Study Protocol with Statistical Analysis Plan

PanECT Study

Study Title
Electrochemotherapy of Posterior Resection Surface for Lowering Disease Recurrence Rate in Pancreatic Cancer (PanECT Study)

ClinicalTrials.gov Identifier: NCT04281290
Institution: University Medical Centre Ljubljana in collaboration with Institute of Oncology Ljubljana
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1. Background and Rationale

Pancreatic cancer remains one of the most lethal malignancies, with poor long-term survival despite improvements in surgical techniques and systemic therapies. Local recurrence occurs in approximately **30% of patients after surgical resection**, contributing significantly to disease progression and mortality.
Electrochemotherapy (ECT) is a treatment modality that combines the administration of cytotoxic agents with locally delivered electric pulses that temporarily permeabilize cell membranes, thereby enhancing drug uptake. Bleomycin is commonly used due to its strong potentiation when combined with electroporation.
The posterior resection margin in pancreatic head carcinoma is located near major vascular structures and represents a frequent site of local recurrence. Application of intraoperative electrochemotherapy to this area may improve local disease control without causing significant damage to surrounding vessels.

The **PanECT study** was therefore designed to evaluate the **safety, feasibility, and preliminary efficacy** of intraoperative electrochemotherapy applied to the posterior pancreatic resection surface following surgical resection.

The methodology and preliminary clinical results of the PanECT study have been previously reported in a peer-reviewed publication. Intraoperative electrochemotherapy applied to the posterior pancreatic resection surface demonstrated feasibility and acceptable safety in patients undergoing surgical treatment for pancreatic cancer.

2. Study Objectives

Primary Objective
To evaluate the **safety and feasibility** of intraoperative electrochemotherapy of the posterior resection surface following pancreaticoduodenectomy.
- To assess **postoperative complications** according to the Clavien-Dindo classification.

- To evaluate **treatment tolerance and quality of life**.

Secondary Objectives
- To evaluate **local recurrence rate** after treatment.
- To evaluate **disease-free survival (DFS)**.
- To evaluate **overall survival (OS)**.

3. Study Design

Prospective **Phase I pilot clinical study**.
Patients undergoing surgical resection for pancreatic head carcinoma will receive additional intraoperative electrochemotherapy applied to the posterior resection surface.

Study phases:
Phase I – safety and feasibility evaluation (10 patients)

4. Study Population

Inclusion Criteria
- Age ≥ 18 years
- Histologically or radiologically confirmed **resectable pancreatic ductal adenocarcinoma**
- Candidate for pancreaticoduodenectomy
- ECOG performance status 0–2
- Adequate organ function
- Written informed consent

Exclusion Criteria
- Metastatic disease
- Severe cardiac arrhythmias
- Known hypersensitivity to bleomycin
- Pregnancy or breastfeeding
- Severe comorbid conditions preventing surgery

5. Treatment Procedure

After surgical removal of the pancreatic tumor, intraoperative electrochemotherapy will be performed on the posterior resection surface.
Bleomycin will be administered intravenously as a bolus at a dose of **15 mg/m^2**.
Electric pulses will be delivered **8–28 minutes after drug administration** using a Cliniporator device with plate electrodes positioned between the following anatomical landmarks:
- lateral border of the inferior vena cava

- resection margin of the common hepatic duct
- truncus coeliacus
- pancreatic resection surface
- level of the left renal vein

Each electrode application will deliver:
- 8 electric pulses
- duration 100 µs
- frequency 5 kHz
- amplitude 960 V

Electric pulse delivery will be synchronized with ECG signals using the AccuSync ECG triggering device to prevent delivery during the vulnerable period of the cardiac cycle.

6. Postoperative Monitoring

Patients will be closely monitored postoperatively.
During the first postoperative days, patients will be treated in the intensive care unit where vital parameters including ECG will be continuously monitored.
Laboratory tests will include:
- hemogram
- electrolytes
- inflammatory markers
- liver function tests

Amylase and lipase levels from abdominal drains will be measured on postoperative days 3 and 7 to detect pancreatic fistula.
Doppler ultrasound will be performed approximately 7 days after surgery to evaluate blood flow through the hepatic artery and portal vein.

7. Follow-Up

Patients will undergo regular follow-up visits including:
- clinical examination
- laboratory tests
- tumor markers (CA19-9 and CEA)
- ultrasound or CT imaging

Follow-up schedule:
- 1 month after surgery
- 3 months
- 6 months
- every 6 months thereafter

These evaluations will be used to detect early local recurrence and assess long-term treatment outcomes.

8. Outcome Measures

Primary Outcome
Safety and feasibility of intraoperative electrochemotherapy, measured by postoperative complications within 30 days after surgery.
Complications will be graded according to the **Clavien-Dindo classification**.

Secondary Outcomes
- Disease-free survival
- Overall survival
- Local recurrence rate
- Quality of life
- Treatment tolerance

9. Statistical Analysis Plan

This study is designed as an exploratory pilot study.
The planned sample size of **10 patients** is based on feasibility considerations rather than formal power calculations.

Continuous variables will be summarized using:
- mean ± standard deviation, or
- median with interquartile range.

Categorical variables will be summarized using frequencies and percentages.
Disease-free survival and overall survival will be estimated using the **Kaplan–Meier method**.
Postoperative complication rates will be analyzed descriptively.

10. Ethical Considerations

The study was approved by the **National Medical Ethics Committee of the Republic of Slovenia**.

All patients provided written informed consent prior to participation.
The study is conducted in accordance with:
- the Declaration of Helsinki
- Good Clinical Practice guidelines

11. Publication

The preliminary results of this clinical study have been published in the following peer-reviewed article:

Čebron Ž, Djokić M, Petrič M, Čemažar M, Bošnjak M, Serša G, Trotovšek B. Intraoperative electrochemotherapy of the posterior resection surface after pancreaticoduodenectomy: Preliminary results of a hybrid approach treatment of pancreatic cancer. Bioelectrochemistry. 2024 Feb;155:108576. doi: 10.1016/j.bioelechem.2023.108576. Epub 2023 Sep 22. PMID: 37748261.