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Treatment of soft tissue tumours through the skin using electrochemotherapy

Submission date	Recruitment status	[_] Prospectively registered
05/09/2019	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
11/09/2019	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
12/02/2020	Cancer	

Plain English summary of protocol

Background and study aims
About 1%-6% of cancer patients experience the spread of their tumour to the skin, subcutaneous tissue or muscle. In these cases, surgical removal is the most effective option, especially when there are no other organs involved. On the contrary, when multiple tumours are present or other organs are involved, multi-disciplinary treatment is preferable. This may combine a systemic treatment (e.g. chemotherapy, immunotherapy, targeted-therapy) coupled with local treatment (radiotherapy, radiofrequency ablation, isolated perfusion, electrochemotherapy [ECT], etc.) aimed at increasing tumour response on critical sites. Among local therapies, ECT has demonstrated high efficacy in the treatment of cutaneous metastases, being capable of achieving local tumour resolution in up to 50%-60% of patient, with acceptable side effects, mainly limited to the skin.
This study aims to explore the feasibility of ECT in the treatment of large or deep tumours located in the fat under the skin or within muscles.

Who can participate?
Cancer patients 18-year-old or older with locally-advanced or metastatic solid tumours

What does the study involve?
The study involves an evaluation visit during which a physician will discuss the opportunity of treatment with the patient along with the eligibility criteria. At the same time, the physician will perform a clinical examination to confirm the eligibility criteria and to verify the feasibility of the procedure. Finally, participants will be requested to fill in a brief (10 minutes) questionnaire on the effects of the disease on the participant's conditions and on the participant's general health. Before treatment, every suitable candidate patient will be investigated with radiologic tests including a computed tomography (CT) scan and a positron emission tomography (PET) scan in the outpatient clinic. If based on these tests, the indication to treatment will be confirmed, the patient will be evaluated by an anaesthetist for deciding the best anesthesiological technique for the procedure (locoregional anaesthesia, general anaesthesia, mild general sedation) and pain management.
The treatment will be administered as an in-hospital procedure and the discharge will follow at 24-48 hours, depending on patient clinical condition (local pain, skin side effects, etc.). The procedure will be performed in the operating room or in the radiology unit by an experienced

team including a surgical oncologist and a radiologist. Briefly, it involves the administration of a low toxic chemotherapy drug into the participant's vein for the duration of one minute, followed by the application of short (some tens of seconds) electric pulses to the tumour by mean of needle electrodes placed through the skin. Indicatively, the total duration of the procedure can range between 60 and 90 minutes.
During the hospital stay, the nursing and the medical team will assess the participant's conditions to detect possible side effects caused by the treatment and will carefully inspect the site of the application of the electrodes. After discharge, participants will be required to attend the outpatient clinic for regular visits (after 1 week, after 1, 2, 3, and 6 months and then every 3 months). Moreover, at one and two months after treatment, participants will be required to undergo new radiological tests (PET-CT and CT or MRI scan) to assess the effect of electrochemotherapy on the tumour and to quantify its effect. Finally, during the follow-up visits, participants will be required to complete the same questionnaire regarding the participant's quality of life to assess any possible influence of the treatment investigated in this study.

What are the possible benefits and risks of participating?
The participation in this study, despite requiring patient availability to attend the clinic for the initial visits and the preparatory test, has the following possible benefits:
- Participants will receive a regular and careful examination from experienced cancer doctors and nurses who will be working together with participants.
- Participants will have access to a treatment that is not available yet.
- The new electrochemotherapy technique proposed in this study may be more effective than standard electrochemotherapy treatment.
- Due to its greater precision, the new electrochemotherapy modality can target the participant's tumour more effectively and participants may be spared from the need of multiple treatment applications
- The chemotherapy drug and dose is the same used in standard electrochemotherapy, which is recognized as an extremely safe procedure. As a result, we don’t expect more systemic side effects.
- By participating, participants will contribute to cancer research and to improving the application of this therapy in the future and in other patients
Along with benefits, there are also some potential risks that should be acknowledged:
- The new treatment may not work for participants, even if it is effective in other patients
- Local pain due to the insertion of needle electrodes that are thicker compared to standard electrochemotherapy
- A longer duration of the procedure and the anaesthesia, due to the novelty of the technique
- More frequent tests and visits because participants will be closely monitored. This could mean also more travels and more time spent in the hospital.

Where is the study run from?
Melanoma and Sarcoma Unit, Department of Surgical Oncological and Gastroenetrological Sciences DISCOG, University of Padova , Italy

When is the study starting and how long is it expected to run for?
September 2009 to August 2018

Who is funding the study?
Investigator initiated and funded. The equipment (disposable material) used during the procedures is kindly provided by IGEA Spa, (Carpi, Italy), which nonetheless is not involved in the conduction of the study

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
N 1886P

Study information

Scientific Title
Percutaneous treatment of large and deep-seated soft tissue tumours by means of variable electrode geometry electrochemotherapy

Study objectives
The study is intended to verify the feasibility, safety, and efficacy (antitumor activity) of electrochemotherapy applied by mean of new equipment. In particular, the use of longer and independent electrodes, and the possibility of their arrangement into a flexible configuration geometry might generate a larger and more homogeneous electric field around tumours than in

standard electrochemotherapy technique. This may allow encompassing the whole tumour mass along with suitable safety margins ("one-shot treatment"), obtaining a better tumour response and local control, even on large and deep-seated soft tissue tumours. No increased in local toxicity is expected since the doses of chemotherapy is the same applied in the standard electrochemotherapy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 13/07/2009, Ethics Committee of the Azienda Ospedaliera of Padova (Comitato Etico per la Sperimentazione Clinica della Provincia di Padova, Via Giustiniani, 1 - 35128 Padova; +39 049 8212341; ce.sperimentazione@aopd.veneto.it), ref: Protocol N 1886P

Study design
Single-centre pilot/phase II study

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 below to request a patient information sheet

Health condition(s) or problem(s) studied
Soft tissue metastases in the soft tissue from any tumour histotype.

