A Phase I/II Study of TheraT® Vector(s) Expressing Human Papillomavirus 16 Positive (HPV 16+) Specific Antigens in Patients with HPV 16+ Confirmed Cancers

Published: 30-09-2021
Last updated: 28-12-2024

Phase I Dose Escalation1.To determine the RP2D in terms of safety and tolerability for:•IV admin of HB-201 in patients with HPV 16+ confirmed HNSCC•IT admin of HB-201 in patients with HPV 16+ confirmed cancers•IV admin of HB-202 in patients with HPV…

Ethical review	Approved WMO
Status	Will not start
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON54432

Source
ToetsingOnline

Brief title
H-200-001

Condition

- Other condition
- Reproductive and genitourinary neoplasms gender unspecified NEC

Synonym
Human papilloma virus (HPV 16) associated cancer

Health condition

HPV16 positive cancers: head and neck squamous cell carcinoma, anal squamous cell

carcinoma, cervical, vulvar, penile, vaginal cancer

Research involving
Human

Sponsors and support

Primary sponsor: Hookipa Biotech GmbH
Source(s) of monetary or material Support: Industry (Hookipa Biotech GmbH)

Intervention

Keyword: E7E6, Gene Therapy, HPV 16+ Confirmed Cancers, TheraT®, Vaccine

Outcome measures

Primary outcome

Phase I Dose Escalation

•Incidence of DLTs from the first study drug administered during the DLT

observation period

Phase II Dose Expansion

Tumor responses will be assessed using RECIST and iRECIST by the Investigator:

•Objective response rate

•Disease control rate

Secondary outcome

Phase I Dose Escalation

•Safety: type, frequency, and severity of AEs and SAEs

•Tolerability: dose interruptions, reductions and dose intensity, and

evaluations of laboratory values

•Tumor responses will be assessed using RECIST and iRECIST by the Investigator:

-Objective response rate

-Disease control rate

Phase II Dose Expansion

Tumor responses will be assessed using RECIST and iRECIST by the Investigator:

•Overall survival

•Progression-free survival

•Duration of response

•Safety: type, frequency, and severity of AEs and SAEs

•Tolerability: dose interruptions, reductions and dose intensity, and

evaluations of laboratory values

Study description

Background summary

Human papilloma virus (HPV) infection is linked to several cancer types. Malignant transformation of cells by HPV necessitates the integration of HPV viral genome elements into the genome of the host. The generation and maintenance of the HPV 16+ malignant state of a cell requires the consistent expression of E7 and E6 proteins from HPV, and therefore, E7 and E6 represent a potential immunotherapy target. HB-201 and HB-202 therapy targets tumors induced by HPV 16, by expression of an artificial antigenic E7 and E6 fusion protein from HPV 16 (E7E6) and is thereby expected to induce a robust CD8+ T cell response.

Significant preclinical data have been generated demonstrating potent efficacy in HPV 16 cancer models using HB-201 and HB-202 both intravenous and intratumoral administration. In animal models, HB-201 and HB-202 were observed to be highly immunogenic, resulting in a robust CD8+ T cell response. Based on the levels of antigen-specific CD8+ T cells induced by HB-201 and HB-202 in preclinical models, notably when compared with the levels induced by other approaches (including adoptive cell therapies), we believe that HB-201 Monotherapy and/or HB-201 & HB-202 sequential alternating two-vector therapy have the potential to provide therapeutic benefit to patients with a wide range of HPV 16+ tumors.

Given the extremely low response rates to existing therapies and limited overall survival of patients with advanced HPV 16 positive cancers, any therapy

with a chance to prolong life should be developed.

Study objective

Phase I Dose Escalation
1.To determine the RP2D in terms of safety and tolerability for:
•IV admin of HB-201 in patients with HPV 16+ confirmed HNSCC
•IT admin of HB-201 in patients with HPV 16+ confirmed cancers
•IV admin of HB-202 in patients with HPV 16+ confirmed HNSCC
•IV admin of HB-202 in patients with HPV 16+ confirmed cancers

