Pharmacokinetic analysis of HPV16 synthetic long peptide vaccination in healthy volunteers using optical imaging

Published: 30-11-2015
Last updated: 19-04-2024

To assess safety, tolerability and pharmacokinetics of a single subcutaneous administration of HPV-NIRD1.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON42729

Source
ToetsingOnline

Brief title
PK imaging of HPV vaccination in healthy volunteers

Condition

- Other condition
- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
HPV / cancer, human papillomavirus, malignant tumors

Health condition

HPV16 associated cancer

Research involving
Human

Sponsors and support

Primary sponsor: Centre for Human Drug Research
Source(s) of monetary or material Support: Investigator Sponsored Study

Intervention

Keyword: HPV16 vaccine, Optical imaging, Pharmacokinetics, Safety

Outcome measures

Primary outcome

Safety and tolerability endpoints

* Treatment-emergent (serious) adverse events ((S)AEs).

* Concomitant medication

* Clinical laboratory tests (Haematology, Chemistry, Urinalysis)

* Vital signs (Pulse Rate (bpm), Systolic blood pressure (mmHg), Diastolic blood pressure (mmHg))

* Injection site status

* Physical examination findings

Pharmacokinetic endpoints

The following endpoints will be determined for HPV-NIRD1 and ICG following administration. They will be derived by imaging of injection site and draining inguinal lymph nodes:

* Absolute fluorescent signal of injection site or draining inguinal lymph node at different time points and doses

* SBR (signal to background ratio), defined as fluorescent signal of injection site or draining inguinal lymph node compared to fluorescence signal of tissue

surrounding the injection side or lymph node, at different time points and

doses.

Secondary outcome

n/a

Study description

Background summary

Following our improved understanding of the cellular and molecular details of the immune system, great progress has been made in the immunotherapy of cancer. An already established example is immunotherapy with monoclonal antibodies that has developed into multiple established cancer therapies. Although successful for treatment of premalignant lesions, the current vaccination approach appears to be insufficient for eradication of established tumors. We aim to develop improved peptide vaccine strategies using better adjuvants, formulations, and dosing schedules to be able to eradicate highly aggressive metastatic cancer. Since the in vivo distribution of peptide vaccine antigens is largely unknown, we propose to track the peptides conjugated with the near-infrared imaging dye 1 (NIRD1). Using this approach, our recent animal data demonstrate major differences in duration and localization of peptide antigen exposure. These pharmacokinetics depend on dose and formulation, and will likely determine the kinetics and extent of subsequent peptide-specific T cell responses and therapeutic efficacy. As animal models have limited predictive value for the design of optimal peptide vaccines that efficiently stimulate human T cell responses in vivo, we produced a clinical grade near-infrared labelled HPV16 peptide (HPV-NIRD1). This labelled peptide can be used as a tool to investigate the effect of dosing schedules and formulations on the pharmacokinetics and T cell kinetics of HPV16 peptide vaccination in clinical studies. In this first clinical trial, we aim to study the safety of HPV-NIRD1 vaccination in healthy adult volunteers, and the feasibility of obtaining pharmacokinetic data by optical imaging.

Study objective

To assess safety, tolerability and pharmacokinetics of a single subcutaneous administration of HPV-NIRD1.

Study design

This is an open label, single ascending dose study in healthy volunteers. Two

ascending dose levels of HPV-NIRD1 (80µg and 400µg) will be investigated in two cohorts of 3 subjects.
After the first dose level, a dose-escalation meeting will take place to review all (safety) data collected up to 24 hours. Escalation to the next dose level will only take place after this review does not indicate a safety concern.

The total duration of the study for each subject will be up to 49 days divided as follows:
* Screening: Up to 21 days before dosing;
* Treatment and study assessments: Days 0 to 28
* In Clinic period: Days 0 to 1 (single subcutaneous administration of HPV-NIRD1 on day 0)
* Follow-up visit: 2,3,7, and 28 days after dose administration.

