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# Obsidian ASG Autologous Platelet-Rich Fibrin Matrix for the prevention of postoperative pancreatic fistula following pancreatic resection: study protocol for a feasibility trial

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## Abstract

**Introduction:** Postoperative pancreatic fistula (POPF) is the most frequent complication after partial pancreatectomy which is by definition associated with clinical consequences requiring changes in postoperative management. Despite numerous scientific efforts, effective procedures to prevent POPF are lacking. Obsidian® ASG Autologous Platelet-Rich Fibrin Matrix has been effectively applied to prevent anastomotic leakage following colorectal surgery. This study is the first to investigate the feasibility of using the sealant in pancreatic surgery.

**Methods and analysis:** Twenty-five consecutive patients scheduled for elective formal partial pancreatectomy due to any underlying disease fulfilling the eligibility criteria will be included. Obsidian® ASG sealant prepared out of 120mL of each patient's whole blood will be applicated to the pancreatic stump or the pancreatic anastomosis respectively. The primary endpoint is the feasibility of the procedure, e.g. proportion of patients undergoing successful trial intervention. Secondary endpoints comprise safety and surgical outcome parameters including rate and severity of POPF as well as further pancreas-specific complications as defined by the International Study Group of Pancreatic Surgery (ISGPS) during 90 days after surgery. Patients will be matched with a historic collective in a 1:2 ratio to gain first data on efficacy.

**Ethics and dissemination:** This trial and the associated study protocol (Version 1.1.1, date 26/03/204) were approved by the institution's Ethics Committee (reference number 2191/2023). All trial procedures are performed in accordance with the ICH harmonized tripartite guideline on Good Clinical Practice (ICH-GCP) and the ethical principles of the Declaration of Helsinki. After completion of the study, results will be published in due course.

**Registration details:** The trial was registered in the German Clinical Trials Register on 06.05.2024 (DRKS-ID: DRKS00034052).

**Strengths and limitations of this trial**

- This is the first trial to investigate the feasibility and safety of intraoperative application of Obsidian® ASG Autologous Platelet-Rich Fibrin Matrix to prevent postoperative pancreatic fistula after partial pancreatectomy.
- One of the strengths of this trial is its novelty and the careful monitoring of adverse events to gain safety besides feasibility data.
- Valid results on efficacy of the trial intervention will not be obtained due to the feasibility study design, however, the results will serve as a basis for future randomized controlled trials.
- The open-label, non-randomized trial design is prone to several sources of bias, especially selection, performance and detection bias.

## Introduction

### *Rationale of the trial*

Formal partial pancreatectomy, i.e. distal pancreatectomy (DP) or partial pancreatoduodenectomy (PD), is the treatment of choice for several malignant and pre-malignant pancreatic diseases including pancreatic cancer and its precursor lesions as well as neuroendocrine tumours[1, 2]. With the centralization of pancreatic surgery in specialized institutions and improvements in perioperative management, procedures have become safe with mortality rates below two percent and low failure-to-rescue rates[3, 4]. However, postoperative morbidity still occurs in 65% of patients and therewith remains unsatisfactorily high[3]. The most frequent and relevant complication is postoperative pancreatic fistula (POPF) resulting from healing disorders of the pancreatic anastomosis after PD or leakage from the pancreatic stump after DP[5]. POPF affects the patient's postoperative course by definition as it may cause intra-abdominal infection or arrosional bleeding requiring changes in clinical management such as anti-infective treatments, re-interventions and re-operations as well as intensive care unit stay

and prolongation of total hospital stay[6]. The rates of clinically relevant POPF, i.e. POPF grades B/C as defined by the International Study Group of Pancreatic Surgery (ISGPS), reported in literature reach up to 27% after DP[7] and 22% after PD[8] (even 38% after robotic PD[9]), illustrating the unsolved problem of POPF. Prevention of POPF is particularly important in patients undergoing extended pancreatic resection including arterial reconstruction, since these patients are at high risk for life-threatening post-pancreatectomy haemorrhage (PPH) caused by intra-abdominal enzyme-rich fluid collections[10, 11].

***Preliminary data***

Numerous previous studies provided evidence that none of the existing surgical techniques and perioperative measures are effective in the prevention of POPF[12-15]. A recent Cochrane review summarizes the available evidence on fibrin sealant use to prevent POPF after PD and DP showing inconclusive results and uncertain evidence on this topic[14]. Further research is therefore mandatory, and the evaluation of new approaches is required to solve the hitherto intractable problem of POPF. The thrombocyte enriched, completely absorbable Obsidian ASG matrix is developed to improve tissue regeneration and healing of gastrointestinal anastomoses by sustained release of an up to 8 times multiplied concentration of non-activated platelets and continuously release of growth factors over a period of 5 to 7 days after surgery[16]. Hence, the application of Obsidian® ASG may accelerate tissue proliferation, and the anti-inflammatory and antimicrobial platelet properties may offer control of potential contamination which may be especially important after PD. Obsidian ASG has already been used to prevent postoperative anastomotic leakages in colorectal surgery and its application has been shown to be safe, feasible and related to low rates of anastomotic leakages[17, 18]. The application has not yet been demonstrated to be superior to standard therapy. This may be due to the low rates of anastomotic leakage in colorectal surgery and the small number of cases in previous trials. This is the first

study to assess the application in pancreatic surgery with the aim to prevent POPF following partial pancreatectomy.

## Methods and analysis

This clinical trial protocol is written according to the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) statement[19]. Adherence to these recommendations is documented in the SPIRIT checklist (see Additional file 1). The trial was registered with the Clinical Trials Register (DRKS00034052) before enrolment of the first patient.

### *Trial design and trial-supporting facilities*

This is an investigator-initiated, single-centre, open-label, phase II clinical trial with one intervention arm and an exploratory study design. Patients in the intervention group will later be matched with a historic control group in a 1:2 ratio. The sponsor of the trial is the Medical University of Vienna, Austria. The sponsor had no role in the design of this study and will not have any role during its execution, analysis of the data, interpretation of the findings, or the decision to submit the results for publication. The coordinating investigator is the sponsor's representative and also the trial's statistician. The trial will be conducted in close cooperation with the Coordinating Centre for Clinical Trials, Medical University of Vienna, Austria, which is in charge of the trial monitoring, including initiation and close-out visits. The site of this trial is the Department of General Surgery, Division of Visceral Surgery, University of Vienna, Austria.

### *Trial population*

Consecutive patients scheduled for elective, partial pancreatic resection, i.e. PD or DP, due to any underlying disease will be screened for eligibility and informed consent will be reached before inclusion of the patient. Inclusion criteria comprise ≥18 years of age, ability to understand character and individual consequences of the clinical trial, as well as written informed consent. In case of withdrawal of informed consent patient data will be excluded from analysis. Patients with severe systemic disease that is a constant threat to life, classified as American Society of Anaesthesiologists' (ASA) score >3 and patients with known hypersensitivity to any component in the formulation of the investigational medical product will be excluded as will be patients with understanding or language problems and patients with inability to comply with the study and/or follow-up procedures. Pregnant and breast-feeding patients as well as patients with concurrent participation in another interventional clinical trial with interference with the trial outcome will also be excluded. For patients with childbearing potential, presence of preoperative negative urine or negative blood pregnancy test and adequate contraception until 14 days after trial intervention is therefore required.

### *Trial intervention and perioperative management*

#### *Preparation*

At the day of surgery, 120 mL of whole blood will be withdrawn from the individual patient. Then, the matrix will be prepared using 300 mg of tranexamic acid and processed through a fully automated Vivostat microprocessor-controlled system (Vivostat A/S, Alleroed, Denmark). The blood will be heated up to 36 °C and separated by centrifugation in the upper reservoir chamber of the processing unit. The resulting plasma will be combined with Batroxobin, leading to the polymerization of acid-soluble fibrin 1. This process will effectively

remove excess fibrinogen and thrombocyte-depleted serum, leaving concentrated fibrin 1 and thrombocytes. To dissolve the available fibrin and create a stable clot matrix with high elasticity, tensile strength, and crack resistance, the fibrin concentrate will be mixed with sodium acetate buffer (pH 4). The resulting thrombocyte-enriched matrix will then be embedded in a fibrin scaffold.

***Surgical procedures***

Surgical steps and techniques will be carried out according to the institutional standard procedures as open, laparoscopic or robotic partial pancreatectomies. After exclusion of distant tumor spread and after confirming local resectability, PD or DP will be performed depending on the localization of the disease. Reconstruction after PD is routinely performed with an omega loop and a double-layer end-to-side pancreatojejunostomy and an end-to-side hepaticojejunostomy, each with 5/0 or 6/0 monofilament atraumatic single sutures. An internal stent is neither recommended nor prohibited. During DP, transection and closure of the pancreas is routinely performed above the portomesenteric axis with any linear stapling device which is selected at the surgeon's discretion. In case of too thick tissue transection will be performed with a surgical scalpel followed by separate ligation of the pancreatic duct and suture of the entire pancreatic remnant. If indicated, additional resections may be performed depending on the individual patient`s intraoperative findings. A ligamentum teres hepatis patch as additional covering of the pancreatic remnant is permitted but not recommended. Any other additional coverage, except for the investigational drug, is not allowed because there is no evidence and therefore it would not be the institution's standard.

***Application of the investigational medicinal product***

At the end of surgery, 5-6 ml of Obsidian ASG sealant will be applicated to the pancreatic stump in DP or to the pancreatic anastomosis in PD. According to the surgical approach, application systems for open or minimal-invasive surgery will be used. After application of the investigational medicinal product, at least one intra-abdominal drainage tube will be placed and left in place at least until postoperative day (POD) three after surgery. Perioperative administration of somatostatin analogues is permitted but not recommended. The administration must be documented in the Case report form (CRF; see Additional file 2).

***Control group***

To serve as a basis for further planning of a randomized controlled trial regarding the secondary outcome parameters, the enrolled patients will be matched with a historic collective (age, procedures, histopathological findings) extracted from the pancreatic surgery database of the Department of Visceral Surgery, Medical University of Vienna in a 1:2 ratio.

***Risk of bias***

The open-label trial design with a single prospective intervention arm and a matched historical control group bears considerable sources of bias, especially selection, performance and detection bias. However, since this is the first trial to use the investigational medicinal product in pancreatic surgery, a small and non-randomized pilot trial focusing on safety and feasibility seems appropriate at this early stage of evaluation of a new surgical intervention[20]. Procedures will be standardized and the trial personnel will be informed and trained at the site initiation visit; hence performance bias will be reduced. In addition, adherence to the trial protocol will be controlled by regularly on-site monitoring.

## Outcome parameters

### *Assessment of feasibility*

Primary outcome is the feasibility of the trial intervention defined as proportion of patients undergoing successful trial intervention.

### *Assessment of safety*

Patients will be closely monitored for the occurrence of adverse events (AE) and serious adverse events (SAE). The incidence of all AE will be ascertained by the investigators using non-leading questions, noted as spontaneously reported by the patients to the medical staff or observed during any measurements on all study days. Only events that occurred after enrolment and during the follow-up will be collected. A SAE is defined as any AE occurring during the observation period that results in death, is life-threatening, requires or prolongs hospitalisation, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, is otherwise medically relevant and/or requires intervention to prevent any of these outcomes. All SAE must be reported to the Coordinating Centre for Clinical Trials, Medical University of Vienna, Austria within 24 hours after becoming known.

### *Secondary outcome parameters*

The secondary outcome parameters comprise all relevant surgical complications, i.e. clinically relevant POPF[6], delayed gastric emptying[21], postpancreatectomy hemorrhage[22], lymphatic fistula[23], postpancreatectomy acute pancreatitis[24], intraabdominal fluid collection/abscess, wound infection, burst abdomen, perioperative sepsis[25], reinterventions and reoperations, 90-day mortality, length of intensive care unit and total hospital stay, as well as readmission to hospital. Postoperative complications will be graduated as proposed by the ISGPS and Clavien-Dindo[26] as applicable.

## Schedule of trial procedures and follow-up visits

As presented in Table 1, there will be seven trial visits from screening to the last follow-up at POD 90. Except the trial intervention on the day of surgery all procedures including assessment of laboratory parameters belong to the perioperative standard procedures after pancreatic resection. In patients with childbearing potential, a pregnancy test will be performed during the routine preoperative laboratory examinations.

