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

Submission date	Recruitment status	[_] Prospectively registered
24/09/2021	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
29/09/2021	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
24/01/2025	Cancer	

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?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2021-000852-21

ClinicalTrials.gov (NCT)
NCT05077033

Protocol serial number
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

Study type(s)
Treatment

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(s)
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

Key secondary outcome(s))
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-γ 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

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 ≥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

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

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 µmol/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
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Slovenia
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Sponsor information

Organisation
Institute of Oncology Ljubljana

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

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?
Results article		06/01/2025	24/01/2025	Yes	No
Protocol article		14/08/2022	07/11/2022	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes