ISRCTN15021247 https://doi.org/10.1186/ISRCTN15021247

Phase II study for the treatment of recurrent and/or metastatic human papillomavirus (HPV16)-associated head and neck cancer

Submission date
28/01/2022

Recruitment status
No longer recruiting

Registration date
06/07/2022

Overall study status
Completed

Last Edited
28/05/2026

Condition category
Cancer

[_] Prospectively registered
[X] Protocol
[X] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
The aim of this study is to test the effectiveness and safety of the combination of an investigational vaccine, PDS0101, given by subcutaneous (beneath the skin) injection and the standard of care, pembrolizumab, given intravenously (into the vein). Participants are being invited to take part in this research study because he/she has been diagnosed with recurrent or metastatic head and neck cancer (HNC) and high-risk human papillomavirus-16 (HPV16) infection. The most common type of HNC is head and neck squamous cell carcinoma (HNSCC), the sixth most common cancer worldwide. HPV has been clearly implicated as the cause in a subset of HNC. The most commonly implicated HPV subtype in HNC is HPV16, accounting for over 80% of HPV+ HNC. PDS0101 is an investigational therapeutic cancer vaccine designed to boost the body's immune response against HPV16. PDS0101 contains two active components: the first is called R-DOTAP and is included in the vaccine to boost the immune system's response against the HPV viral proteins. The second group of active components are selected small pieces of proteins (called peptides) taken from the HPV virus. In order to be able to participate, To participate in this study, participants must have confirmed HPV16-infected head and neck tumors and have the right tumor marker PD-L1 and will need to provide a blood sample to find out their tissue type. Current treatments for HNC can include surgery, radiation therapy, chemotherapy, targeted therapy and immunotherapy.

Who can participate?
Patients aged 18 years or older with recurrent or metastatic head and neck cancer (HNC) and high-risk human papillomavirus-16 (HPV16) infection.

What does the study involve?
All participants will receive the study treatment which will consist of PDS0101 and pembrolizumab on the same day. Pembrolizumab and PDS0101 will be administered every 3 weeks for the first 4 Cycles on Days 1 (Cycle 1), 22 (Cycle 2), 43 (Cycle 3), and 64 (Cycle 4). The fifth and final PDS0101 injection will be administered again on Day 232 (6 months after the 4th

vaccination, Cycle 12 of pembrolizumab). Pembrolizumab treatment will continue every 3 weeks from Day 1, Cycle 1 until unacceptable toxicity or disease progression. Participants without disease progression will be treated for up to 35 Cycles.

What are the possible benefits and risks of participating?
Participants may receive the benefit from information about and monitoring of their health and a chance to be in a research study that may help others. There is no guarantee that the participant will directly benefit from this study. There is no promise that the participant's condition will get better. It might stay the same or it might get worse. The information from this study may help the study doctors learn more about the study vaccine and its effect on HNC caused by persistent infection with HPV16.

Where is the study run from?
Syneos Health (UK)

When is the study starting and how long is it expected to run for?
January 2022 to June 2025

Who is funding the study?
PDS Biotechnology Corporation (USA)

Who is the main contact?
clinical_ops@pdsbiotech.com

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

ClinicalTrials.gov (NCT)
NCT04260126

Clinical Trials Information System (CTIS)
2021-004046-38

Integrated Research Application System (IRAS)

1004811

Central Portfolio Management System (CPMS)
51182

Protocol serial number
PDS0101-HNC-201

Study information

Scientific Title
A Phase II, open-label, multi-center study of PDS0101 (R-DOTAP [Versamune®] + HPVmix) and pembrolizumab (KEYTRUDA®) combination immunotherapy in subjects with recurrent and/or metastatic head and neck cancer and high-risk human papillomavirus-16 (HPV16) infection