## Statistical methods

### *Sample size calculation and timelines*

In this proof-of-concept trial, the focus is on the feasibility and safety of the procedure. Hence, no formal sample size calculation has been performed. We have chosen a number of patients, which is considered valid to obtain first data on feasibility and safety of the trial intervention. Twenty-five patients are planned to be enrolled in this trial. Considering drop-outs of 5 patients (due to inoperability in case of distant metastasis, local inoperability or in case of total pancreatectomy) the remaining 20 patients will be sufficient to evaluate feasibility. The trial preparation phase started in December 2023. The inclusion of the first patient is planned in May 2024. The duration of the clinical trial for each individual patient will be 3 months. The flow chart in Figure 1 illustrates the structure of the trial flow. Nowadays, our centre carries out at least 130 partial pancreatectomies per year. Thus, the time taken to recruit 25 patients out of 50 patients screened for eligibility is expected to be 5 months. Taking into account two months for preparation and another two months for analysis, the duration of the entire trial will be approximately 12 months.

### *Statistical analysis*

All analyses will be of descriptive character and will be performed with the software program SPSS. Quantitative variables will be presented as median and dispersion as interquartile range (IQR) or 95% confidence interval (CI). For comparison with the historical control group, the nonparametric Kruskal-Wallis test will be used to compare continuous parameters. For categorical parameters, absolute and relative frequencies will be calculated and compared using the $X^2$ or Fisher's exact test as appropriate. Mortality will be calculated using the Kaplan-Meier method. Missing data are expected to be rare, so no imputation will be performed. Two-sided P values will be used and a difference will be considered statistically significant at $P < 0.05$. Interim analyses are not planned.

### Data collection and data management

The investigator or a designated representative must enter all protocol-required information in the CRF (see Additional file 2). The CRF should be completed as soon as possible after the information is collected, preferably on the same day when a trial participant is seen for an examination, treatment, or any other trial procedure. The reason for missing data should be provided. The investigator is responsible for ensuring that all sections of the CRF are completed correctly and that entries can be verified in accordance with the source data. In general, all entries in the CRF must be verifiable by source documents. In advance, exceptions to this rule can be defined by the sponsor. A detailed list will be provided in the Investigator Site File (ISF). Finally, there must be no data that are inconsistent between CRF and source documents. Completeness, validity and plausibility of data will be checked in time of data entry. If no further corrections are to be made in the database it will be closed and used for statistical analysis. Any reason for missing data should be documented. The investigator is responsible

for completeness of data as well as the compliance with institutional data management regulations. The investigator will archive all trial data (source data and ISF, including patient identification list) according to Good Clinical Practice and to local law or regulations. All data shall be made available if requested by relevant authorities.

## Monitoring

Monitoring will be done remotely and by a clinical monitor's personal visits as defined by the Coordinating Centre for Clinical Trials, Medical University of Vienna, Austria. During on-site visits, the monitor will review entries into the CRF on the basis of source documents. Additionally, by remote monitoring and frequent communication, the monitor will ensure that the trial is conducted according to the protocol and regulatory requirements. Therefore, the investigator must allow the monitor to verify all essential documents and must provide support at all times to the monitor.

## Ethics and dissemination

This trial was approved by the institution's Ethics Committee (reference number 2191/2023) on 03.05.2024. Every patient participating in the study will be provided a personal injury insurance, as well as subsidiary medical liability and medical professional legal expenses insurance. All trial procedures are performed in accordance with the ICH harmonized tripartite guideline on Good Clinical Practice (ICH-GCP) and the ethical principles of the Declaration of Helsinki. Once the study has been completed, the results will be published in due course.

## Author's contributions

UK conceived the study, drafted the protocol and the manuscript.

CG was involved in the conception of the study, drafted the protocol and the manuscript.

CD was involved in the conception of the study and approved the final manuscript.

CSL conducted revisions and approved the final manuscript.

SR conducted revisions and approved the final manuscript.

KS conducted revisions and approved the final manuscript.

MS conducted revisions and approved the final manuscript.

OS was involved in the conception of the study, supervised revisions of the protocol and approved the final manuscript.

## Funding statement

This study is being funded by the financial resources of the institution. It received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

## Patient and Public involvement statement

Neither patients nor the general public were involved in the design, conduct, reporting, or dissemination of our research.

## Competing interests statement

The authors declare that they have no competing interests.

## Tables and figures

| | |
|---|---|
| **Table 1** | Study visits |
| **Figure 1** | Trial flow chart |

## Additional files

| | |
|---|---|
| **Additional file 1** | SPIRIT checklist |
| **Additional file 2** | Case Report Form |
| **Additional file 3** | Informed consent form |

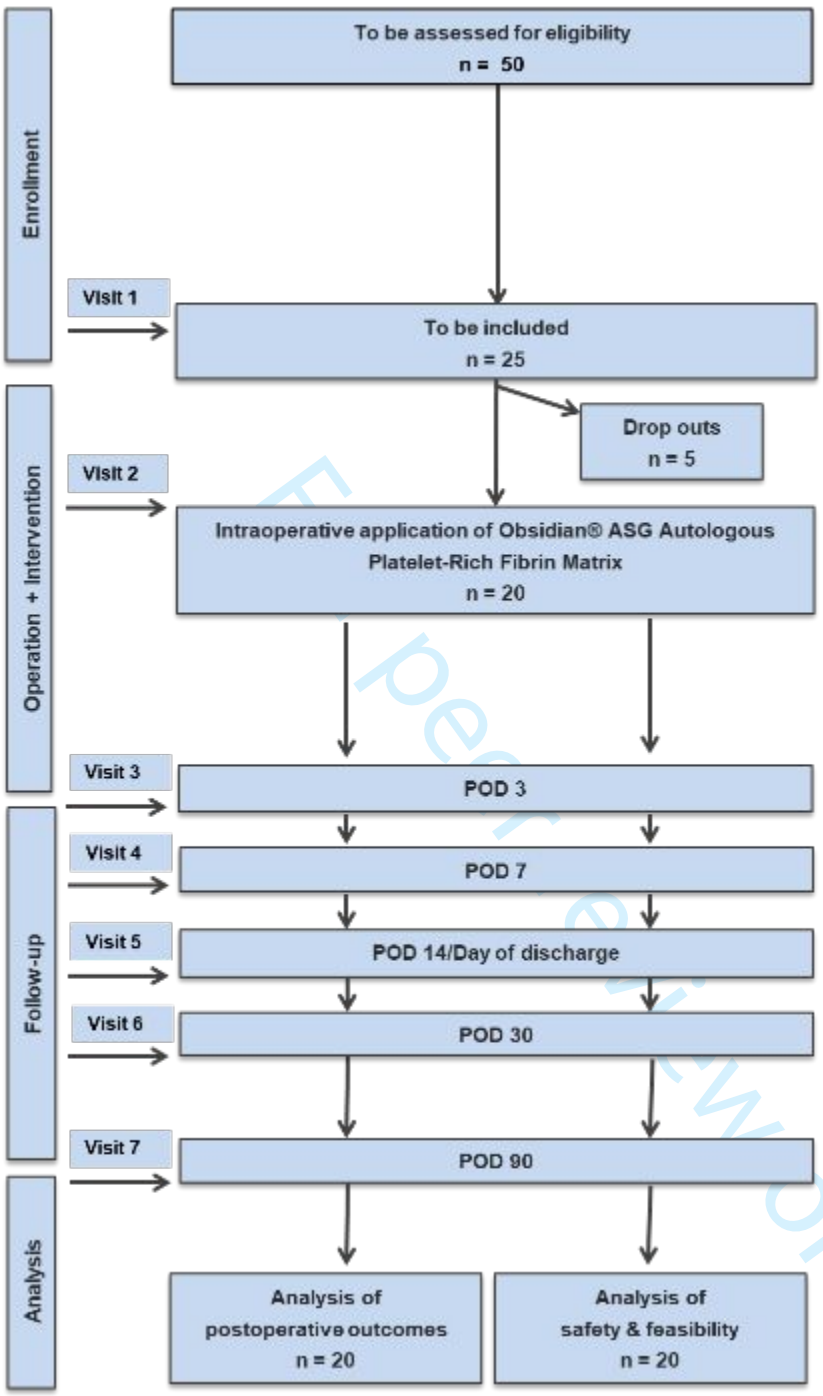


**Figure 1 Trial flow**

**Table 1** Trial visits

| Visit | 1 Enrollment & Randomization | 2 Operation | 3 | 4 | 5 Follow-up | 6 | 7 |
|---|---|---|---|---|---|---|---|
| Day related to index operation | | Day 0 | POD 3 | POD 7 | POD 14/Day of discharge | POD 30 | 3 months post-OP |
| Type of visit | Outpatient | Inpatient | Inpatient | Inpatient | Inpatient | Outpatient | Phone |
| Visit window | ±0 | ±0 | ±0 | ±0 | -2 | ±2 | ±2 |
| Inclusion/exclusion criteria | X | | | | | | |
| Informed consent | X | | | | | | |
| Baseline/demographic data | X | | | | | | |
| Prior/concomitant diseases | X | | | | | | |
| Prior/concomitant medication | X | X | X | X | X | X | X |
| Trial intervention | | X | | | | | |
| Operative procedure | | X | | | | | |
| Laboratory parameters† | | X | X | X | | | |
| Pregnancy test¥¥ | X | | | | | | |
| Drainage amylase | | | X | (X) | (X) | (X) | (X) |
| Primary endpoint | | X | | | | | |
| Secondary endpoints | | | X | X | X | X | X |
| AE/SAE | X | X | X | X | X | X | X |

POD: postoperative day; *In-hospital visit in case of ongoing hospital stay or readmission to hospital.; †Standard periinterventional/perioperative procedures; Documentation of serum values of amylase and/or lipase, bilirubin, hemoglobin, erythrocytes, leucocytes, thrombocytes, International Normalized Ratio (INR), creatinine clearance/glomerular filtration rate, C-reactive protein; ¥¥Females with childbearing potential onl

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# Obsidian ASG Autologous Platelet-Rich Fibrin Matrix for the prevention of postoperative pancreatic fistula following pancreatic resection: study protocol for a feasibility trial

# CASE REPORT FORM

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# Obsidian-Pilottrial

**Visit 1: Screening/Enrolment**

Screening No.: _____ Year of birth: _____

Date of screening: ____ (dd/mm/yyyy)

| **Inclusion criteria** | **yes** | **no** |
|---|---|---|
| 1. Age ≥ 18 years | ○ | ○ |
| 2. Patient undergoing elective partial pancreatic resection for any reason | ○ | ○ |
| 3. Ability to understand character and individual consequences of the trial | ○ | ○ |
| 4. Written informed consent | ○ | ○ |
| 5. Date of written informed consent: | ○ | ○ |

| **Exclusion criteria** | **yes** | **no** |
|---|---|---|
| 1. ASA score > III | ○ | ○ |
| 2. Pregnancy or lactation | ○ | ○ |
| 3. Understanding or language problems | ○ | ○ |
| 4. Inability to comply with study and/or follow-up procedures | ○ | ○ |
| 5. Known hypersensitivity to any component of the formulation | ○ | ○ |
| 6. Concurrent participation in another interventional clinical trial | ○ | ○ |

**Demography**

Gender ○ female ○ male ○ divers

Age: _____ years

**Anamnesis**

Body height and weight: _____ cm _____ kg

Previous abdominal surgery

Previous radio-/chemotherapy within the last 6 months

Relevant comorbidities:

- Coronary heart disease☐
- Congestive heart failure NYHA I/II☐
- Chronic artrial fibrillation☐
- Chronic renal insufficiency☐
- Chronic obstructive pulmonary disease (COPD)☐
- Diabetes mellitus ☐
- Other:☐_____

ASA-classification: ☐ I (healthy patient)☐ II (mild systemic disease)
☐ III (severe systemic disease)

**Pancreas-specific anamnesis**

Indication for the planned surgical procedure

- Pancreatic carcinoma
- Cystic neoplasm
- Neuroendocrine tumor
- Other: _____

If preexisting diabetes mellitus, insulin dependent? Yes ☐ no ☐

Preexisting exocrine pancreatic insufficiency? Yes ☐ no ☐

o

# Obsidian-Pilottrial

**Visit 2: Surgery**

Screening No.: _____ Year of birth: _____

Date of surgery

Performed surgery

- DP☐ PD☐ other☐ _____

Approach

- Laparoscopic☐ robotic☐ open☐
- Conversion: no☐ yes☐, reason for conversion_____

Level of pancreatic transection

- above☐ left to portal vein☐ right to portal vein☐

Transsection technique:_____

Closure technique:_____

Anastomosis technique_____

Texture of pancreatic tissure:

- soft ☐ intermediate ☐ hard☐

Pancreatic ducts size: _____ (mm)

Additional resections: splenectomy☐ lymphadenectomy☐ others ☐ _____

Duration from skin incision to closure: _____ min

Intraoperative blood loss: _____ ml

Intraoperative blood transfusion: _____ml

Placement of abdominal drain: yes ☐ no ☐

Administration of somatostatin-analogues:

- during surgery: yes ☐ no ☐
- after surgery: yes ☐ no ☐

**Serious adverse events** (new events since last visit)

Were there any serious adverse events? Yes☐ no ☐

Were there any other intervention related side effects? Yes ☐ no ☐

If yes, please specify: _____

**Protocol violations**

Were there any protocol violations? Yes ☐ no ☐

If yes, please specify: _____

# Obsidian-Pilottrial

**Visit 3: POD 3**

Screening No.: _____ Year of birth: _____

Date of visit: _____ (dd/mm/yyyy)

**Assessment of postoperative pancreatic fistula**

Pancreatic amylase at POD3: _____ (U/L)

Lipase at POD3: _____ (U/L)

Classification of POPF: no POPF ☐ grade A ☐ grade B ☐ grade C ☐

**Complications** (new events since last visit)

Perioperative sepsis ☐

Postpancreatectomy acute pancreatitis ☐

- associated complications (e.g. bleeding or perforation) ☐ please, specifiy: _____

Delayed gastric emptying

Post-pancreatectomy hemorrhage: no PPH ☐ grade A ☐ grade B ☐ grade C ☐

Intraabdominal fluid collection ☐

Intraabdominal abscess ☐

Lymphatic fistula / chylus ascites ☐

Wound infection ☐

Burst abdomen ☐

Reinterventions / - operations ☐ _____

ICU stay ☐

Transfer to normal ward at ____. POD

**Diagnostics/interventions:** yes ☐ no ☐

CT-scan ☐

Interventional application of drainage ☐

Relaparotomy ☐, state the reason: _____

**Serious adverse events** (new events since last visit)

Were there any serious adverse events? Yes ☐ no ☐

Were there any other intervention related side effects? Yes ☐ no ☐

If yes, please specify: _____

**Protocol violations**

Were there any protocol violations? Yes ☐ no ☐

If yes, please specify: _____

# Obsidian-Pilottrial

**Visit 4: POD 7**

Screening No.: _____ Year of birth: _____

Date of visit: _____ (dd/mm/yyyy)

**Assessment of postoperative pancreatic fistula**

Pancreatic amylase at POD7: _____ (U/L)

Lipase at POD7: _____ (U/L)

Classification of POPF: no POPF ☐ grade A ☐ grade B ☐ grade C ☐

**Complications** (new events since last visit)

Perioperative sepsis ☐

Postpancreatectomy acute pancreatitis ☐

- associated complications (e.g. bleeding or perforation) ☐ please, specifiy: _____

Delayed gastric emptying

Post-pancreatectomy hemorrhage: no PPH ☐ grade A ☐ grade B ☐ grade C ☐

Intraabdominal fluid collection ☐

Intraabdominal abscess ☐

Lymphatic fistula / chylus ascites ☐

Wound infection ☐

Burst abdomen ☐

Reinterventions / - operations ☐ _____

ICU stay ☐

Transfer to normal ward at ____. POD

**Diagnostics/interventions:** yes ☐ no ☐

CT-scan ☐

Interventional application of drainage ☐

Relaparotomy ☐, state the reason: _____

**Serious adverse events** (new events since last visit)

Were there any serious adverse events? Yes ☐ no ☐

Were there any other intervention related side effects? Yes ☐ no ☐

If yes, please specify: _____

**Protocol violations**

Were there any protocol violations? Yes ☐ no ☐

If yes, please specify: _____

# Obsidian-Pilottrial

**Visit 5: POD 14/day of discharge**

Screening No.: _____ Year of birth: _____

Date of visit: _____ (dd/mm/yyyy)

**Assessment of postoperative pancreatic fistula**

Classification of POPF: no POPF ☐ grade A ☐ grade B ☐ grade C ☐

**Complications** (new events since last visit)

Perioperative sepsis ☐

Postpancreatectomy acute pancreatitis ☐

- associated complications (e.g. bleeding or perforation) ☐ please, specifiy: _____

Delayed gastric emptying

Post-pancreatectomy hemorrhage: no PPH ☐ grade A ☐ grade B ☐ grade C ☐

Intraabdominal fluid collection ☐

Intraabdominal abscess ☐

Lymphatic fistula / chylus ascites ☐

Wound infection ☐

Burst abdomen ☐

Reinterventions / - operations ☐ _____

ICU stay ☐

Transfer to normal ward at ____. POD

**Diagnostics/interventions:** yes ☐ no ☐

CT-scan ☐

Interventional application of drainage ☐

Relaparotomy ☐, state the reason: _____

**Serious adverse events** (new events since last visit)

Were there any serious adverse events? Yes ☐ no ☐

Were there any other intervention related side effects? Yes ☐ no ☐

If yes, please specify: _____

**Protocol violations**

Were there any protocol violations? Yes ☐ no ☐

If yes, please specify: _____

# Obsidian-Pilottrial

**Visit 6: POD 30**

Screening No.: _____ Year of birth: _____

Date of visit: _____ (dd/mm/yyyy)

**Assessment of postoperative pancreatic fistula**

Classification of POPF: no POPF ☐ grade A ☐ grade B ☐ grade C ☐

**Complications** (new events since last visit)

Perioperative sepsis ☐

Postpancreatectomy acute pancreatitis ☐

- associated complications (e.g. bleeding or perforation) ☐ please, specifiy: _____

Delayed gastric emptying

Post-pancreatectomy hemorrhage: no PPH ☐ grade A ☐ grade B ☐ grade C ☐

Intraabdominal fluid collection ☐

Intraabdominal abscess ☐

Lymphatic fistula / chylus ascites ☐

Wound infection ☐

Burst abdomen ☐

Reinterventions / - operations ☐ _____

ICU stay ☐

Transfer to normal ward at ____. POD

**Diagnostics/interventions:** yes ☐ no ☐

CT-scan ☐

Interventional application of drainage ☐

Relaparotomy ☐, state the reason: _____

**Serious adverse events** (new events since last visit)

Were there any serious adverse events? Yes ☐ no ☐

Were there any other intervention related side effects? Yes ☐ no ☐

If yes, please specify: _____

**Protocol violations**

Were there any protocol violations? Yes ☐ no ☐

If yes, please specify: _____

# Obsidian-Pilottrial

**Visit 7: POD 90 / premature study termination**

Screening No.: _____ Year of birth: _____

Date of visit: _____ (dd/mm/yyyy)

**Assessment of postoperative pancreatic fistula**

Lipase at POD3: _____ (U/L)

Classification of POPF: no POPF ☐ grade A ☐ grade B ☐ grade C ☐

**Complications** (new events since last visit)

Perioperative sepsis ☐

Postpancreatectomy acute pancreatitis ☐

- associated complications (e.g. bleeding or perforation) ☐ please, specifiy: _____

Delayed gastric emptying

Post-pancreatectomy hemorrhage: no PPH ☐ grade A ☐ grade B ☐ grade C ☐

Intraabdominal fluid collection ☐

Intraabdominal abscess ☐

Lymphatic fistula / chylus ascites ☐

Wound infection ☐

Burst abdomen ☐

Reinterventions / - operations ☐ _____

ICU stay ☐

Transfer to normal ward at ____. POD

**Diagnostics/interventions:** yes ☐ no ☐

CT-scan ☐

Interventional application of drainage ☐

Relaparotomy ☐, state the reason: _____

**Serious adverse events** (new events since last visit)

Were there any serious adverse events? Yes ☐ no ☐

Were there any other intervention related side effects? Yes ☐ no ☐

If yes, please specify: _____

**Protocol violations**

Were there any protocol violations? Yes ☐ no ☐

If yes, please specify: _____

**Hospitalization**

Date of discharge: _____ or hospital stay ongoing ☐

Total intensive care unit stay (postoperative and readmissions): ____ (days)

Total hospital stay: ____ (days)

**Results from final histological examination**

Pancreatic carcinoma ☐

- if yes, please enter pTNM-stage: _____

Cystic neoplasm ☐

Neuroendocrine tumor ☐

Other ☐ _____

I confirm that all data entered in this CRF is complete and accurate to the best of my knowledge.

X

date, investigator's name (block letters)

SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

| Section/item | Item No | Description | Addressed on page number |
|---|---|---|---|
| **Administrative information** | | | |
| Title | 1 | Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym | 1 |
| Trial registration | 2a | Trial identifier and registry name. If not yet registered, name of intended registry | 2, 6 |
| | 2b | All items from the World Health Organization Trial Registration Data Set | 2 |
| Protocol version | 3 | Date and version identifier | 2 |
| Funding | 4 | Sources and types of financial, material, and other support | 5, 14 |
| Roles and responsibilities | 5a | Names, affiliations, and roles of protocol contributors | 1,14, |
| | 5b | Name and contact information for the trial sponsor | 1 |
| | 5c | Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities | 6 |
| | 5d | Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) | 6 |

| | | | |
|---|---|---|---|
| **Introduction** | | | |
| Background and rationale | 6a | Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention | 4, 5, 6 |
| | 6b | Explanation for choice of comparators | 6 |
| Objectives | 7 | Specific objectives or hypotheses | 9, 10 |
| Trial design | 8 | Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) | 6 |
| **Methods: Participants, interventions, and outcomes** | | | |
| Study setting | 9 | Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained | 6 |
| Eligibility criteria | 10 | Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) | 6, 7 |
| Interventions | 11a | Interventions for each group with sufficient detail to allow replication, including how and when they will be administered | 7,8,9 |
| | 11b | Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) | 8 |
| | 11c | Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) | 6 |
| | 11d | Relevant concomitant care and interventions that are permitted or prohibited during the trial | 7, 8 |
| Outcomes | 12 | Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended | 9, 10 |
| Participant timeline | 13 | Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) | 11 |

| | | | |
|---|---|---|---|
| Sample size | 14 | Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations | 11 |
| Recruitment | 15 | Strategies for achieving adequate participant enrolment to reach target sample size | 11 |
| **Methods: Assignment of interventions (for controlled trials)** | | | |
| Allocation: | | | |
| Sequence generation | 16a | Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions | 6,7 |
| Allocation concealment mechanism | 16b | Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned | 6,7 |
| Implementation | 16c | Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions | 7,8 |
| Blinding (masking) | 17a | Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how | 6 |
| | 17b | If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial | - |
| **Methods: Data collection, management, and analysis** | | | |
| Data collection methods | 18a | Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol | 9, 10 |
| | 18b | Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols | 7 |

| | | | |
|---|---|---|---|
| Data management | 19 | Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol | 12 |
| Statistical methods | 20a | Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol | 11, 12 |
| | 20b | Methods for any additional analyses (eg, subgroup and adjusted analyses) | 12 |
| | 20c | Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) | 12 |
| **Methods: Monitoring** | | | |
| Data monitoring | 21a | Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed | 13 |
| | 21b | Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial | 12 |
| Harms | 22 | Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct | 9,10 |
| Auditing | 23 | Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor | 13 |
| **Ethics and dissemination** | | | |
| Research ethics approval | 24 | Plans for seeking research ethics committee/institutional review board (REC/IRB) approval | 13 |
| Protocol amendments | 25 | Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) | 2 |

| | | | |
|---|---|---|---|
| Consent or assent | 26a | Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) | 6 |
| | 26b | Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable | - |
| Confidentiality | 27 | How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial | 12 |
| Declaration of interests | 28 | Financial and other competing interests for principal investigators for the overall trial and each study site | 14 |
| Access to data | 29 | Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators | 12 |
| Ancillary and post-trial care | 30 | Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation | 13 |
| Dissemination policy | 31a | Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions | 13 |
| | 31b | Authorship eligibility guidelines and any intended use of professional writers | not applicable |
| | 31c | Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code | not applicable |
| **Appendices** | | | |
| Informed consent materials | 32 | Model consent form and other related documentation given to participants and authorised surrogates | 15 |
| Biological specimens | 33 | Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable | 15 |

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

# *PatientInneninformation[1] und Einwilligungserklärung zur Teilnahme an der klinischen Prüfung*

## *Obsidian® - ASG Autologe plättchenreiche Fibrinmatrix zur Vorbeugung einer postoperativen Pankreasfistel nach Pankreasresektion – Eine Machbarkeitsstudie*

Sehr geehrte Patientin, sehr geehrter Patient!

Wir laden Sie ein an der oben genannten klinischen Prüfung teilzunehmen. Die Aufklärung darüber erfolgt in einem ausführlichen ärztlichen Gespräch.

**Ihre Teilnahme an dieser klinischen Prüfung erfolgt freiwillig. Sie können jederzeit ohne Angabe von Gründen aus der Studie ausscheiden. Die Ablehnung der Teilnahme oder ein vorzeitiges Ausscheiden aus dieser Studie hat keine nachteiligen Folgen für Ihre medizinische Betreuung.**

Klinische Prüfungen sind notwendig, um verlässliche neue medizinische Forschungsergebnisse zu gewinnen. Unverzichtbare Voraussetzung für die Durchführung einer klinischen Prüfung ist jedoch, dass Sie Ihr Einverständnis zur Teilnahme an dieser klinischen Prüfung schriftlich erklären. Bitte lesen Sie den folgenden Text als Ergänzung zum Informationsgespräch mit Ihrem Prüfarzt sorgfältig durch und zögern Sie nicht Fragen zu stellen.

Bitte unterschreiben Sie die Einwilligungserklärung nur

- wenn Sie Art und Ablauf der klinischen Prüfung vollständig verstanden haben,
- wenn Sie bereit sind, der Teilnahme zuzustimmen und
- wenn Sie sich über Ihre Rechte als Teilnehmer an dieser klinischen Prüfung im Klaren sind.

Zu dieser klinischen Prüfung, sowie zur Patienteninformation und Einwilligungserklärung wurde von der zuständigen Ethikkommission eine befürwortende Stellungnahme abgegeben.

# 1. Was ist der Zweck der klinischen Prüfung?

Der Zweck dieser klinischen Prüfung ist die Überprüfung der Machbarkeit einer neuartigen Methode zur Vermeidung von Komplikationen nach Ihrer Operation. Sie werden in der Universitätsklinik für Allgemeinchirurgie (Klinische Abteilung für Viszeralchirurgie) der Medizinischen Universität Wien auf Grund einer Erkrankung der Bauchspeicheldrüse (Pankreas) aufgenommen, die durch eine Operation demnächst werden in der Universitätsklinik für Allgemeinchirurgie (Klinische Abteilung für Viszeralchirurgie) der Medizinischen Universität Wien auf behandelt werden soll. Ziel dieser Operation ist, den erkrankten Teil Ihrer Bauchspeicheldrüse zu entfernen. Im Rahmen dieser Operation muss die Bauchspeicheldrüse etwa in der Mitte durchtrennt werden. Ziel ist es, einen Teil der Drüse zu erhalten. Im Verlauf kommt es nach der Operation an der

[1] Wegen der besseren Lesbarkeit wird im weiteren Text zum Teil auf die gleichzeitige Verwendung weiblicher und männlicher Personenbegriffe verzichtet. Gemeint und angesprochen sind – sofern zutreffend – immer beide Geschlechter.

Stelle der Durchtrennung der Bauchspeicheldrüse häufig zu einer Undichtigkeit, sodass Bauchspeicheldrüsensaft in die Bauchhöhle austritt. Dies wird „Pankreasfistel“ genannt. Dies stellt auch gleichzeitig die häufigste Komplikation der Operation dar und erfordert eine – meist länger (evtl. mehrere Wochen) dauernde – Ableitung dieser Flüssigkeit nach außen. Hierzu ist oft auch die Einlage einer zusätzlichen Drainage von außen im Rahmen einer Röntgenuntersuchung (Computertomographie) erforderlich. Selten können auch schwerwiegendere Probleme (Blutungen, Infektionen) durch die Pankreasfistel verursacht werden. Ein wichtiges Ziel ist daher, das Auftreten einer solchen Pankreasfistel zu verhindern, was durch chirurgische Maßnahmen bei der Operation jedoch trotz größter Sorgfalt bei jedem vierten Patienten nicht gelingt.

Wir wollen Sie daher einladen, an einer Studie teilzunehmen, mit der wir versuchen möchten, das Auftreten einer Pankreasfistel auf einem völlig neuartigen Weg zu verhindern. Es gibt die Möglichkeit, aus körpereigenem Blut eine Flüssigkeit herzustellen, welche während der Operation auf die Schnittstelle der Bauchspeicheldrüse aufgebracht wird und die Heilung und Dichtigkeit der Schnittstelle unterstützen soll. Diese Flüssigkeit wurde bereits erfolgreich bei Operationen am Darm angewandt. Bislang gibt es keine Untersuchungen zum Einsatz bei Bauchspeicheldrüsenoperationen. Wir nehmen an, dass sich durch die beschriebene Maßnahme die Häufigkeit und Schwere einer Pankreasfistel deutlich senken lässt und möchten zunächst die Machbarkeit der Verabreichung in einer klinischen Studie untersuchen.

## 2. Welche anderen Behandlungsmöglichkeiten gibt es?

Zur Behandlung Ihrer Erkrankung stehen **stattdessen auch** die folgenden Möglichkeiten zur Verfügung: wenn Sie an der Studie nicht teilnehmen möchten, findet die Operation ohne Anwendung der zusätzlichen Methode statt.

## 3. Wie läuft die klinische Prüfung ab?

Diese klinische Prüfung wird an der Klinik für Viszeralchirurgie durchgeführt, und es werden insgesamt ungefähr 25 Personen daran teilnehmen.

Vor Aufnahme in diese klinische Prüfung wird die Vorgeschichte Ihrer Krankheit erhoben, und Sie werden einer umfassenden ärztlichen Untersuchung unterzogen.

Ihre Teilnahme an dieser klinischen Prüfung wird voraussichtlich 12 Wochen dauern.

Eine Reihe von Untersuchungen und Eingriffen werden im Zuge Ihrer Behandlung durchgeführt, gleichgültig, ob Sie nun an dieser klinischen Prüfung teilnehmen oder nicht. Diese werden von Ihrem Prüfarzt im Rahmen des üblichen ärztlichen Aufklärungsgespräches mit Ihnen besprochen.

Folgende Maßnahmen werden ausschließlich aus Studiengründen durchgeführt:

Während dieser klinischen Prüfung werden Ihnen am Tag der Operation 120ml Blut abgenommen (dies entspricht etwa 8 Esslöffel). Mit diesem Blut wird dann die Flüssigkeit hergestellt, die bei Ihrer Operation zur Abdichtung der Schnittstelle der Bauchspeicheldrüse verwendet werden soll. Sie werden nach der Operation regelmäßig von Studienärzten besucht, damit wir Ihren Verlauf beobachten können. Nachdem Sie nach Hause entlassen werden, würden wir Sie am 30. und 90. Tag nach der Operation nochmals einbestellen bzw. telefonisch kontaktieren. Insgesamt sind 7 Studienbesuche angedacht, wobei die ersten 5 in jedem Fall stattfinden, während Sie ohnehin im Krankenhaus sind. Weitere Maßnahmen sind nicht studienspezifisch, sondern würden auch ohne Teilnahme an der Operation durchgeführt werden.

## 4. Was ist „Obsidian® - ASG Autologe plättchenreiche Fibrinmatrix“?

Obsidian®-ASG Autologe plättchenreiche Fibrinmatrix ist ein Medizinprodukt, welches bereits zugelassen ist für die Anwendung bei Operationen. Dieses Medizinprodukt wird gegenwärtig insbesondere bei der Behandlung von Darmerkrankungen verwendet. Es wurde bisher bei über 200 Patienten angewendet.

## 5. Worin liegt der Nutzen einer Teilnahme an der Klinischen Prüfung?

Mit der Anwendung von Obsidian®-ASG Autologe plättchenreiche Fibrinmatrix kann möglicherweise der Verlauf Ihrer Operation verbessert werden, indem Komplikationen gänzlich verhindert oder zumindest deren Schwergrad deutlich reduziert werden können. Es ist jedoch auch möglich, dass Sie durch Ihre Teilnahme an dieser klinischen Prüfung keinen direkten Nutzen für Ihre Gesundheit ziehen. Es ist jedoch ein Erkenntnisgewinn in der Wissenschaft und Nutzen für die zukünftige Behandlung von Patient:innen möglich.

## 6. Gibt es Risiken, Beschwerden und Begleiterscheinungen?

Die Behandlung mit Obsidian®-ASG Autologe plättchenreiche Fibrinmatrix kann zu Nebenwirkungen oder Beschwerden führen. Die bislang beobachteten Nebenwirkungen und Beschwerden umfassen Nachwirkungen der Blutabnahme wie Schmerzen im Bereich der Einstichstelle oder einem Bluterguss. Dies tritt häufig auf (bei mehr als der Hälfte der Patient:innen), heilt aber in aller Regel folgenlos und rasch ab. Sehr selten (bei 5 von 100 Patient:innen) kann bei der Blutabnahme auch ein kleiner Nerv verletzt werden. Es können sehr selten (bei 5 von 100 Patient:innen) allergische Reaktionen auf Inhaltsstoffe des Produktes auftreten. Wenn eine dementsprechende Allergie bekannt ist, dürfen Sie nicht an der Studie teilnehmen. Wie mit jeder neuen Substanz können auch bei der Anwendung von Obsidian®-ASG Autologe plättchenreiche Fibrinmatrix neue, bisher unbekannte Nebenwirkungen auftreten.

## 7. Zusätzliche Einnahme von Arzneimitteln?

Aufgrund der Teilnahme an der Studie ist keine Änderung Ihrer Medikation erforderlich.

## 8. Hat die Teilnahme an der klinischen Prüfung sonstige Auswirkungen auf die Lebensführung und welche Verpflichtungen ergeben sich daraus?

Nein.

## 9. Was ist zu tun beim Auftreten von Symptomen, Begleiterscheinungen und/oder Verletzungen?

Sollten im Verlauf der klinischen Prüfung irgendwelche Symptome, Begleiterscheinungen oder Verletzungen auftreten, müssen Sie diese Ihrem Prüfarzt mitteilen, bei schwerwiegenden Begleiterscheinungen umgehend, ggf. telefonisch (Telefonnummern, etc. siehe unten).

# 10. Versicherung

Als Teilnehmer an dieser klinischen Prüfung besteht für Sie der gesetzlich vorgeschriebene verschuldensunabhängige Versicherungsschutz (Personenschadenversicherung gemäß § 20 Medizinproduktegesetz, der alle Schäden abdeckt, die an Ihrem Leben oder Ihrer Gesundheit durch die an Ihnen durchgeführten Maßnahmen der klinischen Prüfung verursacht werden können, mit Ausnahme von Schäden auf Grund von Veränderungen des Erbmaterials in Zellen der Keimbahn.

Die Versicherung wurde für Sie bei der Zürich Versicherungs-Aktiengesellschaft im Rahmen einer Rahmenversicherung der Medizinischen Universität Wien für klinische Studien abgeschlossen (Polizze-Nr. 07229622-2).

Auf Wunsch können Sie in die Versicherungsunterlagen Einsicht nehmen.

Im Schadensfall können Sie sich direkt an den Versicherer wenden und Ihre Ansprüche selbständig geltend machen. Für den Versicherungsvertrag ist österreichisches Recht anwendbar, die Versicherungsansprüche sind in Österreich einklagbar.

Zur Unterstützung können Sie sich auch an die Patientenanwaltschaft, Patientenvertretung oder Patientenombudsschaft wenden.

Um den Versicherungsschutz nicht zu gefährden

- dürfen Sie sich während der Dauer der klinischen Prüfung einer anderen medizinischen Behandlung nur im Einvernehmen mit Ihrem behandelnden Prüfarzt unterziehen **(ausgenommen davon sind Notfälle).** Dies gilt auch für die zusätzliche Einnahme von Medikamenten oder die Teilnahme an einer anderen Studie.
- müssen Sie dem behandelnden Prüfarzt - oder der oben genannten Versicherungsgesellschaft - eine Gesundheitsschädigung, die als Folge der klinischen Prüfung eingetreten sein könnte, unverzüglich mitteilen.
- müssen Sie alles Zumutbare tun um Ursache, Hergang und Folgen des Versicherungsfalles aufzuklären und den entstandenen Schaden gering zu halten. Dazu gehört ggf. auch, dass Sie Ihre behandelnden Ärzte ermächtigen, vom Versicherer geforderte Auskünfte zu erteilen.

# 11. Informationen für gebärfähige Frauen – Schwangerschaftstest

Schwangere und stillende Frauen dürfen an dieser klinischen Prüfung NICHT teilnehmen.

Als gebärfähige Frau dürfen Sie an der klinischen Prüfung nur teilnehmen,

- wenn ein Arzt vor der klinischen Prüfung das Nichtvorliegen einer Schwangerschaft (Schwangerschaftstest) feststellt.
- wenn Sie sich verpflichten während der Dauer eine zuverlässige Art der Empfängnisverhütung (Pille, Spirale) zu praktizieren.

Sollten Sie dennoch während der klinischen Prüfung schwanger werden oder den Verdacht haben, dass Sie schwanger geworden sind, informieren Sie bitte umgehend Ihren Prüfarzt. Es wird dann umgehend Kontakt mit der Gynäkologie aufgenommen.

# 12. Wann wird die klinische Prüfung vorzeitig beendet?

Sie können jederzeit auch ohne Angabe von Gründen, Ihre Teilnahmebereitschaft widerrufen und aus der klinischen Prüfung ausscheiden ohne dass Ihnen dadurch irgendwelche Nachteile für Ihre weitere medizinische Betreuung entstehen.

Ihr Prüfarzt wird Sie über alle neuen Erkenntnisse, die in Bezug auf diese klinische Prüfung bekannt werden, und für Sie wesentlich werden könnten, umgehend informieren. Auf dieser Basis können Sie dann Ihre Entscheidung zur **weiteren** Teilnahme an dieser klinischen Prüfung neu überdenken.

Es ist aber auch möglich, dass Ihr Prüfarzt (oder gegebenenfalls der Auftraggeber dieser klinischen Prüfung) entscheidet, Ihre Teilnahme an der klinischen Prüfung vorzeitig zu beenden, ohne vorher Ihr Einverständnis einzuholen. Die Gründe hierfür können sein:

a) Sie können den Erfordernissen der Klinischen Prüfung nicht entsprechen;

b) Ihr Prüfarzt hat den Eindruck, dass eine weitere Teilnahme an der klinischen Prüfung nicht in Ihrem Interesse ist;

c) der Auftraggeber trifft die Entscheidung, die gesamte klinische Prüfung abzubrechen, oder lediglich Ihre Teilnahme vorzeitig zu beenden.

Sofern Sie sich dazu entschließen, vorzeitig aus der klinischen Prüfung auszuscheiden, oder Ihre Teilnahme aus einem der oben genannten Gründe vorzeitig beendet wird, ist es für Ihre eigene Sicherheit wichtig, dass Sie sich einer normalen Kontrolluntersuchung unterziehen. Diese besteht meistens aus einer körperlichen Untersuchung sowie aus Laboruntersuchungen.

# 13. Datenschutz

Im Rahmen dieser klinischen Prüfung werden Daten über Sie erhoben und verarbeitet. Es ist grundsätzlich zu unterscheiden zwischen

1) jenen personenbezogenen Daten, anhand derer eine Person direkt identifizierbar ist (z.B. Name, Geburtsdatum, Adresse, Sozialversicherungsnummer, Bildaufnahmen...),
2) pseudonymisierten personenbezogenen Daten, das sind Daten, bei denen alle Informationen, die direkte Rückschlüsse auf die konkrete Person zulassen, entweder entfernt, durch einen Code (z. B. eine Zahl) ersetzt oder (z.B. im Fall von Bildaufnahmen) unkenntlich gemacht werden. Es kann jedoch trotz Einhaltung dieser Maßnahmen nicht vollkommen ausgeschlossen werden, dass es unzulässigerweise zu einer Re-Identifizierung kommt.
3) anonymisierten Daten, bei denen eine Rückführung auf die konkrete Person ausgeschlossen werden kann.

Zugang zu den Daten, anhand derer Sie direkt identifizierbar sind (siehe Punkt 1), haben der Prüfarzt und andere Mitarbeiter des Prüfzentrums, die an der klinischen Prüfung oder Ihrer medizinischen Versorgung mitwirken. Zusätzlich können autorisierte und zur Verschwiegenheit verpflichtete Beauftragte des Sponsors, der Medizinischen Universität Wien, sowie Beauftragte von in- und/ oder ausländischen Gesundheitsbehörden und jeweils zuständige Ethikkommissionen in diese Daten Einsicht nehmen, soweit dies für die Überprüfung der ordnungsgemäßen Durchführung der klinischen Prüfung notwendig ist. Sämtliche Personen, die Zugang zu diesen Daten erhalten, unterliegen im Umgang mit den Daten den jeweils geltenden nationalen Datenschutzbestimmungen und/oder der EU-Datenschutz-Grundverordnung (DSGVO).

Der Code, der eine Zuordnung der pseudonymisierten Daten zu Ihrer Person ermöglicht, wird nur an Ihrem Prüfzentrum aufbewahrt.

Eine Weitergabe der Daten erfolgt nur in pseudonymisierter oder anonymisierter Form.

Für etwaige Veröffentlichungen werden nur die pseudonymisierten oder anonymisierten Daten verwendet.

Im Rahmen dieser klinischen Prüfung ist keine Weitergabe von Daten in Länder außerhalb der EU (Drittland) vorgesehen.

Ihre Einwilligung bildet die Rechtsgrundlage für die Verarbeitung Ihrer personenbezogenen Daten. Sie können die Einwilligung zur Erhebung und Verarbeitung Ihrer Daten jederzeit ohne Begründung widerrufen. Nach Ihrem Widerruf werden

keine weiteren Daten mehr über Sie erhoben. Die bis zum Widerruf erhobenen Daten können allerdings weiter im Rahmen dieser klinischen Prüfung verarbeitet werden.

Nach der DSGVO stehen Ihnen grundsätzlich die Rechte auf Auskunft, Berichtigung, Löschung, Einschränkung der Verarbeitung, Datenübertragbarkeit und Widerspruch zu, soweit dies die Ziele der klinischen Prüfung nicht unmöglich macht oder ernsthaft beeinträchtigt und soweit dem nicht andere gesetzliche Vorschriften widersprechen.

Das gemäß DSGVO vorgesehene Recht auf Löschung Ihrer im Rahmen dieser klinischen Prüfung verarbeiteten Daten steht Ihnen aufgrund von Regelungen nach dem Arzneimittelgesetz und Medizinproduktegesetz nicht zu. Zusätzlich ist bei einer klinischen Prüfung nach dem Arzneimittelgesetz das Recht auf Datenübertragbarkeit außer Kraft gesetzt.

Die voraussichtliche Dauer der klinischen Prüfung ist 12 Monate. Die Dauer der Speicherung Ihrer Daten über das Ende oder den Abbruch der klinischen Prüfung hinaus ist durch Rechtsvorschriften geregelt.

Falls Sie Fragen zum Umgang mit Ihren Daten in dieser klinischen Prüfung haben, wenden Sie sich zunächst an Ihren Prüfarzt. Dieser kann Ihr Anliegen ggf. an die Personen, die für den Datenschutz verantwortlich sind, weiterleiten.

Kontaktdaten der Datenschutzbeauftragten der an dieser klinischen Prüfung beteiligten Institutionen:

Datenschutzbeauftragte/r der MedUni Wien: datenschutz@meduniwien.ac.at

Datenschutzverantwortliche/r des AKH: datenschutz@akhwien.at

Sie haben das Recht, bei der österreichischen Datenschutzbehörde eine Beschwerde über den Umgang mit Ihren Daten einzubringen (www.dsb.gv.at; E-Mail: dsb@dsb.gv.at ).

# 14. Entstehen für die Teilnehmer Kosten? Gibt es einen Kostenersatz oder eine Vergütung?

Durch Ihre Teilnahme an dieser klinischen Prüfung entstehen für Sie keine zusätzlichen Kosten mit Ausnahme der Fahrtkosten für die Verlaufskontrolle 30 Tage nach der Operation. Allerdings ist zu diesem Zeitpunkt auch unabhängig von der Teilnahme an der Studie eine Kontrolle empfohlen. Es ist keine Vergütung vorgesehen.

# 15. Möglichkeit zur Diskussion weiterer Fragen

Für weitere Fragen im Zusammenhang mit dieser klinischen Prüfung stehen Ihnen Ihr Prüfarzt und seine Mitarbeiter gern zur Verfügung. Auch Fragen, die Ihre Rechte als Patient und Teilnehmer an dieser klinischen Prüfung betreffen, werden Ihnen gerne beantwortet.

I. Name der Kontaktperson: Priv.-Doz. Dr. Ulla Klaiber

Ständig erreichbar unter: .Mobil: +43 67764384772

II. Name der Kontaktperson: Dr. Charlotte Gustorff

Ständig erreichbar unter: Mobil: +43 6703501743

# 19. Einwilligungserklärung

Name des Patienten:

Geb.Datum:

Ich erkläre mich bereit, an der klinischen Prüfung Obsidian zur Reduktion der Pankreasfistel teilzunehmen. Ich bin darüber aufgeklärt worden, dass ich die Teilnahme ohne nachteilige Folgen, insbesondere für meine medizinische Betreuung, ablehnen kann.

Ich bin von Frau/Herrn (Dr.med.) .....ausführlich und verständlich über die klinische Prüfung, mögliche Belastungen und Risiken, sowie über Wesen, Bedeutung und Tragweite der klinischen Prüfung, die bestehende Versicherung sowie die sich für mich daraus ergebenden Anforderungen aufgeklärt worden. Ich habe darüber hinaus den Text dieser Patientenaufklärung und Einwilligungserklärung, die insgesamt 7 Seiten umfasst, gelesen. Aufgetretene Fragen wurden mir vom Prüfarzt verständlich und zufriedenstellend beantwortet. Ich hatte ausreichend Zeit, mich zu entscheiden. Ich habe zurzeit keine weiteren Fragen mehr.

Ich werde den ärztlichen Anordnungen, die für die Durchführung der klinischen Prüfung erforderlich sind, Folge leisten, behalte mir jedoch das Recht vor, meine freiwillige Mitwirkung jederzeit zu beenden, ohne dass mir daraus Nachteile, insbesondere für meine medizinische Betreuung, entstehen.

Ich stimme ausdrücklich zu, dass meine im Rahmen dieser klinischen Prüfung erhobenen Daten wie im Abschnitt „Datenschutz“ dieses Dokuments beschrieben verarbeitet werden.

Eine Kopie dieser Patienteninformation und Einwilligungserklärung habe ich erhalten. Das Original verbleibt beim Prüfarzt.

.....
(Datum und Unterschrift des Patienten)

.....
(Datum, Name und Unterschrift des verantwortlichen Prüfarztes)

(Der Patient erhält eine unterschriebene Kopie der Patienteninformation und Einwilligungserklärung, das Original verbleibt im Studienordner des Prüfarztes.)

BMJ Open

# Obsidian ASG Autologous Platelet-Rich Fibrin Matrix for the prevention of postoperative pancreatic fistula following pancreatic resection: Study protocol for a feasibility trial at the Medical University of Vienna



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# Obsidian ASG Autologous Platelet-Rich Fibrin Matrix for the prevention of postoperative pancreatic fistula following pancreatic resection: Study protocol for a feasibility trial at the Medical University of Vienna

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## Abstract

**Introduction:** Postoperative pancreatic fistula (POPF) is the most frequent complication after partial pancreatectomy which is by definition associated with clinical consequences requiring changes in postoperative management. Despite numerous scientific efforts, effective procedures to prevent POPF are lacking. Obsidian® ASG Autologous Platelet-Rich Fibrin Matrix has been effectively applied to prevent anastomotic leakage following colorectal surgery. This study is the first to investigate the feasibility of using the sealant in pancreatic surgery.

**Methods and analysis:** Twenty-five consecutive patients scheduled for elective formal partial pancreatectomy due to any underlying disease fulfilling the eligibility criteria will be included. Obsidian® ASG sealant prepared out of 120mL of each patient's whole blood will be applicated to the pancreatic stump or the pancreatic anastomosis respectively. The primary endpoint is the feasibility of the procedure, e.g. proportion of patients undergoing successful trial intervention. Secondary endpoints comprise safety and surgical outcome parameters including rate and severity of POPF as well as further pancreas-specific complications as defined by the International Study Group of Pancreatic Surgery (ISGPS) during 90 days after surgery. Patients will be matched with a historic collective in a 1:2 ratio to gain first data on efficacy.

**Ethics and dissemination:** This trial and the associated study protocol (Version 1.1.1, date 26/03/2024) were approved by the institution's Ethics Committee (reference number 2191/2023). All trial procedures are performed in accordance with the ICH harmonized tripartite guideline on Good Clinical Practice (ICH-GCP) and the ethical principles of the Declaration of Helsinki. After completion of the study, results will be published in due course.

**Registration details:** The trial was registered in the German Clinical Trials Register on 06.05.2024 (DRKS-ID: DRKS00034052).

**Strengths and limitations of this trial**

- One of the strengths of this trial is the careful monitoring of adverse events to gain safety besides feasibility data.
- Valid results on efficacy of the trial intervention will not be obtained due to the feasibility study design with a small number of interventions.
- The open-label, non-randomized trial design is prone to several sources of bias, especially selection, performance and detection bias.

## Introduction

### *Rationale of the trial*

Formal partial pancreatectomy, i.e. distal pancreatectomy (DP) or partial pancreatoduodenectomy (PD), is the treatment of choice for several malignant and pre-malignant pancreatic diseases including pancreatic cancer and its precursor lesions as well as neuroendocrine tumours[1, 2]. With the centralization of pancreatic surgery in specialized institutions and improvements in perioperative management, procedures have become safe with mortality rates below two percent and low failure-to-rescue rates[3, 4]. However, postoperative morbidity still occurs in 65% of patients and therewith remains unsatisfactorily high[3]. The most frequent and relevant complication is postoperative pancreatic fistula (POPF) resulting from healing disorders of the pancreatic anastomosis after PD or leakage from the pancreatic stump after DP[5]. POPF affects the patient's postoperative course by definition as it may cause intra-abdominal infection or arrosional bleeding requiring changes in clinical management such as anti-infective treatments, re-interventions and re-operations as well as intensive care unit stay and prolongation of total hospital stay[6]. The rates of clinically relevant POPF, i.e. POPF grades B/C as defined by the International Study Group of Pancreatic Surgery (ISGPS), reported in literature reach up to 27% after DP[7] and 22% after PD[8] (even 38% after robotic PD[9]), illustrating the unsolved problem of POPF. Prevention of POPF is particularly important in patients

undergoing extended pancreatic resection including arterial reconstruction, since these patients are at high risk for life-threatening post-pancreatectomy haemorrhage (PPH) caused by intra-abdominal enzyme-rich fluid collections[10, 11].

***Preliminary data***

Numerous previous studies provided evidence that none of the existing surgical techniques and perioperative measures are effective in the prevention of POPF[12-15]. A recent Cochrane review summarizes the available evidence on fibrin sealant use to prevent POPF after PD and DP showing inconclusive results and uncertain evidence on this topic[14]. Further research is therefore mandatory, and the evaluation of new approaches is required to solve the hitherto intractable problem of POPF. The thrombocyte enriched, completely absorbable Obsidian ASG matrix is developed to improve tissue regeneration and healing of gastrointestinal anastomoses by sustained release of an up to 8 times multiplied concentration of non-activated platelets and continuously release of growth factors over a period of 5 to 7 days after surgery[16]. Hence, the application of Obsidian® ASG may accelerate tissue proliferation, and the anti-inflammatory and antimicrobial platelet properties may offer control of potential contamination which may be especially important after PD. Obsidian ASG has already been used to prevent postoperative anastomotic leakages in colorectal surgery and its application has been shown to be safe, feasible and related to low rates of anastomotic leakages[17, 18]. The application has not yet been demonstrated to be superior to standard therapy. This may be due to the low rates of anastomotic leakage in colorectal surgery and the small number of cases in previous trials. This is the first study to assess the application in pancreatic surgery with the aim to prevent POPF following partial pancreatectomy.

## Methods and analysis

This clinical trial protocol is written according to the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) statement[19]. Adherence to these recommendations is documented in the SPIRIT checklist (see Additional file 1). The trial was registered with the Clinical Trials Register (DRKS00034052) before enrolment of the first patient. The trial is scheduled for completion in December 2025, with the results to be published in due course.

***Trial design and trial-supporting facilities***

This is an investigator-initiated, single-centre, open-label, phase II clinical trial with one intervention arm and an exploratory study design. There will be a 1:2 matching with patients from a historic collective on the basis of their main characteristics (age, procedures and histopathological findings) in order to receive two comparable study groups. The sponsor of the trial is the Medical University of Vienna, Austria. The sponsor had no role in the design of this study and will not have any role during its execution, analysis of the data, interpretation of the findings, or the decision to submit the results for publication. The coordinating investigator is the sponsor's representative and also the trial's statistician. The trial will be conducted in close cooperation with the Coordinating Centre for Clinical Trials, Medical University of Vienna, Austria, which is in charge of the trial monitoring, including initiation and close-out visits. The site of this trial is the Department of General Surgery, Division of Visceral Surgery, University of Vienna, Austria.

***Trial population***

Consecutive patients scheduled for elective, partial pancreatic resection, i.e. PD or DP, due to any underlying disease will be screened for eligibility and informed consent will be reached before inclusion of the patient. Inclusion criteria comprise ≥18 years of age, ability to understand character and individual consequences of the clinical trial, as well as written

informed consent. See Additional file 3 for the informed consent form. In case of withdrawal of informed consent patient data will be excluded from analysis. Patients with severe systemic disease that is a constant threat to life, classified as American Society of Anaesthesiologists' (ASA) score >3 and patients with known hypersensitivity to any component in the formulation of the investigational medical product will be excluded as will be patients with understanding or language problems and patients with inability to comply with the study and/or follow-up procedures. Pregnant and breast-feeding patients as well as patients with concurrent participation in another interventional clinical trial with interference with the trial outcome will also be excluded. For patients with childbearing potential, presence of preoperative negative urine or negative blood pregnancy test and adequate contraception until 14 days after trial intervention is therefore required.

### *Trial intervention and perioperative management*

#### *Preparation*

At the day of surgery, 120 mL of whole blood will be withdrawn from the individual patient. Then, the matrix will be prepared using 300 mg of tranexamic acid and processed through a fully automated Vivostat microprocessor-controlled system (Vivostat A/S, Alleroed, Denmark). The blood will be heated up to 36 °C and separated by centrifugation in the upper reservoir chamber of the processing unit. The resulting plasma will be combined with Batroxobin, leading to the polymerization of acid-soluble fibrin 1. This process will effectively remove excess fibrinogen and thrombocyte-depleted serum, leaving concentrated fibrin 1 and thrombocytes. To dissolve the available fibrin and create a stable clot matrix with high elasticity, tensile strength, and crack resistance, the fibrin concentrate will be mixed with sodium acetate buffer (pH 4). The resulting thrombocyte-enriched matrix will then be embedded in a fibrin scaffold.

### *Surgical procedures*

Surgical steps and techniques will be carried out according to the institutional standard procedures as open, laparoscopic or robotic partial pancreatectomies. After exclusion of distant tumor spread and after confirming local resectability, PD or DP will be performed depending on the localization of the disease. PD is usually performed open using an arterial or uncinate first approach and including the TRIANGLE procedure in patients with cancer. Reconstruction after PD is routinely performed with an omega loop and a double-layer end-to-side pancreatojejunostomy and an end-to-side hepaticojejunostomy, each with 5/0 or 6/0 monofilament atraumatic single sutures. An internal stent is neither recommended nor prohibited. During DP, transection and closure of the pancreas is routinely performed above the portomesenteric axis with any linear stapling device which is selected at the surgeon's discretion. In case of too thick tissue transection will be performed with a surgical scalpel followed by separate ligation of the pancreatic duct and suture of the entire pancreatic remnant. If indicated, additional resections may be performed depending on the individual patient`s intraoperative findings. Frozen section specimen will standardly be taken from the pancreatic and bile duct remnant. A ligamentum teres hepatis patch as additional covering of the pancreatic remnant is permitted but not recommended. Any other additional coverage, except for the investigational drug, is not allowed because there is no evidence and therefore it would not be the institution's standard.

### *Application of the investigational medicinal product*

At the end of surgery, 5-6 ml of Obsidian ASG sealant will be applicated to the pancreatic stump in DP or to the pancreatic anastomosis in PD. According to the surgical approach, application systems for open or minimal-invasive surgery will be used. After application of the

investigational medicinal product, at least one intra-abdominal drainage tube will be placed and left in place at least until postoperative day (POD) three after surgery. Perioperative administration of somatostatin analogues is permitted but not recommended. The administration must be documented in the Case report form (CRF; see Additional file 2).

### *Control group*

To serve as a basis for further planning of a randomized controlled trial regarding the secondary outcome parameters, the enrolled patients will be matched with a historic collective (age, procedures, histopathological findings) extracted from the pancreatic surgery database of the Department of Visceral Surgery, Medical University of Vienna in a 1:2 ratio.

### *Risk of bias*

The open-label trial design with a single prospective intervention arm and a matched historical control group bears considerable sources of bias, especially selection, performance and detection bias. However, since this is the first trial to use the investigational medicinal product in pancreatic surgery, a small and non-randomized pilot trial focusing on safety and feasibility seems appropriate at this early stage of evaluation of a new surgical intervention[20]. Procedures will be standardized and the trial personnel will be informed and trained at the site initiation visit; hence performance bias will be reduced. In addition, adherence to the trial protocol will be controlled by regularly on-site monitoring.

## Outcome parameters

### *Assessment of feasibility*

Primary outcome is the feasibility of the trial intervention defined as proportion of patients undergoing successful trial intervention. The successful application of Obsidian intraoperatively to the pancreatic anastomosis or pancreatic stump will be considered a successful trial intervention.

***Assessment of safety***

Patients will be closely monitored for the occurrence of adverse events (AE) and serious adverse events (SAE). The incidence of all AE will be ascertained by the investigators using non-leading questions, noted as spontaneously reported by the patients to the medical staff or observed during any measurements on all study days. Only events that occurred after enrolment and during the follow-up will be collected. A SAE is defined as any AE occurring during the observation period that results in death, is life-threatening, requires or prolongs hospitalisation, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, is otherwise medically relevant and/or requires intervention to prevent any of these outcomes. All SAE must be reported to the Coordinating Centre for Clinical Trials, Medical University of Vienna, Austria within 24 hours after becoming known.

***Secondary outcome parameters***

The secondary outcome parameters comprise all relevant surgical complications, i.e. clinically relevant POPF[6], delayed gastric emptying[21], postpancreatectomy hemorrhage[22], lymphatic fistula[23], postpancreatectomy acute pancreatitis[24], intraabdominal fluid collection/abscess, wound infection, burst abdomen, perioperative sepsis[25], reinterventions and reoperations, 90-day mortality, length of intensive care unit and total hospital stay, as well as readmission to hospital. Postoperative complications will be graduated as proposed by the ISGPS and Clavien-Dindo[26] as applicable.

## Schedule of trial procedures and follow-up visits

As presented in Table 1, there will be seven trial visits from screening to the last follow-up at POD 90. Except the trial intervention on the day of surgery all procedures including assessment of laboratory parameters belong to the perioperative standard procedures after pancreatic resection. In patients with childbearing potential, a pregnancy test will be performed during the routine preoperative laboratory examinations.

| Visit | 1 Enrollment & Randomization | 2 Operation | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| | | | ---------- Follow-up---------- | | | | |
| Day related to index operation | | Day 0 | POD 3 | POD7 | POD14/Day of discharge | PDO 30 | 3 months post-OP |
| Type of visit | Outpatient | Inpatient | Inpatient | Inpatient | Inpatient | Outpatient | Phone * |
| Visit window | ±0 | ±0 | ±0 | ±0 | ±2 | ±2 | ±2 |
| Inclusion/exclusion criteria | X | | | | | | |
| Baseline/demographic data | X | | | | | | |
| Prior / concomitant diseases | X | | | | | | |
| Prior/concomitant medication | X | X | X | X | X | X | X |
| Trial intervention | | X | | | | | |
| Operative procedure | | X | | | | | |
| Laboratory parameters† | | X | X | X | | | |
| Pregnancy test¥¥ | X | | | | | | |
| Drainage amylase | | | X | (X) | (X) | (X) | (X) |
| Primary endpoint | | X | | | | | |
| Secondary endpoints | | | | | | | |
| Ae/SAE | X | X | X | X | X | X | X |

Table 1: POD: postoperative day; *In-hospital visit in case of ongoing hospital stay or readmission to hospital.; †Standard periinterventional/perioperative procedures. Documentation of serum values of amylase and/or lipase, bilirubin, hemoglobin, erythrocytes, leucocytes, thrombocytes, International Normalized Ratio (INR), creatinine clearance/glomerular filtration rate, C-reactive protein; ¥¥Females with childbearing potential only

## Statistical methods

### *Sample size calculation and timelines*

In this proof-of-concept trial, the focus is on the feasibility and safety of the procedure. Hence, no formal sample size calculation has been performed. We have chosen a number of patients, which is considered valid to obtain first data on feasibility and safety of the trial intervention. Twenty-five patients are planned to be enrolled in this trial. Considering drop-outs of 5 patients (due to inoperability in case of distant metastasis, local inoperability or in case of total pancreatectomy) the remaining 20 patients will be sufficient to evaluate feasibility. The trial preparation phase started in December 2023. The inclusion of the first patient is planned in May 2024. The duration of the clinical trial for each individual patient will be 3 months. The flow chart in Figure 1 illustrates the structure of the trial flow. Nowadays, our centre carries out at least 130 partial pancreatectomies per year. Thus, the time taken to recruit 25 patients out of 50 patients screened for eligibility is expected to be 5 months. Taking into account two months for preparation and another two months for analysis, the duration of the entire trial will be approximately 12 months.

