A first-in-human, open-label, dose escalation followed by dose expansion phase I/IIa trial to evaluate the safety, preliminary efficacy and pharmacokinetics of intratumoral CyPep-1 monotherapy and in combination with pembrolizumab in patients with advanced solid cancers.

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The primary objectives are:- To evaluate the safety and tolerability of IT administration of CyPep-1 as monotherapy and in combination with pembrolizumab.- To identify the recommended phase II dose (RP2D) of CyPep-1 as monotherapy and in combination…

Ethical review	Approved WMO
Status	Completed
Health condition type	Miscellaneous and site unspecified neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON54523

Source
ToetsingOnline

Brief title
CICILIA

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
Solid malignant tumors

Research involving
Human

Sponsors and support

Primary sponsor: Cytovation ASA
Source(s) of monetary or material Support: Cytovation ASA

Intervention

Keyword: Advanced solid cancers, CICILIA, intratumoral CyPep-1, phase I/IIa

Outcome measures

Primary outcome

Primary endpoints:

- Type and number of adverse events (AEs) according to National Cancer Institute (NCI) - Common Terminology Criteria for Adverse Events (CTCAE) criteria v5.0, and additional safety parameters of CyPep-1 as monotherapy and in combination with pembrolizumab.

- Dose limiting toxicities (DLTs) and the maximum tolerated dose (MTD) for determination of RP2D of CyPep-1 as monotherapy and treatment-limiting toxicities (TLTs) of CyPep-1 in combination with pembrolizumab.

Secondary outcome

Secondary endpoints:

- Objective response rate (ORR), defined by complete and partial responses, according to immune Response Evaluation Criteria in Solid Tumors (iRECIST) based on investigator's assessment.

- Time to and duration of response and duration of stable disease.

- The plasma concentration time profile of CyPep-1 and, if detectable, the derived PK parameters (i.e., area under the curve [AUC], peak plasma concentration [Cmax], time to reach Cmax [tmax], systemic clearance (CL), elimination half-life (t1/2) and volume of distribution [VD]).

Exploratory endpoints:

• For all Phase IIa arms: ORR in injected lesions and non-injected lesions separately, per itRECIST

• Progression-free survival (PFS) per iRECIST based on investigator's assessment.

• Overall survival (OS).

• The relative change in number of tumor infiltrating CD8+ T-cells in the injected and, whenever available, non-injected tumor biopsies.

• The association between the relative change in tumor infiltrating CD8+ T-cells and response rate in the injected lesions (per itRECIST) and all lesions (per iRECIST).

• The change in T-cell receptor (TCR) clonality levels in peripheral blood and (when available) biopsied lesions.

• Changes in the tumor microenvironment (injected and, whenever available, non-injected tumor biopsies) via expression of selected candidate immune markers: CD3, CD4, CD8, programmed death ligand 1 (PD-L1), programmed cell death protein 1 (PD-1), dendritic cell markers (CD80, CD86), immune suppressive cell markers (anti-FoxP3 for regulatory T-cells, anti-CD68 antibody for macrophages, anti-CD14 for monocytes, anti-CD15 for granulocytes, anti-CD56

for NK cells).

• For Arms A, B and C: Changes in the levels of peripheral blood cytokines

(IFN-γ, IL-2, IL-4, IL-6, IL-10, IL-15, TNF-α, TGF-β1).

• Peripheral blood phenotyping of selected immune cell markers

Study description

Background summary

CyPep-1 has been shown to selectively target tumor cell membranes based on their altered molecular composition, which in turn leads to lysis of tumor cells by removal of the cell membrane. This mode of action of CyPep-1 induces tumor cell death resulting in the release of tumor antigens, and potentially induces a tumor-specific immune response by in-situ immunization.
Preclinical toxicology studies have shown a favorable safety profile and potent anti-tumor activity of CyPep-1 in several tumor models. CyPep-1 was shown to modulate the tumor microenvironment by increasing the presence of CD8+ T-cells and by potentiating the effects of immune checkpoint inhibitors (ICIs). As such, we hypothesize that intratumoral (IT) injection with CyPep-1 leads to transformation of immunological *cold* and ICI treatment-resistant tumors into *hot* and immunological active tumors that can be successfully treated with immune-modulating agents.