Subjects will be admitted to the study unit on Day 0 and will be discharged approximately 24 hours after study drug administration.

Intervention

HPV-NIRD1 contains HPV-16 E6 peptide 71-95 conjugated to Near-Infrared Dye 1 and has been manufactured at the Interdivisional GMP Facility LUMC (IGFL) of the department of Clinical Pharmacy and Toxicology, LUMC. For technical details reference is made to the IMPD that accompanies this protocol. Study drug HPV-NIRD1 will be administered as a single subcutaneous injection to the subjects on day 0 of the study. Two strengths of HPV-NIRD1 will be administered: 80ug, which corresponds to 60 ug of the HPV peptide and 20 ug NIRD1 label and 400ug which corresponds to 300 ug HPV peptide and 100 ug NIRD1 label.
ICG is registered for diagnostic assessment of heart, circulation, microcirculation, liver function and perfusion of the choroidea. ICG is a 775 Da di-sulfonated small molecule. It has a spectral absorption peak at 800 nm and a spectral emission peak at 810 nm. ICG can be used as a lymphatic tracer. A solution of 1mL containing either 20*g or 100*g ICG will be administered as a single subcutaneous injection to the subjects on day 0 of the study.

Study burden and risks

Burden: The burden for participants consists of a time investment of 1 full day and 5 1-hour visits, possible side effects and compliance with lifestyle restriction.

Risks: The risks of participation for the subjects in the trial include local injection site reactions
and hypersensitivity reactions. In the absence of any adjuvants and based on the low and local dose of the study drug, the risks are deemed very limited. Nevertheless precautionary measures (supervised administration by qualified

staff and availability of medical treatment to treat hypersensitivity reactions) are in place and these effects are generally well manageable

Benefits: There are no expected direct benefits to subjects who participate in this trial, but participants may
help others prospectively by contributing to the knowledge base for designing future studies to
improve therapeutic HPV vaccination in cancer patients.

Contacts

Public
Centre for Human Drug Research

Zernikedreef 8
Leiden 2333CL
NL
Scientific
Centre for Human Drug Research

Zernikedreef 8
Leiden 2333CL
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. The subject is 18-65 years old at screening.
2. The subject is able and willing to comply with study procedures, and signed and dated

informed consent is obtained before any study-related procedure is performed.
3. Female subjects need to be either surgically sterile, post-menopausal or pre-menopausal with a negative urine pregnancy test at screening and just before administration of HPV-NIRD1.Pre-menopausal female subjects who are not surgically sterile should also employ an effective method of birth control for at least three months post dosing.
4. The subject*s body mass index is 18-22 kg/m2.
5. The subject has a normal or clinically acceptable medical history, physical examination, and
vital signs findings at screening (within 21 days before administration of study drug).
6. The subject*s screening ECG and clinical laboratory test results are within normal limits, or if
any are outside of normal limits they are considered to be clinically insignificant.
7. The subject has negative screening test results for hepatitis B, hepatitis C, and human immunodeficiency virus.
8. The subject has negative test results for drug and alcohol screening.

Exclusion criteria

1. The subjects uses prescription drugs or OTC-drugs that may have an impact on the study objectives.
2. Previous exposure to the investigational drug.
3. Participation in a clinical trial within 90 days of screening or more than 4 times in the previous year.
4. Known hypersensitivity to the investigational drug or comparative drug or drugs of the same class, or any of their excipients.
5. Any known factor, condition, or disease that might interfere with treatment compliance, study conduct or interpretation of the results such as drug or alcohol dependence or psychiatric disease.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-05-2016
Enrollment:	6
Type:	Actual

Medical products/devices used

Generic name:	optoacoustic imaging system
Registration:	No
Product type:	Medicine
Brand name:	HPV-NIRD1
Generic name:	n.v.t.
Product type:	Medicine
Brand name:	ICG-PULSION
Generic name:	Indocyanine Green
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	30-11-2015
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	06-04-2016
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	EUCTR2015-004995-31-NL
CCMO	NL55681.058.15