Acronym
VERSATILE-002

Study objectives
To assess the preliminary activity of the combination of pembrolizumab (KEYTRUDA) and PDS0101 in checkpoint inhibitor (CPI) naïve or refractory subjects with recurrent and/or metastatic head and neck cancer (HNSCC) and high-risk HPV16 infection.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 07/04/2022, London-Surrey Borders Research Ethics Committee (Equinox House, City Link, Nottingham, NG2 4LA, UK; +44 (0)2071048057; surreyborders.rec@hra.nhs.uk), ref: 22/LO/0124

Primary study design
Interventional

Study design
Open-label non-randomized trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Recurrent and/or metastatic head and neck cancer and high-risk human papillomavirus-16 (HPV16) infection

Interventions
This is an open-label, non-randomized trial. All eligible patients will receive the study treatment which will consist of PDS0101 (2.7 mg HPVmix mixed with 3.0 mg R-DOTAP) administered by subcutaneous (SC) injection, as well as 200 mg of pembrolizumab (KEYTRUDA) administered by IV infusion on the same day. A regimen of pembrolizumab (200 mg) and PDS0101 will be administered every 3 weeks for the first 4 Cycles: intravenous (IV) infusion of pembrolizumab

followed by subcutaneous (SC) injections of PDS0101 on Days 1 (Cycle 1), 22 (Cycle 2), 43 (Cycle 3), and 64 (Cycle 4).

The fifth and final PDS0101 injection will be administered again on Day 232 (6 months after the 4th vaccination, Cycle 12 of pembrolizumab). Intravenous infusion of pembrolizumab will occur first followed by SC injection of PDS0101. Pembrolizumab administration will continue every 3 weeks from Day 1, Cycle 1 until unacceptable toxicity or disease progression. Subjects without disease progression will be treated for up to 35 Cycles.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
PDS0101, pembrolizumab

Primary outcome(s)
In both CPI naïve and CPI refractory subjects the primary outcome measure will be the best overall response (BOR) of confirmed complete response (CR) or confirmed partial response (PR) using Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 guidelines, evaluated in all patients at 24 months

Key secondary outcome(s)
In both CPI naïve and CPI refractory subjects:
1. Progression-free survival per RECIST 1.1 in all subjects at 12 and 24 months
2. Overall survival measured using EDC data (subjects who are still alive) at 24 months
3. Safety and tolerability of pembrolizumab and PDS0101 measured using reported adverse events (AEs), changes in clinical laboratory findings, changes in electrocardiogram (ECGs), changes in vital signs, and any signs of dose-limiting toxicities (DLTs) from the combination therapy at 12 and 24 months

Completion date
14/06/2025

Eligibility

Key inclusion criteria
1. The subject (or legally acceptable representative if applicable) provides written informed consent for the study
2. ≥18 years of age on the day of signing the informed consent.
3. Checkpoint-naïve subjects: have a history of histologically-confirmed diagnosis of squamous cell cancer of the head and neck (HNSCC) that is recurrent, metastatic, or persistent with:
3.1. Confirmed HPV16 infection
3.2. Confirmed tumor PDL1 expression defined as a combined positive score (CPS) ≥1 using the FDA-approved Dako PD-L1 immunohistochemistry (IHC) 22C3 PharmDx Assay
3.3. No prior receipt of any immunological therapy for metastatic disease
4. Checkpoint experienced subjects have a history of histologically-confirmed diagnosis of HNSCC that is recurrent, metastatic, or persistent with:
4.1. Confirmed HPV16 infection