Study objective

The primary objectives are:
- To evaluate the safety and tolerability of IT administration of CyPep-1 as monotherapy and in combination with pembrolizumab.
- To identify the recommended phase II dose (RP2D) of CyPep-1 as monotherapy and in combination with pembrolizumab.
The secondary objectives are:
- To assess the preliminary anti-tumor efficacy of CyPep-1, as monotherapy and in combination with pembrolizumab.
- To characterize the pharmacokinetics (PK) of CyPep-1.
The additional exploratory objectives are:
- To assess the preliminary anti-tumor efficacy of CyPep-1, as monotherapy and in combination with pembrolizumab, in injected lesions and non-injected lesions, separately.
- To assess survival after treatment with CyPep-1, as monotherapy and in combination with pembrolizumab.
- To assess the immune modulating properties of treatment with CyPep-1, as

monotherapy and in combination with pembrolizumab.

Study design

OVERALL TRIAL DESIGN:
This is a combined Phase I/IIa, open-label, dose escalation followed by dose expansion trial in subjects with advanced solid cancers. The trial consists of two phases and multiple arms, as shown in Figure 2 (see protocol page 18).

Phase I - dose escalation:
In this phase of the trial, safety and tolerability will be documented and the MTD/RP2D will be determined. Cohorts of 3 subjects will receive IT injections with CyPep-1. The DLT observation period for each dose level will be 6 weeks (5 weeks of trial treatment and 1 week of safety follow-up).
Screening will occur during the 4 weeks prior to start of CyPep-1 treatment.
In three dose cohorts of 3 subjects each, subjects will receive CyPep-1 IT at different concentrations (dose escalation) and volumes (depending on tumor size), i.e., 0.5 mg/mL, 2 mg/mL, or 5 mg/mL, respectively. These dose concentrations have been selected based on previous preclinical experience with CyPep-1.
Each subject will receive IT injection(s) with CyPep-1 on Day 1 of Weeks 1, 3, and 5, respectively. After each CyPep-1 administration, subjects will be required to stay at the clinic for at least 4 hours for safety and for those in which PK will be assessed, also for PK monitoring. The data from the additional three subjects in cohort 3 will be used for further confirmation of RP2D. The following CyPep-1 administrations are planned as continuous bi-weekly administrations.
For each dose cohort, at least 24 hours must elapse between each subject to start treatment with CyPep-1. No intra-subject dose escalation is allowed.
The decisions on dose escalation and MTD will be taken by the Dose Escalation Committee (DEC) after reviewing safety data (including DLTs) from all subjects who have entered the previous dose cohort and have completed the DLT observation period. The DEC will review all the data after all subjects in the highest dose cohort completed DLT observation period and before enrolment of subjects in the expansion cohort at RP2D in monotherapy can be initiated. The DEC is comprised of all the investigators or designees, as well as the medical monitor and representatives of the sponsor.
In Phase I, subject replacement for subjects who drop out for any reason, except DLTs, will only occur before the DLT observation period is completed and is allowed if a subject does not receive all three CyPep-1 administrations, unless due to CyPep-1-related toxicity. No subject replacement will occur for subjects who withdraw later.
After completion of Phase I, all results will be evaluated by the DEC. This will include safety data and if available, other supportive clinical data (e.g., efficacy, pharmacokinetics, tumor biopsy analyses) from all subjects included in Phase I of the trial. The DEC will confirm the MTD or RP2D (in case the MTD is not reached).

All additional arms for Phase IIa can start once Phase I data has been evaluated by the DEC and RP2D is confirmed for CYPep-1.
Phase I has been completed in August 2021, and the RP2D of CyPep-1 was determined at 5 mg/mL

Phase IIa - dose expansion (Arm A):
In this phase, safety and tolerability will be further evaluated in an expanded cohort of 9 subjects at the RP2D of CyPep-1, determined in Phase I. Screening- and treatment schedules will be the same as in Phase I, except for the 24-h observation period before start of treatment of the next subject, which is not applicable.
At the RP2D, in case of a responder per iRECIST or 2 subjects with stable disease per iRECIST, the number of subjects will be expanded to a total of 24 (CyPep-1 monotherapy).

Phase IIa - combination arm (ArmB):
The safety and tolerability of CyPep-1 in combination with pembrolizumab will be evaluated in a cohort of 15 subjects in total, using a staggered approach. Initially, 3 subjects will receive CyPep-1 at RP2D in combination with pembrolizumab Q6W and each subject will be observed for 24 h before the next subject can be administered with CyPep-1. After the first 3 subjects completed the TLT observation period of 6 weeks with no TLTs observed and after reviewing the safety data (including TLTs) by the DEC the inclusion of all remaining subjects at RP2D of CyPep-1 in combination with pembrolizumab can be initiated. In the absence of any TLTs in the initial 3 subjects, the 24-h observation period before start of treatment of the next subject is no longer applicable. Should any TLTs be observed in the first 3 subjects at the RP2D of CyPep-1 in combination with pembrolizumab, an additional 3 subjects in this dose group will be included. If <=1 out of 6 subjects have a TLT, the remainder of the 15 subjects will be treated at the RP2D. In the unlikely case that 2 or more of the 6 subjects experience any TLTs at RP2D of CyPep-1, a recommendation to dose de-escalate CyPep-1 and to what dose or to continue the combination part of the trial will be made by the DEC. The same screening schedule is planned and CyPep-1 will be administered according to the same treatment schedule as in Phase I.

For arm B, replacement of the first three subjects is allowed if a subject drops out for any reason, and does not receive all three CyPep-1 injections during the TLT observation period, unless due to CyPep-1- and/or pembrolizumab-related toxicity. No subject replacement will occur for subjects who discontinue later.

Phase IIa - dose expansion liver metastases (Arm C):
The safety and tolerability of at least two dose levels of CyPep-1, the RP2D and the dose immediately below that, are planned to be evaluated when CyPep-1 is administered intratumorally using ultrasound guidance to one metastatic lesion in the liver. The two dose levels are planned to be investigated

adhering to the *3+3* design and will follow the procedures as described for the dose escalation (Phase I). The first three subjects will receive CyPep-1 at the lower dose level and each subject will be observed for 24 h before CyPep-1 administration to a next subject (cohort 4). After the third subject at that dose finished the DLT observation period of 6 weeks (5 weeks CyPep-1 treatment plus 1 week safety follow-up), the DEC will recommend on the start of the cohort to be administered at RP2D based on the review of the safety data (cohort 5). After the DLT observation period for the first three subjects at RP2D for CyPep-1 and the review of all safety data, the DEC will recommend on the inclusion of all remaining subjects. In the absence of any DLTs in the first 3 subjects, the 24-h observation period before start treatment of the next subject is not applicable. Should a DLT be observed in the first three subjects at the RP2D of CyPep-1, an additional three subjects in this dose group will be included. In case that two or more subjects experience DLTs at RP2D of CyPep-1, a decision to dose de-escalate and to what dose and how to continue Arm C will be made by the DEC.

For Arm C, replacement for subjects who drop out for any reason, except DLTs, before the DLT observation period is completed is allowed when a subject did not receive all three CyPep-1 administrations. No subject replacement will occur for subjects who discontinue later.

Phase IIa - dose expansion melanoma (Arm D):
The safety and tolerability of CyPep-1 at RP2D will be further evaluated with focus on assessing efficacy signals of CyPep-1 monotherapy in up to 30 subjects with melanoma. Although safety information will be collected, there will not be a formal DLT observation period.