Phase II Dose Expansion
1. To assess the preliminary antitumor activity of:
•IV admin of HB-201 in patients with HPV 16+ confirmed HNSCC
•IT admin of HB-201 followed by IV administration of HB-201 in patients with HPV 16+ confirmed cancers
•IV administration of HB 201 in combination with pembrolizumab in patients with HPV 16+ confirmed HNSCC
•Sequential alternating IV admin of HB-201 & HB-202 in patients with HPV 16+ confirmed HNSCC
•IT admin of HB-201 followed by sequential alternating IV admin of HB 201 & HB 202 in patients with HPV 16+ confirmed cancers
•Sequential alternating IV administration of HB-201 & HB-202 in combination with pembrolizumab in patients with HPV 16+ confirmed HNSCC

Study design

This is a first in human Phase I/II, multinational, multicenter, open-label study of HB-201 monotherapy and HB-201 & HB-202 alternating two-vector therapy in patients with HPV 16+ confirmed cancers comprising two parts: Phase I Dose Escalation and Phase II Dose Expansion. The proposed Phase I Dose Escalation will evaluate the safe recommended Phase II dose (RP2D) of HB-201 monotherapy and HB-201 & HB-202 alternating therapy in both intravenous and - for HB-201 - intratumoral administrations (first dose only).

The Phase II Dose Expansion will evaluate the safety and efficacy of intravenous administrations of HB-201 monotherapy and HB-201 & HB-202 alternating two-vector therapy alone and in combination with pembrolizumab. It will also evaluate the safety and efficacy of an initial intratumoral administration of HB-201 followed either by HB-201 iv monotherapy or HB-201 & HB-202 iv alternating two-vector therapy alone and in combination with pembrolizumab.

Patients with HPV 16+ Head and Neck Squamous Cell Carcinoma (HNSCC) will be enrolled in the intravenous treatment groups. Patients with HPV 16+ HNSCC and other HPV 16+ confirmed cancers who have an accessible tumor lesion will be

included in the intratumoral treatment groups.

The study will take approximately 5 years to complete including a long-term follow up, and will be performed as a multicenter, multinational, open label, safety and efficacy study.

Intervention

Patients with HPV 16+ Head and Neck Squamous Cell Carcinoma (HNSCC) will be enrolled in the intravenous treatment groups. Patients with HPV 16+ HNSCC and other HPV 16+ confirmed cancers who have an accessible tumor lesion will be included in the intratumoral treatment groups.
The type of treatment the patient receives will depend on which phase of the study they joined.
At Phase I, the patient will be receiving either all doses of the study drug intravenously (into a vein) or the first dose of the study drug regimen intratumorally (into the tumor) and all later doses of the study drug will be given intravenously.
Four different doses of the study drugs are planned to be studied.

At Phase II, the *recommended doses* of the study drugs as determined in Phase I will be used. Depending on the group that the patients will be assigned they will be receiving either the study drugs alone, or together with Pembrolizumab intravenously. Patients who have an accessible tumor lesion will receive the first dose of the study drugs intratumorally.
Pembrolizumab will be administered on a 200 mg once every 3 weeks or 400 mg once every 6 weeks schedule, overlapping with study visits.

Study burden and risks

Based on the levels of antigen-specific CD8 cytotoxic T cells induced by HB-201 and HB-201 & HB-202 in nonclinical models, notably when compared with the levels induced by other approaches (including adoptive cell therapies), HB-201 monotherapy as well as HB-201 & HB-202 alternating two-vector therapy have the potential to provide therapeutic benefit to patients with a wide range of HPV 16+ tumors.
Given the extremely low response rates to existing therapies and limited OS of patients with advanced HPV 16+ cancers, any therapy with a chance to prolong life should be developed.
Thus, it is expected that the benefits of HB-201 monotherapy and HB-201 & HB-202 alternating two-vector therapy significantly outweigh the negligible risk of developing any AEs.

Subject*s participation in this study will last years and consists of a screening period, treatment period and a follow-up period.
During the treatment period, subjects will need to visit the study site to

receive their treatment and take their safety/efficacy assessments as well as sample collection for biomarker analyses.
During the follow-up period, subjects will be contacted every 6-8 weeks for progression-free survival follow-up and every 12 weeks for long term FU. Aside from the intervention described above, participation in this study involves blood draws at multiple visits, and might involve tumor biopsy at screening and on the day of their first study drug administration and involve exposure through CT or MRI. Also samples from saliva, feces (e.g., fecal swab) and urine will be collected.

