 2, and in preventative management of ADRs, such as adequate hydration and use of paracetamol pre and post vaccination. Footers in the schedule of observations have been updated to clarify when end of treatment and follow up visits should occur, there is also a new appendix 7 with a table of follow up visit schedule for patients who continue to maintenance treatment. The dose escalation diagram has been updated to clarify whether to dose escalate or reduce following a significant adverse drug reaction. Covid-19 vaccination status will now be collected as part of medical history.
19 December 2022	Study Title updated, ref to anti CD40 removed ; Arm 1B eligibility inclusion HPV16+ unknown primary; Window for weight, phys exam, ECOG - 3 days, New Stage 1 Consent added, Clarification scheduling of scans during maintenance treatment, Removed 24h overnight stays, Clinical Safety updates to wording (BNT)
02 August 2023	Change to Eligibility, cancer survivals free of disease for 1 year eligible, mandatory biopsies removed, definition of vaccine immunogenicity clarified, decrease in maintenance from 12 to 6 months.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
18 March 2020	COVID-19 lockdown	05 October 2020
12 January 2021	COVID-19 lockdown	01 February 2021
12 February 2021	Clinical Trial Unit resource issue (Arm 1B only)	01 July 2021
05 April 2022	Pause to recruitment until revised IMPD approved to enable QP release of IMP	27 April 2022
19 April 2023	Fungal contamination of the outer packaging of HARE-40 IMP Kit B	-

Notes:

Limitations and caveats

None reported