As part of the continuous safety monitoring of the trial, reports with cumulative safety data of Arm D subjects will be shared with all investigators, competent authorities, and ethical committees of countries where the trial is conducted at the following time points:
• After the first three subjects completed three weeks of treatment with CyPep-1.
• After the first three, six, and 12 subject

Intervention

Not applicable

Study burden and risks

Refer to protocol section 1.9 'Potential Risks and Benefits'.

Contacts

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Scientific
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NO

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

For Phase I and Phase IIa Arms A and C: 1. Histologically or cytologically confirmed locally advanced (unresectable) or metastatic tumors (solid tumor or lymphoma) with an accessible tumor lesion for intratumoral injection of CyPep-1 malignancy (including lymphomas) that is either: a. Refractory to standard-of-care treatment b. Have a disease for which there is no standard therapy considered appropriate. Metastatic deposits (including cutaneous/subcutaneous lesions and metastatic deposits in lymph nodes) of tumors for which IT injections may be performed are eligible. Pure cutaneous infiltrations (e.g., breast cancer cutaneous carcinomatosis) are ineligible. 2. 1 to 3 non-ulcerated transcutaneously accessible lesion(s) for injection and measurable as defined by iRECIST. All other tumor lesion(s) may be selected for efficacy follow-up, but will not be subjected to treatment with CyPep-1. 3. Presence of tumor lesion(s) (that have not been previously irradiated) suitable for biopsy at screening and at Week 6. For Arm C: 4. Confirmation of the presence of at least 1 liver

metastasis by imaging. 5. Subjects must have measurable disease which is equal to one or more metastatic liver lesions that can be accurately and serially measured that are greater than 1 cm dimension and for which the longest diameter is greater or equal to 1 cm as measured by CT (computed tomography)scan or magnetic resonance imaging (MRI). The metastatic liver lesion must not be in an area that received prior localized therapies. 6. Metastatic liver lesion for injection with >50% radiological visible necrosis must be avoided and the lesion must be located where any tumor swelling will not lead to gall bladder tract obstruction or lead to bleeding risk. For Arm D: 7. Histologically or cytologically confirmed diagnosis of advanced (unresectable Stage III) or metastatic (Stage IV: M1a and/or M1b) melanoma considered incurable by Standard of Care. For metastatic melanoma, only cutaneous, subcutaneous, lymph node, or lung metastases are allowed. 8. Previously exposed to ICI(s) and be categorized following the SITC Immunotherapy Resistance Taskforce (Kluger 2020) meeting one of the following: a. Have primary resistance: PD-(L)-1 inhibitor exposure >=6 weeks and have the best response as one of the following: i. PD, ii. SD for <6 months. b. Have secondary resistance: PD-(L)-1 inhibitor exposure >=6 weeks and best response CR, PR, or SD >6 months. c. Have adjuvant therapy resistance: recurrence subcategorized into primary resistance/early relapse occurred <12 weeks after the last dose, and late relapse occurred >=12 weeks after the last dose. If BRAF mutated, patients must have progressed to treatment with BRAF inhibitors. d. Have neoadjuvant therapy resistance including subjects with or without major pathologic response and subsequent PD that fulfills criteria for primary or secondary resistance e. Discontinued from ICI(s) therapy due to immune-related adverse events grade 3 or 4 other than endocrine insufficiencies treatable with hormonal replacement therapy, and meet one of the following: i. Remain on SD at discontinuation of PD-(L)1 inhibitor in combination with ipilimumab or show regrowth after <12 weeks of the last dose ii. Have not achieved a CR with single-agent PD-(L)1 inhibitor or combination of PD-(L)1 with LAG-3 inhibitor 9. At least 1 non-ulcerated lesion, not exceeding 5 cm in (the longest) diameter, for intratumoral injection(s) and measurable as defined by iRECIST. 10. Resolution of toxicity due to prior therapy returned to baseline or < Grade 2, except for alopecia or other irreversible immune-mediated AEs, as defined by CTCAE v5.0. and SITC ICI-related AEs (Brahmer et al, 2021). 11. Prior treatment(s) delivered by IT injection to the to-be injected lesion(s), including investigational agents, is allowed. For Phase I and Phase IIa Arms A, C and D in addition: 12. Age >= 18 years. 13. Estimated life expectancy of at least 3 months. 14. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1 (Appendix B). 15. Resolution of toxicity due to prior therapy to Grade < 2 (except for alopecia and transaminases in case of liver metastases) as defined by CTCAE v5.0 (Appendix C). 16. Ability to give written informed consent and to comply with the protocol. 17. All subjects of childbearing potential (defined as < 2 years after last menstruation or not surgically sterile) must have a negative highly sensitive pregnancy test at screening (urine/serum) and agree to use highly effective method for contraception according to the EU Clinical Trial Facilitation Group guidance from time of signing the informed consent form (ICF) until at least 120 days after the last administration of CyPep-1. The partners of subjects with childbearing potential must also apply contraceptive methods and are recommended not to donate sperm. 18. A male participant must agree to use contraception and refrain from sperm donation during the treatment period and for at least 120 days after the last dose of trial medication. 19. Adequate bone marrow, liver, and renal function: a. Platelet count >= 100 x 109/L b. Hemoglobin >= 6.0 mmol/L or 9.67 g/dL c. Absolute Neutrophil Count (ANC) >= 1.5 x 109/L d. Total bilirubin <= 1.5 x ULN, except for subjects with familial bilirubinemia

(Gilbert*s disease) e. Serum ASAT and ALAT <= 2.5 x ULN (<= 5 x ULN in case of liver metastases) f. Creatinine clearance >= 30 mL/min (Glomerular Filtration Rate [GFR] to be calculated by CKD-EPI formula) For Phase IIa Arm B: Participants are eligible to be included in Arm B of the trial only if all of the following criteria apply: Type of Participant and Disease Characteristics 1. The participant provides written informed consent for the trial. 2. Be >= 18 years of age on day of signing informed consent. 3. Participant with histologically or cytologically confirmed diagnosis of advanced (unresectable Stage III) or metastatic (Stage IV) solid tumor malignancy (including lymphomas) that is refractory to standard-of-care treatment or for which there is no standard therapy considered appropriate. Metastatic deposits (including cutaneous/subcutaneous lesions and metastatic deposits in lymph nodes) of tumors for which IT injections may be performed are eligible. Pure cutaneous infiltrations (e.g., breast cancer cutaneous carcinomatosis) are ineligible. 4. Subjects must have progressed on treatment with an anti-PD1/L1 monoclonal antibody (mAb) administered either as monotherapy, or in combination with other checkpoint inhibitors or other therapies. Treatment progression is defined by meeting all of the following criteria: a. Has received at least 2 doses of an approved anti-PD-1/L1 mAb. b. Has demonstrated clinical or radiological disease progression (PD) after PD-1/L1 5. A male participant must agree to use contraception and refrain from sperm donation during the treatment period and for at least 120 days after the last dose of trial medication. 6. A female participant is eligible to participate if she is not pregnant, not breastfeeding, and at least one of the following conditions applies: a.) Not a woman of childbearing potential (WOCBP) b.) A WOCBP (defined as < 2 years after last menstruation or not surgically sterile) must have a negative highly sensitive pregnancy test at screening (urine/serum) and must follow contraceptive guidance (highly effective method for contraception according to the EU Clinical Trial Facilitation Group guidance) from time of signing the ICF until at least 120 days after the last administration of trial medication. The partners of subjects with childbearing potential must also apply contraceptive methods, and are recommended not to donate sperm. 7. 1 to 3 non-ulcerated transcutaneously accessible lesion(s) for injection and measurable as defined by iRECIST. All other tumor lesion(s) may be selected for efficacy follow-up, but will not be subjected to treatment with CyPep-1. 8