4.2. Characterization of tumor PDL1 expression using the FDA-approved PD-L1 IHC 22C3 PharmDx Assay
4.3. Receipt of prior treatment with checkpoint inhibitors as a single agent or in combination, and have received at least 2 doses of the agent or a minimum of 6 weeks on treatment
4.4. Have documented clinical progression or recurrence that has been radiologically confirmed
5. Have recurrent and/or metastatic measurable disease based on RECIST 1.1 as assessed by the local Principal Investigator/radiology. There must be confirmation that the subject's imaging shows at least 1 lesion that is appropriate for selection as a target lesion per RECIST 1.1. Lesions situated in a previously irradiated area are considered measurable if progression has been demonstrated in such lesions.
6. Have adequate organ function as defined in hematological: ANC ≥1500/µl, platelets ≥100 000 /µl; hemoglobin ≥9.0 g/dl or ≥5.6 mmol/l; renal: creatinine ≤1.5 × ULN or >1.5 × institutional ULN; hepatic: total bilirubin ≤1.5 × ULN or direct bilirubin ≤ULN for subjects with total bilirubin levels >1.5 × ULN, AST and ALT ≤2.5 ULN (5 × ULN for subjects with liver metastases); coagulation: INR, PTT ≤1.5 × ULN. Specimens must be collected within 10 days prior to the start of the study combination treatment.
7. If the subject received major surgery or radiation therapy of >30 Gy, they must have recovered from the toxicity and/or complications from the intervention
8. For female subjects defined as women of childbearing potential (WOCBP), a negative urine pregnancy test must be obtained during screening. Women who are surgically sterile or at least 2 years postmenopausal do not require pregnancy testing. Note: Female subjects of childbearing potential must be willing to use an effective method of contraception for the course of the study through 120 days after the last dose of study medication.
9. Male subjects of childbearing potential must agree to use a condom as an effective method of contraception starting with the first dose of study therapy through 120 days after the last dose of study therapy
10. Have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
100 Years

Sex
All

Total final enrolment
87

Key exclusion criteria

1. A female subject defined as a WOCBP who has a positive urine pregnancy test (within 72 hours) prior to treatment. If the urine test is positive or cannot be confirmed as negative, a serum pregnancy test will be required.
2. Has received prior therapy with an anti-PD-1, anti-PD- L1, or anti PD L2 agent with an agent directed to another stimulatory or co-inhibitory T-cell receptor (eg, CTLA-4, OX40, CD137) and was discontinued from that treatment due to a Grade 3 or higher adverse events (AE)
3. Has received prior systemic anticancer therapy including investigational agents within 30 days prior to treatment. Note: Subjects must have recovered from all AEs due to previous therapies to <Grade 1 or baseline. Subjects with <Grade 2 neuropathy and <Grade 2 alopecia are an exception to this criterion and may qualify for therapy. Note: If subjects received major surgery, they must have recovered adequately from the toxicity and/or complications from the intervention prior to starting treatment.
4. Coordination and timing of coronavirus disease 2019 (COVID-19) vaccination should be based on local investigator clinical assessment and judgment. Note: Whenever possible, it is recommended to avoid COVID vaccination on the day of PDS0101 and/or pembrolizumab dosing because it may be difficult to attribute certain AEs (eg, fever, infusion reaction) to the study drug (s) or the COVID vaccine if they are both administered on the same day.
5. Has received prior radiotherapy within 2 weeks of the start of study treatment. Subjects must have recovered from all-radiation-related toxicities, not require corticosteroids and not have had radiation pneumonitis. A 1-week washout is permitted for palliative radiation (<2 weeks of radiotherapy) to non-CNS disease.
6. Has received a live vaccine within 30 days prior to the first dose of treatment. Examples of live vaccines include, but are not limited to, the following: measles, mumps, rubella, varicella/zoster (chicken pox), yellow fever, rabies, Bacillus Calmette-Guérin (BCG), and typhoid vaccine. Seasonal influenza vaccines for injection are generally killed-virus vaccines and are allowed; however, intranasal influenza vaccines (eg, FluMist®) are live attenuated vaccines and are not allowed.
7. Received immunotherapy/immunomodulatory or immunosuppressive agents (eg, IFNs, tumor necrosis factor, interleukins, immunoglobulins or other biological response modifiers [GM-CSF, granulocyte colony-stimulating factor, macrophage colony-stimulating factor]) within 6 weeks prior to administration of the first study combination treatment
8. Is currently participating in or has participated in a study of an investigational agent or has used an investigational device within 30 days prior to the first dose of study treatment. Note: Subjects who entered the follow-up phase of an investigational study may participate as long as it has been 30 days after the last dose of the previous investigational agent.
9. Has undergone prior allogeneic hematopoietic stem cell transplantation within the last 5 years. (Subjects who have had a transplant greater than 5 years ago are eligible as long as there are no symptoms of graft-versus-host disease [GVHD]).Diagnostic Assessments
10. Has a diagnosis of immunodeficiency or is receiving chronic systemic steroid therapy
11. Has a known additional malignancy that is progressing or has required active treatment within the past 3 years. Note: Subjects with basal cell carcinoma of the skin, squamous cell carcinoma of the skin or carcinoma in situ (eg, breast carcinoma, cervical cancer in situ) or other malignant tumors that have undergone potentially curative therapy are not excluded.
12. Has known active central nervous system (CNS) metastases and/or carcinomatous meningitis
13. Has severe hypersensitivity (>Grade 3) to pembrolizumab and/or any of its excipients
14. Has an active autoimmune disease that has required systemic treatment in the past 2 years
15. Has a history of (non-infectious) pneumonitis that required steroids or has current pneumonitis
16. Has an active infection requiring systemic therapy
17. Subjects with known human immunodeficiency virus and/or history of hepatitis B or C infections
18. Has a history or current evidence of any condition, therapy, or laboratory abnormality that might confound the results of the study

