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Optimizing the concentration of a cancer-treating drug (bleomycin) in patients undergoing electrochemotherapy

Submission date
17/10/2019

Recruitment status
No longer recruiting

Registration date
21/10/2019

Overall study status
Completed

Last Edited
30/08/2022

Condition category
Cancer

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Bleomycin is a treatment for a number of types of cancer. Bleomycin is a type of antibiotic that is poisonous to cells. It binds to the cancer cells' DNA so that the cells can't divide or grow. Electrochemotherapy is a cancer treatment. The definition of therapeutic window of lectrochemotherapy is based on the observed responses of the tumors that were treated at different time points after the drug injection. To refine the method, thorough knowledge is needed about the pharmacokinetics and pharmacodynamics of bleomycin, which would base on sensitive analytical method. This method was not available until recently. The aim of the study is therefore to determine pharmacokinetics and pharmacodynamics of bleomycin in patients treated with electrochemotherapy, for optimization of the treatment protocol

Who can participate?
Patients aged over 18 eligible for electrochemotherapy of cutaneous tumors (basal cell carcinoma, squamous cell carcinoma, melanoma) and cutaneus metastases of melanoma and adenocarcinoma of the breast

What does the study involve?
All participants have electrochemotherapy treatment. The procedure is standardized and is performed according to the published Standard Operating Procedure (SOP) for electrochemotherapy. The chemotherapy drug bleomycin is injected intravenously (through a needle in a vein) in dose of 15 000 IU/m2. After 8 minutes, electric pulses are delivered to the tumour in order to send the bleomycin into the cancer cells. Before the bleomycin application blood will be collected as well as 5, 10 ,20 and 30 minutes after bleomycin injection, for bleomycin pharmacokinetics and pharmacodynamics analysis. Moreover collection of tumor tissue of the same patients at the time of application of electric pulses for determination of BLM concentration in treated tumors.

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 anaesthesia will be needed. There may be some reddening of the skin but no pain after the treatment is complete is expected.

Where is the study run from?
1. Institute of Oncology Ljubljana, Slovenia
2. Department of Otorhinolaryngology and Cervicofacial Surgery, University Medical Centre Ljubljana, Slovenia
3. Department of Dermatology and Allergology, University of Szeged, Hungary

When is the study starting and how long is it expected to run for?
August 2018 to June 2021

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
Zaloska 2
Ljubljana
Slovenia
1000
+386 15879434
gsersa@onko-i.si

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
Clinico-pharmacological approach to optimize the therapeutic bleomycin concentration in patients undergoing electrochemotherapy

Acronym
ECT-BLM

Study objectives
The aim of the study is to determine pharmacokinetics and pharmacodynamics of bleomycin in patients treated with electrochemotherapy, for optimization of the treatment protocol

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 13/07/2017, Republic of Slovenia National Ethics Committee (Štefanova 5, 1000 Ljubljana, Slovenia; +386 01 478 69 13), ref: KME 39/06/17

Study design
Multicentre interventional non-randomized study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Basal cell carcinoma, squamous cell carcinoma, melanoma or metastases of adenocarcinoma of the breast, treated with electrochemotherapy

Interventions
All patients are treated with electrochemotherapy with bleomycin (BLM), according to European Standard Operating Procedures of Electrochemotherapy. Bleomycin will be injected intravenously in a dose of 15,000 IU/m2 skin surface. The electric pulses will be delivered by electrodes to the tumors generated by electric pulse generator Cliniporator (IGEA, Carpi, Italy) 8-

28 minutes after bleomycin injection. During the procedure tumor tissue and blood samples will be collected for the purpose of pharmacological analysis.

Data analysis for determination of:
• Pharmacokinetics of BLM in patients within different age groups.
• Correlation between the tumor response and BLM concentration in the tumors.
• Possible variability in drug concentration according to the tumor type.
• Impact of previous treatment(s) (radiotherapy, systemic therapies, surgery) on drug accumulation in the tumors.
• Optimization of the therapeutic window.

Intervention Type
Procedure/Surgery

Primary outcome measure
Pharmacokinetics and pharmacodynamics of bleomycin assessed by:
1. Collection of patient's sera undergoing electrochemotherapy according to the SOP (5, 10, 20 and 30 min after ECT) and in compliance with the NICE recommendations for determination of in vivo BLM pharmacokinetics.
2. Collection of tumor tissue of the same patients at the time of application of electric pulses (8 min after intravenous 15 000 IU/m2 BLM injection) for determination of BLM concentration in treated tumors.

Secondary outcome measures
n/a

Overall study start date
01/09/2016

Completion date
30/06/2021

Eligibility

Key inclusion criteria
1. Eligible for electrochemotherapy of cutaneous tumors (basal cell carcinoma, squamous cell carcinoma, melanoma) and cutaneus metastases of melanoma and adenocarcinoma of the breast
2. Age ≥18 years
3. Agree to participate in this study and signed informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex

Both

Target number of participants
80

Total final enrolment
26

Key exclusion criteria
1. Do not comply with requirements for the blood collection, or samples were not collected according to the SOP for blood collection
2. Do not comply with the requirements for tumor biopsy, or samples were not collected according to the SOP for tissue sampling

Date of first enrolment
01/07/2018

Date of final enrolment
04/06/2021

Locations

Countries of recruitment
Hungary

Slovenia

Study participating centre
Department of Otorhinolaryngology and Cervicofacial Surgery, University Medical Centre Ljubljana
Zaloska 2
Ljubljana
Slovenia
1000

Study participating centre
Institute of Oncology Ljubljana
Zaloska 2
Ljubljana
Slovenia
1000

Study participating centre
Department of Dermatology and Allergology, University of Szeged
Korányi fasor 6

Szeged
Hungary
6720

Sponsor information

Organisation
Department of Otorhinolaryngology and Cervicofacial Surgery University Medical Centre

Sponsor details
Zaloska 2
Ljubljana
Slovenia
1000
+38615222153
ales.groselj@kclj.si

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/01nr6fy72

Funder(s)

Funder type
Government

Funder Name
Slovenian Research Agency, ARRS

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
04/06/2022

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository. International Network for Sharing Practices on

Electrochemotherapy (INSPECT) group database;http://www.insp-ect.org/default.aspx
The database will be private, only available to Slovenian and Hungarian researchers designated for the study. Written informed consent will be signed. Patients will be anonymous, coded according to the standard InspECT coding system. Slovenian researchers together with Hungarian researchers will perform analysis of the results.
Other participants in InspECT group will not have access to the patients' files but will be informed about the progress in the study at regular yearly meetings

IPD sharing plan summary

Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		24/08/2021	26/08/2021	Yes	No
Protocol file	version 3	21/10/2019	30/08/2022	No	No