Interventions
Enrolled patients will be treated under regional/general anaesthesia or general sedation as appropriate according to tumour location and patient preference. They will receive the same dose of chemotherapy (bleomycin 15,000 IU/m2) used in standard electrochemotherapy according to the European Standard Operating Procedure of Electrochemotherapy (ESOPE; Mir LM, Eur J Cancer Suppl. Nov 2016) The target tumour, instead, will be electroporated by means of the percutaneous insertion of 2-6 independent needle electrode probes connected with a dedicated pulse generator (Cliniporator-Vitae, IGEA, Carpi, Italy). The electrode probes will be positioned by a radiologist under ultrasound (US) or computed tomography (CT) guidance.

The duration of the investigated procedure is expected to be slightly longer compared to standard electrochemotherapy due to the more challenging nature (size, anatomical location) of the treated tumours and the novelty of the technique. Indicatively, we estimate that it could take between 60 and 90 minutes.

The follow-up includes clinical evaluation at 1 week, 1, 2, 3 and 6 months and then every three months. The radiological evaluation includes PET-CT scan at one month and CT or MRI scan at one and two months after treatment in accordance with the Response Evaluation Criteria In Solid Tumors (RECIST, J Natl Cancer Inst 2000). Subsequent radiological follow-up (with CT or MRI scan) will be every three months, but will be agreed with the referring medical oncologist based to reduce the number of examinations.

Intervention Type
Mixed

Primary outcome measure
1. Antitumor activity (tumour response) assessed by Radiological (PET-CT and CT / MR scan) at baseline, 1 month, 2 months, then every 3 months
2. Feasibility of the procedure (rate of procedures achieving tumour coverage with electric pulses) assessed by review of procedural data from the electric pulse generator at intraoperative (electric current flowed into the tumour) and postoperative (actual distribution of the electric field intensity around the target lesion)
3. Safety assessed by clinical and anamnestic at baseline, intraoperative, at the conclusion of the procedure, during hospital stay (12h and/or 24h depending on discharge), and at every follow-up visit (1 week, 1, 2, 3, 6 months and every 3 months thereafter)

Secondary outcome measures
1. Local control (local progression-free survival) assessed by clinical and radiological methods 3 months after treatment and every 3 months thereafter
2. Patient-reported outcomes assessed by Health-related quality of life questionnaire (EQ-5D-3L) at baseline, 1 month, 2 months
3. Improvement of the procedure assessed by study dedicated multidisciplinary audit meeting (including an anaesthetist, a surgeon, a radiologist and a medical engineer) aimed at discussing critical technical/clinical aspects, after every 3 performed procedures

Overall study start date
20/03/2009

Completion date
31/08/2018

Eligibility

Key inclusion criteria
1. Cancer patients 18-year-old or older with locally-advanced or metastatic solid tumours of any histotypes
2. At least one measurable, well-demarcated soft tissue tumour (histologically proven) not amenable to surgical treatment and suitable for percutaneous electrode insertion
3. Tumour size has to be comprised between 3 cm and 7 cm, tumour depth between 3 cm and 20 cm
4. Patient performance status of ≤ 2 according to the Eastern Cooperative Oncology Group (ECOG) scale
5. Agreement to local treatment with electrochemotherapy at the multidisciplinary team meeting
6. Signed informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
30

Total final enrolment
30

Key exclusion criteria
1. Clinically relevant lung disease, in particular, lung fibrosis
2. Severe heart, kidney or liver impairment
3. History of epilepsy
4. Short life expectancy (< 3 months)
5. Active infection
6. Previous treatment with bleomycin up to the maximal dosage (400,000 IU)
7. Concomitant local/systemic anticancer therapies administered within 4 weeks before and 8 weeks after ECT (unless agreed at the MDT meeting as being in the interest of the patient)
8. Clinically relevant abnormalities in coagulation tests
9. No infiltration of the target lesions across fascial planes at pre-operative radiological imaging (CT, MRI scan)

Date of first enrolment
01/09/2009

Date of final enrolment
31/12/2016

Locations

Countries of recruitment
Italy

Study participating centre
Melanoma and Sarcoma Unit, Department of Surgical Oncological and Gastroenetrological Sciences DISCOG, University of Padova
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Sponsor information

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Sponsor type
University/education

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ROR
https://ror.org/00240q980

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded. The equipment (disposable material) used during the procedures is kindly provided by IGEA Spa, (Carpi, Italy), which nonetheless is not involved in the conduction of the study

Results and Publications

Publication and dissemination plan

We intend to communicate the preliminary results at surgical and oncological scientific events. Moreover, at the end of patient accrual and analysis of data, we will prepare a final report that will be submitted for publication to a scientific journal.

The preliminary results of this trial have been presented at the following scientific events:
- European Society of Medical Oncology (ESMO) Congress 2014 (Madrid, September 26-30)
- 2nd World Congress of Electroporation (Norfolk, VA, September 24-28 2017)
- European Society of Surgical Oncology (ESSO) 38th annual congress (Budapest, October 10-12 2018)
- 3rd World Congress of Electroporation (Toulouse, September 3-6 2019).

Intention to publish date
01/10/2019

Individual participant data (IPD) sharing plan
The data collected during this study will not publicly available due to ethical and privacy restrictions. The dataset generated with anonymized patient data will be available upon detailed and reasonable request from the principal investigator after the publication of the final results (Dr Luca Giovanni Campana, Email: luca.campana@unipd.it)

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	10/02/2020	12/02/2020	Yes	No