Exclusion criteria

For Phase I and Phase IIa Arms A, C and D: subjects who meet ANY of the following criteria at screening will be excluded from trial entry: 1. There is no limit to the number of prior treatment regimens, but prior treatment(s) should not include compounds delivered by IT injection to the to-be injected lesion(s), including investigational agents. Subjects with prior IT therapies are allowed in Arm D. 2. Participation in another clinical trial within 4 weeks prior to first dose of CyPep-1. 3. Anti-cancer therapy within 4 weeks prior to the first dose of CyPep-1 (within 2 weeks for palliative radiotherapy, within 1 week for endocrine therapy). 4. Major surgical procedure within 14 days prior to the first dose of CyPep-1. 5. Live vaccine within 30 days prior to first dose of CyPep-1. 6. Expected to require any other form of systemic or localized antineoplastic therapy while in this trial. Localized palliative radiotherapy for pain relief is allowed on tumor lesions that are not selected for evaluation of treatment response. 7. Clinical evidence of an active second malignancy that is progressing or requires active treatment, except for curatively treated early stage (carcinoma in situ or stage 1) carcinomas

or non-melanoma skin cancer. 8. Active autoimmune disease requiring immunosuppressive therapy. 9. Any condition requiring continuous systemic treatment with either corticosteroids (> 10 mg daily prednisone equivalents) or other immunosuppressive agents within 2 weeks prior to first dose of CyPep-1. Inhaled, intranasal or topical (only on areas outside the injected lesion(s)) and physiological replacement doses of up to 10 mg daily prednisone equivalent are permitted in the absence of active auto-immune disease. 10. Abnormal or clinically significant coagulation parameters: a. Prothrombin Time - International Normalized Ratio (PT-INR)) >= 1.5 ULN b. Activated Partial Thromboplastin Time (APTT)) >= 1.5 ULN Subjects being treated with anticoagulants are excluded if the coagulation parameters are outside the therapeutic intervals as described in the SmPC for the administered treatment. 11. Subjects on anticoagulants with temporarily stop and start, supported by low molecular weight heparin (or other anticoagulation therapy at the discretion of the investigator and/or per local standard of care) during treatment period. 12. Known hypersensitivity to any component of CyPep-1. 13. Prior allogeneic tissue/solid organ transplant, stem cell or bone marrow transplant. 14. Known active human immunodeficiency virus (HIV). Subject is eligible when normal levels of CD4 are present. 15. Central nervous system (CNS) metastasis that is symptomatic or progressing or that requires current therapy (e.g., evidence of new or enlarging CNS metastasis, carcinomatous meningitis or new neurological symptoms attributable to CNS metastasis). 16. QTcF > 480 ms, history of long or short QT syndrome, Brugada syndrome, or known history of QTc prolongation, or Torsade de Pointes. 17. Women who are pregnant or breastfeeding. 18. Any serious and/or unstable pre-existing medical, psychiatric or other condition which in the investigator*s opinion could interfere with subject safety, obtaining written informed consent, or compliance with the trial protocol. 19. Has an active acute or chronic infection requiring systemic therapy at the time of CyPep-1 injection. Note: Subjects treated for mild/moderate infection with oral antibiotics only may be included based on consultation with the study medical monitor and the sponsor. Additional exclusion criteria for Phase IIa Arm C: 20. Subject is a candidate for hepatic surgery or local regional therapy of liver metastases with curative intent. 21. More than one third of the liver is estimated to be involved with metastases. 22. There is invasion by cancer into the main blood vessels such as the portal vein, hepatic vein or the vena cava. 23. Subject is currently receiving or has received liver metastatic-directed therapy (eg: radiation, ablation, embolization) less than 4 weeks prior to enrolmentor hepatic surgery. Exclusion criteria specific for Phase IIa Arm B: Participants are excluded from the trial if ANY of the following criteria apply at screening: Pregnancy Exclusion 1. A WOCBP who has a positive urine pregnancy test (within 72 hours) prior to trial treatment. If the urine test is positive or cannot be confirmed as negative, a serum pregnancy test will be required. Prior/Concomitant Therapy 2. Has received prior therapy with an anti-PD-1, anti-PD-L1, or anti PD-L2 agent or with an agent directed to another stimulatory or co-inhibitory T-cell receptor (e.g., CTLA 4, OX 40, CD137), and was discontinued from that treatment due to a Grade 3 or higher irAE. 3. Has received prior systemic anti-cancer therapy including investigational agents within 4 weeks (within 1 week for endocrine therapy) prior to first dose of CyPep-1. Note: Participants must have recovered from all AEs due to previous therapies to <=Grade 1 or baseline as defined by CTCAE v5.0 (Appendix C). Participants with <=Grade 2 neuropathy may be eligible. Participants with endocrine-related AEs Grade <=2 requiring treatment or hormone replacement may be eligible. Note: If the participant had major surgery, this should not have been within 14 days prior to the first dose of CyPep-1 and the participant must have recovered adequately from the procedure and/or any complications from the surgery prior to