### *Statistical analysis*

All analyses will be of descriptive character and will be performed with the software program SPSS. Quantitative variables will be presented as median and dispersion as interquartile range (IQR) or 95% confidence interval (CI). For comparison with the historical control group, the nonparametric Kruskal-Wallis test will be used to compare continuous parameters. For categorical parameters, absolute and relative frequencies will be calculated and compared using the $X^2$ or Fisher's exact test as appropriate. Mortality will be calculated using the Kaplan-Meier method. Missing data are expected to be rare, so no imputation will be performed. Two-sided

P values will be used and a difference will be considered statistically significant at P <0.05. Interim analyses are not planned.

**Data collection and data management**

The investigator or a designated representative must enter all protocol-required information in the CRF (see Additional file 2). The CRF should be completed as soon as possible after the information is collected, preferably on the same day when a trial participant is seen for an examination, treatment, or any other trial procedure. The reason for missing data should be provided. The investigator is responsible for ensuring that all sections of the CRF are completed correctly and that entries can be verified in accordance with the source data. In general, all entries in the CRF must be verifiable by source documents. In advance, exceptions to this rule can be defined by the sponsor. A detailed list will be provided in the Investigator Site File (ISF). Finally, there must be no data that are inconsistent between CRF and source documents. Completeness, validity and plausibility of data will be checked in time of data entry. If no further corrections are to be made in the database it will be closed and used for statistical analysis. Any reason for missing data should be documented. The investigator is responsible for completeness of data as well as the compliance with institutional data management regulations. The investigator will archive all trial data (source data and ISF, including patient identification list) according to Good Clinical Practice and to local law or regulations. All data shall be made available if requested by relevant authorities.

**Monitoring**

Monitoring will be done remotely and by a clinical monitor's personal visits as defined by the Coordinating Centre for Clinical Trials, Medical University of Vienna, Austria. During on-site visits, the monitor will review entries into the CRF on the basis of source documents.

Additionally, by remote monitoring and frequent communication, the monitor will ensure that the trial is conducted according to the protocol and regulatory requirements. Therefore, the investigator must allow the monitor to verify all essential documents and must provide support at all times to the monitor.

## Ethics and dissemination

This trial was approved by the institution's Ethics Committee (reference number 2191/2023) on 03.05.2024. Every patient participating in the study will be provided a personal injury insurance, as well as subsidiary medical liability and medical professional legal expenses insurance. All trial procedures are performed in accordance with the ICH harmonized tripartite guideline on Good Clinical Practice (ICH-GCP) and the ethical principles of the Declaration of Helsinki. Once the study has been completed, the results will be published in due course.

## Author's contributions

UK conceived the study, drafted the protocol and the manuscript.

CG was involved in the conception of the study, drafted the protocol and the manuscript.

CD was involved in the conception of the study and approved the final manuscript.

CSL conducted revisions and approved the final manuscript.

SR conducted revisions and approved the final manuscript.

KS conducted revisions and approved the final manuscript.

MS conducted revisions and approved the final manuscript.

OS was involved in the conception of the study, supervised revisions of the protocol and approved the final manuscript.

Guarantor is Oliver Strobel

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**Patient and Public involvement statement**

Neither patients nor the general public were involved in the design, conduct, reporting, or dissemination of our research.

**Competing interests statement**

All authors declare that they have no competing interests.

## Tables and figures

| | |
|---|---|
| **Table 1** | Study visits |
| **Figure 1** | Trial flow chart |

## Additional files

| | |
|---|---|
| **Additional file 1** | SPIRIT checklist |
| **Additional file 2** | Case Report Form |
| **Additional file 3** | Informed consent form |

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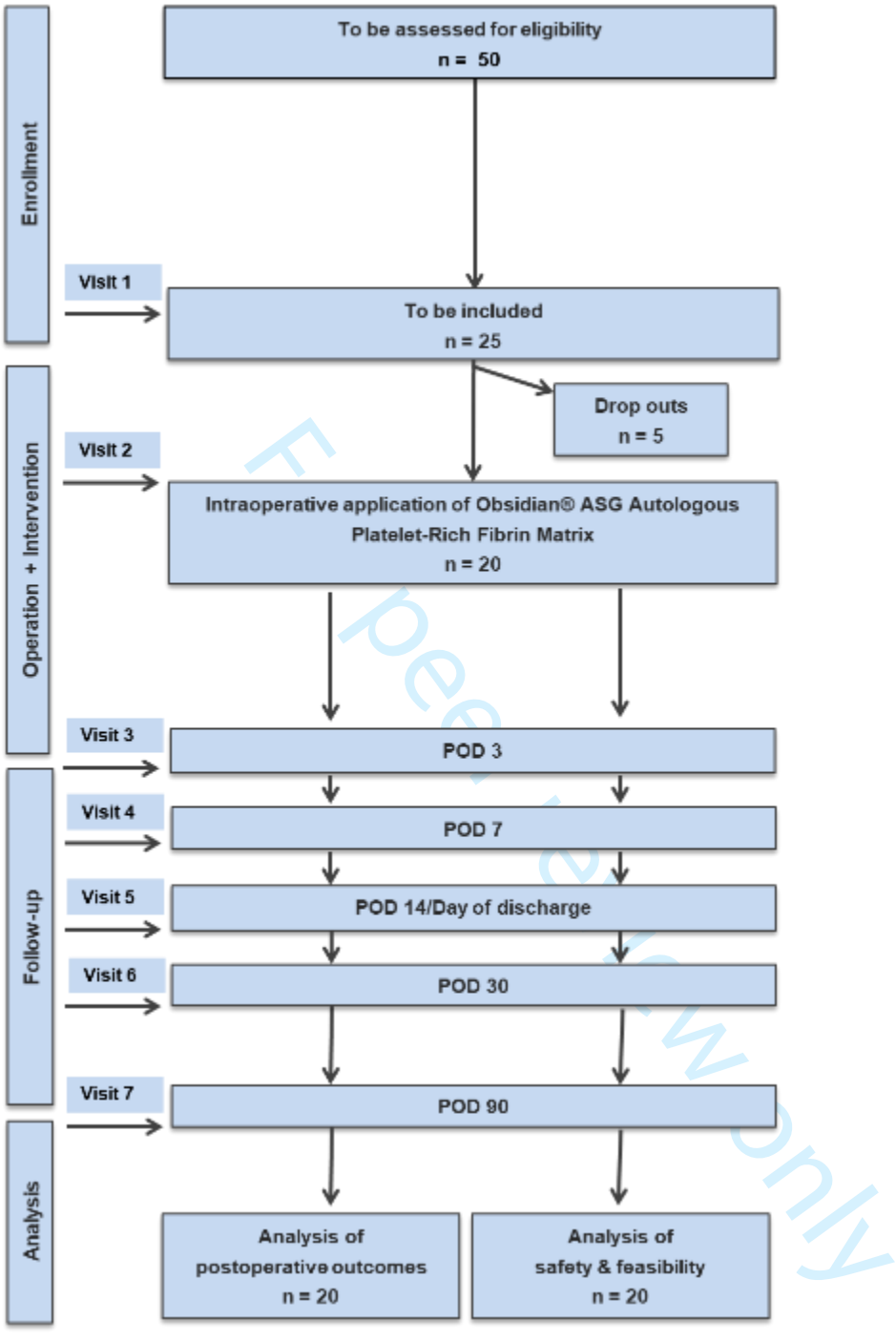
## Legends:

## Legend Figure 1: Trial flow

**Legend Table 1:** POD: postoperative day; *In-hospital visit in case of ongoing hospital stay or readmission to hospital.; †Standard periinterventional/perioperative procedures. Documentation of serum values of amylase and/or lipase, bilirubin, hemoglobin, erythrocytes, leucocytes, thrombocytes, International Normalized Ratio (INR), creatinine clearance/glomerular filtration rate, C-reactive protein; ¥¥Females with childbearing potential only



| Visit | 1 Enrollment & Randomization | 2 Operation | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| | | | | ----------Follow-up---------- | | | |
| Day related to index operation | | Day 0 | POD 3 | POD7 | POD14/Day of discharge | PDO 30 | 3 months post-OP |
| Type of visit | Outpatient | Inpatient | Inpatient | Inpatient | Inpatient | Outpatient | Phone* |
| Visit window | ±0 | ±0 | ±0 | ±0 | ±2 | ±2 | ±2 |
| Inclusion/exclusion criteria | X | | | | | | |
| Baseline/demographic data | X | | | | | | |
| Prior / concomitant diseases | X | | | | | | |
| Prior/concomitant medication | X | X | X | X | X | X | X |
| Trial intervention | | X | | | | | |
| Operative procedure | | X | | | | | |
| Laboratory parameters† | | X | X | X | | | |
| Pregnancy test¥¥ | X | | | | | | |
| Drainage amylase | | | X | (X) | (X) | (X) | (X) |
| Primary endpoint | | X | | | | | |
| Secondary endpoints | | | | | | | |
| Ae/SAE | X | X | X | X | X | X | X |

POD: postoperative day; *In-hospital visit in case of ongoing hospital stay or readmission to hospital.; †Standard periinterventional/perioperative procedures. Documentation of serum values of amylase and/or lipase, bilirubin, hemoglobin, erythrocytes, leucocytes, thrombocytes, International Normalized Ratio (INR), creatinine clearance/glomerular filtration rate, C-reactive protein; ¥¥Females with childbearing potential only

# Obsidian ASG Autologous Platelet-Rich Fibrin Matrix for the prevention of postoperative pancreatic fistula following pancreatic resection: study protocol for a feasibility trial

## CASE REPORT FORM

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# Obsidian-Pilottrial

**Visit 1: Screening/Enrolment**

Screening No.: _____ Year of birth: _____

Date of screening: ____ (dd/mm/yyyy)

| **Inclusion criteria** | **yes** | **no** |
|---|---|---|
| 1. Age ≥ 18 years | ○ | ○ |
| 2. Patient undergoing elective partial pancreatic resection for any reason | ○ | ○ |
| 3. Ability to understand character and individual consequences of the trial | ○ | ○ |
| 4. Written informed consent | ○ | ○ |
| 5. Date of written informed consent: | ○ | ○ |

| **Exclusion criteria** | **yes** | **no** |
|---|---|---|
| 1. ASA score > III | ○ | ○ |
| 2. Pregnancy or lactation | ○ | ○ |
| 3. Understanding or language problems | ○ | ○ |
| 4. Inability to comply with study and/or follow-up procedures | ○ | ○ |
| 5. Known hypersensitivity to any component of the formulation | ○ | ○ |
| 6. Concurrent participation in another interventional clinical trial | ○ | ○ |

**Demography**

Gender ○ female ○ male ○ divers

Age: _____ years

**Anamnesis**

Body height and weight: _____ cm _____ kg

Previous abdominal surgery

Previous radio-/chemotherapy within the last 6 months

Relevant comorbidities:

- Coronary heart disease☐
- Congestive heart failure NYHA I/II☐
- Chronic artrial fibrillation☐
- Chronic renal insufficiency☐
- Chronic obstructive pulmonary disease (COPD)☐
- Diabetes mellitus ☐
- Other:☐_____

ASA-classification: ☐ I (healthy patient)☐ II (mild systemic disease)
☐ III (severe systemic disease)