19. Has a known psychiatric or substance abuse disorder
20. Is pregnant or breastfeeding or expecting to conceive or father children within the projected duration of the study
21. Has had an allogenic tissue/solid organ transplant
22. Has received administration of colony-stimulating factors within 30 days prior to Day 1
23. Has a history of interstitial lung disease
24. Female subjects defined as WOCBP unwilling or unable to use highly effective contraception method(s) for the duration of the study:
24.1. Combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation
24.2. Progestogen-only hormonal contraception
24.3. Intrauterine device
24.4. Intrauterine hormone-releasing system
24.5. Bilateral tubal occlusion
24.6. Vasectomized partner is a highly effective birth control method provided that the partner is the sole sexual partner of the WOCBP trial participant and that the vasectomised partner has received a medical assessment of the surgical success

Added 02/09/2022:
25. Any prior Grade ≥3 immune-related adverse event (irAE) while receiving any previous checkpoint inhibitor or immunotherapy agent, or any unresolved irAE >Grade 1 except for endocrine AEs managed with replacement therapy
26. Developed immune-related toxicity while on prior checkpoint inhibitor therapy that has not yet returned to Grade 1 or better
27. History of any drug allergies or significant adverse reactions to any components of PDS0101

Date of first enrolment
01/03/2021

Date of final enrolment
12/05/2023

Locations

Countries of recruitment
United Kingdom

England

Scotland

Ireland

Puerto Rico

United States of America

Study participating centre

The Royal Marsden NHS Foundation Trust
Fulham Road
London
England
SW3 6JJ

Study participating centre
Christie Hospital NHS Foundation Trust
550 Wilmslow Road
Manchester
England
M20 4BX

Study participating centre
NHS Lothian
Waverley Gate
2-4 Waterloo Place
Edinburgh
Scotland
EH1 3EG

Sponsor information

Organisation
Syneos Health

Funder(s)

Funder type
Industry

Funder Name
PDS Biotechnology Corporation

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study will be included in the subsequent results publication. The sponsor will maintain anonymity when publishing data by publishing aggregate data only. Identifiable personal data will not be published.

IPD sharing plan summary

Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		27/05/2026	27/05/2026	No	No
HRA research summary			28/06/2023	No	No
Participant information sheet	version 7		03/05/2022	No	Yes
Plain English results		02/04/2026	27/05/2026	No	Yes
Protocol file	version 4.1	10/10/2022	28/05/2026	No	No
Statistical Analysis Plan	version 40	06/05/2025	28/05/2026	No	No