starting study intervention. 4. Has received prior (palliative) radiotherapy within 2 weeks of start of trial treatment. Participants 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. 5. Has received a live or live-attenuated vaccine within 30 days prior to the first dose of CyPep-1. Note: Administration of killed vaccines are allowed. 6. Has received prior compounds delivered by IT injection to the to-be injected lesion(s), including investigational agents. 7. Expected to require any other form of systemic or localized antineoplastic therapy while in this trial. Localized palliative radiotherapy for pain relief is allowed on tumor lesions that are not selected for evaluation of treatment response. 8. Ongoing pembrolizumab-related toxicity event(s) as per TLT definition. Prior/Concurrent Clinical Trial Experience 9. Is currently participating in or has participated in a trial of an investigational agent or has used an investigational device within 4 weeks prior to the first dose of trial treatment. Note: Participants who have entered the follow-up phase of an investigational trial may participate as long as it has been 4 weeks after the last dose of the previous investigational agent. 10. Has had an allogeneic tissue/solid organ transplant. Diagnostic assessments 11. Has a diagnosis of immunodeficiency or is receiving chronic systemic steroid therapy (in dosing exceeding 10 mg daily of prednisone equivalent) or any other form of immunosuppressive therapy within 7 days prior the first dose of CyPep-1. 12. Has a known additional malignancy that is progressing or has required active treatment within the past 3 years, except for curatively treated early stage (carcinoma in situ or stage 1) carcinomas or non-melanoma skin cancer. Note: Participants with basal cell carcinoma of the skin, squamous cell carcinoma of the skin or carcinoma in situ (e.g., breast carcinoma, cervical cancer in situ) that have undergone potentially curative therapy are not excluded. 13. Has known active CNS metastases and/or carcinomatous meningitis. Participants with previously treated brain metastases may participate provided they are radiologically stable, i.e., without evidence of progression for at least 4 weeks by repeat imaging (note that the repeat imaging should be performed during study screening), clinically stable and wi

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Completed

Start date (anticipated):	30-04-2020
Enrollment:	65
Type:	Actual

Ethics review

Approved WMO Date:	09-10-2019
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	31-12-2019
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	21-01-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-03-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-04-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-07-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-07-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-10-2020

Application type:	Amendment
Review commission:	METC NedMec
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Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-07-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-08-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-09-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-09-2021
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Review commission:	METC NedMec
Approved WMO Date:	02-11-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-11-2021
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Approved WMO Date:	01-12-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-12-2021

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	17-03-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	04-04-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-07-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-08-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-01-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-02-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-02-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-02-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-12-2023

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	19-01-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	EUCTR2019-003317-33-NL
CCMO	NL71369.031.19