

# Treatment of skin cancer using gene therapy with intratumoral gene electrotransfer of a plasmid coding for IL-12

<b>Submission date</b> 24/09/2021	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 29/09/2021	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 24/01/2025	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Electroporation is a local drug delivery method that uses an electric pulse to deliver drugs such as bleomycin or cisplatin (called electrochemotherapy) or genetic material such as RNA or DNA (called gene electrotransfer). In this study, the researchers want to use gene electrotransfer to deliver the medicine pHIL12 to the tumor site (intratumoral pHIL12 gene electrotransfer). pHIL12 is a medicine consisting of plasmid DNA which can produce IL-12 protein in the body that can help the immune system to fight against cancer. Intratumoral gene electrotransfer with a plasmid coding IL-12 has been proven to be safe and effective for the treatment of melanoma skin metastases in the USA. EU directives recommend the use of plasmids without the gene for antibiotic resistance. For this purpose, the researchers constructed a plasmid coding for IL-12 in accordance with the EU regulatory requirements. The aim of this study is to assess the safety and tolerability of the constructed plasmid, pHIL12, in the treatment of basal cell carcinoma in patients with tumors in the head and neck region, where surgery is also feasible.

### Who can participate?

Adults (aged over 18 years) with untreated cutaneous basal cell carcinoma located in the head and neck region. Patients with only one tumor with the largest diameter up to 3 cm, in the region where surgery is feasible, will be included.

### What does the study involve?

Patients will be treated with a single intratumoral pHIL12 gene electrotransfer. Three different dose levels will be tested, starting with the lowest dose in three patients. If that dose is well tolerated, a higher dose will be used for next three patients and another higher dose for the last three patients.

### What are the possible benefits and risks of participating?

So far minimal or no side effects have been reported. Due to the pain caused by the electric pulses, local or general anesthetic will be needed. There may be some reddening of the skin but no pain after the treatment is complete is expected. The possible benefit is complete tumor regression.

Where is the study run from?

The University Medical Centre Ljubljana and Institute of Oncology Ljubljana (Slovenia)

When is the study starting and how long is it expected to run for?

December 2019 to December 2023

Who is funding the study?

Slovenian Research Agency (ARRS) (Slovenia)

Who is the main contact?

Prof. Gregor Sersa

gsersa@onko-i.si.

## Contact information

### Type(s)

Scientific

### Contact name

Prof Gregor Sersa

### ORCID ID

<http://orcid.org/0000-0002-7641-5670>

### Contact details

Institute of Oncology Ljubljana

Zaloška cesta 2

Ljubljana

Slovenia

SI-1000

+386 (0)1 5879 434

gsersa@onko-i.si

### Type(s)

Scientific

### Contact name

Prof Primoz Strojan

### ORCID ID

<http://orcid.org/0000-0002-0445-112X>

### Contact details

Institute of Oncology Ljubljana

Zaloška cesta 2

Ljubljana

Slovenia

SI-1000

+386 (0)1 5879 290

pstrojan@onko-i.si

# Additional identifiers

## EudraCT/CTIS number

2021-000852-21

## IRAS number

## ClinicalTrials.gov number

NCT05077033

## Secondary identifying numbers

ERIDEK-0086/2020

# Study information

## Scientific Title

Treatment of skin tumours with intratumoral interleukin 12 gene electrotransfer in the head and neck region

## Acronym

SmartGeneH&N

## Study objectives

In the proposed study the researchers intend to study the safety and tolerability of the constructed plasmid, pHIL12, in the treatment of basal cell carcinomas in patients with operable tumors in the head and neck region. The study is designed as exploratory, dose-escalating with the aim to determine the dose of plasmid that produces IL-12 expression in the tumours with the best biological activity, infiltration of the immune cells and no toxicity.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Approved 14/07/2021, Slovenian National Medical Ethics Committee (Štefanova ulica 5, 1000 Ljubljana; +386 (0)1 478 69 06; kme.mz@gov.si), ref: 0120-524/2020-12

## Study design

Clinical interventional open-label single-arm exploratory Phase I trial

## Primary study design

Interventional

## Secondary study design

Non randomised study

## Study setting(s)

Hospital

## Study type(s)

## Treatment

### Participant information sheet

Not available in web format, please use the contact details to request a participant information sheet

### Health condition(s) or problem(s) studied

Basal cell carcinoma of the skin in the head and neck region

### Interventions

Patients with operable basal cell carcinoma of the skin in the head and neck region will be treated with a single intratumoral pHIL12 gene electrotransfer (GET). The study is designed as a Phase I study with 3-6 patients per dose level, three dose levels, for a total estimated number of 9 patients (3-18 patients). The drug product, a plasmid p21-hIL-12-ORT, is prepared at a final concentration of 0.5 mg/ml, 1 mg/ml and 2 mg/ml diluted in physiological saline, ready for injection.

### Intervention Type

Drug

### Phase

Phase I

### Drug/device/biological/vaccine name(s)

pHIL12

### Primary outcome measure

1. Safety of the intratumoral pHIL12 GET measured by recording adverse events according to Common Terminology Criteria for Adverse Events (CTCAE) v.5.0 criteria right after the therapy and at each follow-up 2, 7 and 30 days after the therapy
2. Tolerability of the therapy determined by patient-reported outcomes using the quality of life questionnaire (EORTC QLQ-C30) before the therapy and at follow-up 7 and 30 days after the therapy

### Secondary outcome measures

1. Pharmacokinetics determined by measuring IL-12 serum levels at 2, 7 and 30 days after the therapy
2. Pharmacodynamics determined by measuring IL-12 and IFN- $\gamma$  tumor levels in tumor biopsies at 7 and 30 days after the therapy
3. Feasibility of recruitment evaluated by assessing the process of recruitment, treatment and follow-up visits at the end of the study
4. Determination of recommended dose for confirmatory studies based on pharmacodynamic data at the end of the study. The dose that produces IL-12 expression in the tumors with the best biological activity, infiltration of the immune cells and no toxicity will be selected

### Overall study start date

01/12/2019

### Completion date

31/12/2023

# Eligibility

## Key inclusion criteria

1. Histologically or cytologically confirmed, previously untreated cutaneous basal cell carcinoma located in head and neck region
2. Solitary tumours, with the largest diameter up to 3 cm, in the region where curative surgery is feasible
3. Age 18 years or older
4. Life expectancy >3 months
5. Physical performance in accordance with the Karnofsky scale  $\geq 70$  or  $< 2$  in accordance with World Health Organization (WHO) scale
6. The patient must be capable of understanding the treatment procedure and possible adverse events, which may arise during treatment
7. The patient must be capable of signing the informed consent to participate in the clinical study (voluntary and conscientious consent after education)
8. Prior to inclusion in the trial, the patient must be presented at a multidisciplinary advisory team meeting

## Participant type(s)

Patient

## Age group

Adult

## Lower age limit

18 Years

## Sex

Both

## Target number of participants

9

## Total final enrolment

9

## Key exclusion criteria

1. Known malignancy elsewhere in/on the body
2. Lesions not suitable for treatment with GET (invasion into the bone, infiltration of large vessels)
3. A life-threatening infection and/or severe heart failure and/or liver failure and/or other life-threatening systemic diseases
4. Significantly reduced lung function, which requires the determination of diffusing capacity for carbon monoxide (DLCO). Patients should not be treated if DLCO is abnormal
5. Treatment with immunosuppressive drugs, steroids and other drugs that would affect poor wound healing
6. Age under 18-years
7. Major disruptions in the coagulation system (who does not respond to the standard therapy – replacement of vitamin K or freshly frozen plasma)
8. A chronic decline in kidney function (creatinine  $> 150 \mu\text{mol/l}$ )

- 9. Epilepsy
- 10. Pregnancy and breastfeeding
- 11. Patient's incapable of comprehending the purpose or course of the trial, or not agreeing to be included in the trial
- 12. Patients unwilling or unable to comply with the protocol requirements and scheduled visits

**Date of first enrolment**

28/09/2021

**Date of final enrolment**

01/09/2023

## **Locations**

**Countries of recruitment**

Slovenia

**Study participating centre**

**Institute of Oncology Ljubljana**

Zaloška cesta 2

Ljubljana

Slovenia

1000

## **Sponsor information**

**Organisation**

Institute of Oncology Ljubljana

**Sponsor details**

Zaloska 2

Zaloska

Ljubljana

Slovenia

1000

+386 (0)1 5879 434

gsersa@onko-i.si

**Sponsor type**

Hospital/treatment centre

**Website**

[https://www.onko-i.si/eng/sectors/research\\_and\\_education/department\\_of\\_experimental\\_oncology/employees](https://www.onko-i.si/eng/sectors/research_and_education/department_of_experimental_oncology/employees)

ROR

<https://ror.org/00y5zsg21>

## Funder(s)

### Funder type

Government

### Funder Name

Javna Agencija za Raziskovalno Dejavnost RS

### Alternative Name(s)

Slovenian Research Agency, Javna agencija za raziskovalno dejavnost RS v angleškem jeziku: Slovenian Research Agency, Javna Agencija za Raziskovalno Dejavnost RS, The Slovenian Research and Innovation Agency (ARIS), Javna agencija za znanstvenoraziskovalno in inovacijsko dejavnost Republike Slovenije, ARRS, ARIS

### Funding Body Type

Government organisation

### Funding Body Subtype

National government

### Location

Slovenia

## Results and Publications

### Publication and dissemination plan

Planned publication of the results in a high-impact peer-reviewed journal. The protocol is also planned to be published in a high-ranked peer-reviewed journal in the next few months.

### Intention to publish date

31/03/2025

### Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

### IPD sharing plan summary

Other

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol article</a>		14/08/2022	07/11/2022	Yes	No

[Results article](#)

06/01/2025

24/01/2025

Yes

No