Contacts

Public
Hookipa Biotech GmbH

Helmut-Qualtinger-Gasse 2
Vienna 1030
AT
Scientific
Hookipa Biotech GmbH

Helmut-Qualtinger-Gasse 2
Vienna 1030
AT

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

All Patients:

- 18 years of age or older
- >= 1 measurable lesion by imaging for tumor response following RECIST and iRECIST
- ECOG performance status of 0 to 1.
- Prior curative radiation therapy must have been completed >= 4 weeks prior to study treatment administration. Prior focal palliative radiotherapy must have been completed >= 2 weeks prior to study treatment administration.
- Screening laboratory values must meet protocol-specified criteria
- Female patients who are of childbearing potential must have a negative serum β-human chorionic gonadotropin (β-hCG) pregnancy test prior to the first administration of study treatment or be surgically/biologically sterile (hysterectomy or bilateral oophorectomy) or postmenopausal.
- Male patients with sexual partners of childbearing potential can participate in the study if they agree to use barrier contraception from signing of the ICF through 5 months after the last study treatment administration.

Treatment Group 1, Group 3, Group 4, Group 5 Group A, or Group D:
- Documentation of confirmed HPV 16+ HNSCC via genotype testing
- Tumor progression or recurrence on standard of care therapy, including >= 1 systemic therapy or be a patient for whom standard of care therapy is contraindicated.

Treatment Group 2, Group 4, Group C, or Group F:
- Documentation of confirmed HPV 16+ cancer via genotype testing
- Tumor progression or recurrence on standard of care therapy, including >= 1 systemic therapy
- Safe and accessible tumor site amenable for biopsy and IT administration
- Apart from the tumor site(s) amenable for biopsy and IT administration >= 1 measurable lesion for RECIST assessment

Treatment Group B or Group E:
- Documentation of confirmed HPV 16+ HNSCC via genotype testing
- Must be eligible, as per standard of care, to receive pembrolizumab

Exclusion criteria

- Untreated and/or symptomatic metastatic central nervous system (CNS) disease, and/or carcinomatous meningitis. With some exceptions for treated and stable brain/CNS metastases
- Any serious or uncontrolled medical disorder that, in the opinion of the Investigator, may increase the risk associated with study participation / treatment administration
- Concurrent malignancy that is clinically significant or requires active intervention
- Active, known or suspected, autoimmune or inflammatory disorders requiring

immunosuppressive therapy
- Toxicity attributed to systemic prior anticancer therapy, including radiation and surgery, other than alopecia and fatigue that has not resolved to Grade 1 or Baseline prior to the first administration of study
- Not meeting the protocol-specified washout periods for prohibited medications per the protocol
- Treatment with any chemotherapy, biological, or investigational therapy for cancer within 28 days of the first administration of study treatment., unless agreed otherwise between the Sponsor and the Investigator on a case-by-case basis based on the half-life of the anticancer therapy.
Exception: Ongoing treatment with pembrolizumab is permitted if the subject is enrolling in a backfill cohort continuing pembrolizumab and adding either HB-201 monotherapy or HB-201 & HB-202 alternating two vector therapy.
- Prior anaphylactic or other severe reaction to human immunoglobulin or antibody formulation administration
- Positive hepatitis B surface antigen (HBsAg) or hepatitis C virus (HCV) antibody, indicating acute or chronic infection
- Known history of AIDS.
For patients receiving pembrolizumab:
- History of severe hypersensitivity reaction to pembrolizumab
- Any contraindication to receiving pembrolizumab per package insert or SmPC
- Allogeneic tissue/solid organ transplant.
- History of (non-infectious) pneumonitis that required steroids or current pneumonitis.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	2
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Generic name:	Genetic modified organism
Product type:	Medicine
Brand name:	HB-201
Generic name:	Not available
Product type:	Medicine
Brand name:	HB-202
Generic name:	Not available
Product type:	Medicine
Brand name:	KEYTRUDA 25 mg/ml concentrate for solution for infusion
Generic name:	Pembrolizumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	KEYTRUDA 50 mg Powder for concentrate for solution for infusion
Generic name:	Pembrolizumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Platinol
Generic name:	Cisplatin
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	30-09-2021
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	13-04-2022
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO Date:	01-11-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	11-11-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-12-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	21-12-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	10-05-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	14-07-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	10-01-2024
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	31-01-2024
Application type:	Amendment

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	19-04-2024
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	18-06-2024
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2019-000907-34-NL
ClinicalTrials.gov	NCT04180215
CCMO	NL78667.000.21

Study results

Summary results
Trial never started