**Pancreas-specific anamnesis**

Indication for the planned surgical procedure

- Pancreatic carcinoma
- Cystic neoplasm
- Neuroendocrine tumor
- Other: _____

If preexisting diabetes mellitus, insulin dependent? Yes ☐ no ☐

Preexisting exocrine pancreatic insufficiency? Yes ☐ no ☐

o

# Obsidian-Pilottrial

**Visit 2: Surgery**

Screening No.: _____ Year of birth: _____

Date of surgery

Performed surgery

- DP☐ PD☐ other☐ _____

Approach

- Laparoscopic☐ robotic☐ open☐
- Conversion: no☐ yes☐, reason for conversion_____

Level of pancreatic transection

- above☐ left to portal vein☐ right to portal vein☐

Transsection technique:_____

Closure technique:_____

Anastomosis technique_____

Texture of pancreatic tissure:

- soft ☐ intermediate ☐ hard☐

Pancreatic ducts size: _____ (mm)

Additional resections: splenectomy☐ lymphadenectomy☐ others ☐ _____

Duration from skin incision to closure: _____ min

Intraoperative blood loss: _____ ml

Intraoperative blood transfusion: _____ml

Placement of abdominal drain: yes ☐ no ☐

Administration of somatostatin-analogues:

- during surgery: yes ☐ no ☐
- after surgery: yes ☐ no ☐

**Serious adverse events** (new events since last visit)

Were there any serious adverse events? Yes☐ no ☐

Were there any other intervention related side effects? Yes ☐ no ☐

If yes, please specify: _____

**Protocol violations**

Were there any protocol violations? Yes ☐ no ☐

If yes, please specify: _____

# Obsidian-Pilottrial

**Visit 3: POD 3**

Screening No.: _____ Year of birth: _____

Date of visit: _____ (dd/mm/yyyy)

**Assessment of postoperative pancreatic fistula**

Pancreatic amylase at POD3: _____ (U/L)

Lipase at POD3: _____ (U/L)

Classification of POPF: no POPF ☐ grade A ☐ grade B ☐ grade C ☐

**Complications** (new events since last visit)

Perioperative sepsis ☐

Postpancreatectomy acute pancreatitis ☐

- associated complications (e.g. bleeding or perforation) ☐ please, specifiy: _____

Delayed gastric emptying

Post-pancreatectomy hemorrhage: no PPH ☐ grade A ☐ grade B ☐ grade C ☐

Intraabdominal fluid collection ☐

Intraabdominal abscess ☐

Lymphatic fistula / chylus ascites ☐

Wound infection ☐

Burst abdomen ☐

Reinterventions / - operations ☐ _____

ICU stay ☐

Transfer to normal ward at ____. POD

**Diagnostics/interventions:** yes ☐ no ☐

CT-scan ☐

Interventional application of drainage ☐

Relaparotomy ☐, state the reason: _____

**Serious adverse events** (new events since last visit)

Were there any serious adverse events? Yes ☐ no ☐

Were there any other intervention related side effects? Yes ☐ no ☐

If yes, please specify: _____

**Protocol violations**

Were there any protocol violations? Yes ☐ no ☐

If yes, please specify: _____

# Obsidian-Pilottrial

**Visit 4: POD 7**

Screening No.: _____ Year of birth: _____

Date of visit: _____ (dd/mm/yyyy)

**Assessment of postoperative pancreatic fistula**

Pancreatic amylase at POD7: _____ (U/L)

Lipase at POD7: _____ (U/L)

Classification of POPF: no POPF ☐ grade A ☐ grade B ☐ grade C ☐

**Complications** (new events since last visit)

Perioperative sepsis ☐

Postpancreatectomy acute pancreatitis ☐

- associated complications (e.g. bleeding or perforation) ☐ please, specifiy: _____

Delayed gastric emptying

Post-pancreatectomy hemorrhage: no PPH ☐ grade A ☐ grade B ☐ grade C ☐

Intraabdominal fluid collection ☐

Intraabdominal abscess ☐

Lymphatic fistula / chylus ascites ☐

Wound infection ☐

Burst abdomen ☐

Reinterventions / - operations ☐ _____

ICU stay ☐

Transfer to normal ward at ____. POD

**Diagnostics/interventions:** yes ☐ no ☐

CT-scan ☐

Interventional application of drainage ☐

Relaparotomy ☐, state the reason: _____

**Serious adverse events** (new events since last visit)

Were there any serious adverse events? Yes ☐ no ☐

Were there any other intervention related side effects? Yes ☐ no ☐

If yes, please specify: _____

**Protocol violations**

Were there any protocol violations? Yes ☐ no ☐

If yes, please specify: _____

# Obsidian-Pilottrial

**Visit 5: POD 14/day of discharge**

Screening No.: _____ Year of birth: _____

Date of visit: _____ (dd/mm/yyyy)

**Assessment of postoperative pancreatic fistula**

Classification of POPF: no POPF ☐ grade A ☐ grade B ☐ grade C ☐

**Complications** (new events since last visit)

Perioperative sepsis ☐

Postpancreatectomy acute pancreatitis ☐

- associated complications (e.g. bleeding or perforation) ☐ please, specifiy: _____

Delayed gastric emptying

Post-pancreatectomy hemorrhage: no PPH ☐ grade A ☐ grade B ☐ grade C ☐

Intraabdominal fluid collection ☐

Intraabdominal abscess ☐

Lymphatic fistula / chylus ascites ☐

Wound infection ☐

Burst abdomen ☐

Reinterventions / - operations ☐ _____

ICU stay ☐

Transfer to normal ward at ____. POD

**Diagnostics/interventions:** yes ☐ no ☐

CT-scan ☐

Interventional application of drainage ☐

Relaparotomy ☐, state the reason: _____

**Serious adverse events** (new events since last visit)

Were there any serious adverse events? Yes ☐ no ☐

Were there any other intervention related side effects? Yes ☐ no ☐

If yes, please specify: _____

**Protocol violations**

Were there any protocol violations? Yes ☐ no ☐

If yes, please specify: _____

# Obsidian-Pilottrial

**Visit 6: POD 30**

Screening No.: _____ Year of birth: _____

Date of visit: _____ (dd/mm/yyyy)

**Assessment of postoperative pancreatic fistula**

Classification of POPF: no POPF ☐ grade A ☐ grade B ☐ grade C ☐

**Complications** (new events since last visit)

Perioperative sepsis ☐

Postpancreatectomy acute pancreatitis ☐

- associated complications (e.g. bleeding or perforation) ☐ please, specifiy: _____

Delayed gastric emptying

Post-pancreatectomy hemorrhage: no PPH ☐ grade A ☐ grade B ☐ grade C ☐

Intraabdominal fluid collection ☐

Intraabdominal abscess ☐

Lymphatic fistula / chylus ascites ☐

Wound infection ☐

Burst abdomen ☐

Reinterventions / - operations ☐ _____

ICU stay ☐

Transfer to normal ward at ____. POD

**Diagnostics/interventions:** yes ☐ no ☐

CT-scan ☐

Interventional application of drainage ☐

Relaparotomy ☐, state the reason: _____

**Serious adverse events** (new events since last visit)

Were there any serious adverse events? Yes ☐ no ☐

Were there any other intervention related side effects? Yes ☐ no ☐

If yes, please specify: _____

**Protocol violations**

Were there any protocol violations? Yes ☐ no ☐

If yes, please specify: _____

# Obsidian-Pilottrial

**Visit 7: POD 90 / premature study termination**

Screening No.: _____ Year of birth: _____

Date of visit: _____ (dd/mm/yyyy)

**Assessment of postoperative pancreatic fistula**

Lipase at POD3: _____ (U/L)

Classification of POPF: no POPF ☐ grade A ☐ grade B ☐ grade C ☐

**Complications** (new events since last visit)

Perioperative sepsis ☐

Postpancreatectomy acute pancreatitis ☐

- associated complications (e.g. bleeding or perforation) ☐ please, specifiy: _____

Delayed gastric emptying

Post-pancreatectomy hemorrhage: no PPH ☐ grade A ☐ grade B ☐ grade C ☐

Intraabdominal fluid collection ☐

Intraabdominal abscess ☐

Lymphatic fistula / chylus ascites ☐

Wound infection ☐

Burst abdomen ☐

Reinterventions / - operations ☐ _____

ICU stay ☐

Transfer to normal ward at ____. POD

**Diagnostics/interventions:** yes ☐ no ☐

CT-scan ☐

Interventional application of drainage ☐

Relaparotomy ☐, state the reason: _____

**Serious adverse events** (new events since last visit)

Were there any serious adverse events? Yes ☐ no ☐

Were there any other intervention related side effects? Yes ☐ no ☐

If yes, please specify: _____

**Protocol violations**

Were there any protocol violations? Yes ☐ no ☐

If yes, please specify: _____

**Hospitalization**

Date of discharge: _____ or hospital stay ongoing ☐

Total intensive care unit stay (postoperative and readmissions): ____ (days)

Total hospital stay: ____ (days)

**Results from final histological examination**

Pancreatic carcinoma ☐

- if yes, please enter pTNM-stage: _____

Cystic neoplasm ☐

Neuroendocrine tumor ☐

Other ☐ _____

I confirm that all data entered in this CRF is complete and accurate to the best of my knowledge.

X

date, investigator's name (block letters)

SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

| Section/item | Item No | Description | Addressed on page number |
|---|---|---|---|
| **Administrative information** | | | |
| Title | 1 | Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym | 1 |
| Trial registration | 2a | Trial identifier and registry name. If not yet registered, name of intended registry | 2, 6 |
| | 2b | All items from the World Health Organization Trial Registration Data Set | 2 |
| Protocol version | 3 | Date and version identifier | 2 |
| Funding | 4 | Sources and types of financial, material, and other support | 5, 14 |
| Roles and responsibilities | 5a | Names, affiliations, and roles of protocol contributors | 1,14, |
| | 5b | Name and contact information for the trial sponsor | 1 |
| | 5c | Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities | 6 |
| | 5d | Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) | 6 |

| | | | |
|---|---|---|---|
| **Introduction** | | | |
| Background and rationale | 6a | Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention | 4, 5, 6 |
| | 6b | Explanation for choice of comparators | 6 |
| Objectives | 7 | Specific objectives or hypotheses | 9, 10 |
| Trial design | 8 | Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) | 6 |
| **Methods: Participants, interventions, and outcomes** | | | |
| Study setting | 9 | Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained | 6 |
| Eligibility criteria | 10 | Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) | 6, 7 |
| Interventions | 11a | Interventions for each group with sufficient detail to allow replication, including how and when they will be administered | 7,8,9 |
| | 11b | Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) | 8 |
| | 11c | Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) | 6 |
| | 11d | Relevant concomitant care and interventions that are permitted or prohibited during the trial | 7, 8 |
| Outcomes | 12 | Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended | 9, 10 |
| Participant timeline | 13 | Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) | 11 |

| | | | |
|---|---|---|---|
| Sample size | 14 | Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations | 11 |
| Recruitment | 15 | Strategies for achieving adequate participant enrolment to reach target sample size | 11 |
| **Methods: Assignment of interventions (for controlled trials)** | | | |
| Allocation: | | | |
| Sequence generation | 16a | Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions | 6,7 |
| Allocation concealment mechanism | 16b | Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned | 6,7 |
| Implementation | 16c | Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions | 7,8 |
| Blinding (masking) | 17a | Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how | 6 |
| | 17b | If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial | - |
| **Methods: Data collection, management, and analysis** | | | |
| Data collection methods | 18a | Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol | 9, 10 |
| | 18b | Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols | 7 |

| | | | |
|---|---|---|---|
| Data management | 19 | Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol | 12 |
| Statistical methods | 20a | Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol | 11, 12 |
| | 20b | Methods for any additional analyses (eg, subgroup and adjusted analyses) | 12 |
| | 20c | Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) | 12 |
| **Methods: Monitoring** | | | |
| Data monitoring | 21a | Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed | 13 |
| | 21b | Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial | 12 |
| Harms | 22 | Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct | 9,10 |
| Auditing | 23 | Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor | 13 |
| **Ethics and dissemination** | | | |
| Research ethics approval | 24 | Plans for seeking research ethics committee/institutional review board (REC/IRB) approval | 13 |
| Protocol amendments | 25 | Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) | 2 |

| | | | |
|---|---|---|---|
| Consent or assent | 26a | Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) | 6 |
| | 26b | Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable | - |
| Confidentiality | 27 | How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial | 12 |
| Declaration of interests | 28 | Financial and other competing interests for principal investigators for the overall trial and each study site | 14 |
| Access to data | 29 | Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators | 12 |
| Ancillary and post-trial care | 30 | Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation | 13 |
| Dissemination policy | 31a | Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions | 13 |
| | 31b | Authorship eligibility guidelines and any intended use of professional writers | not applicable |
| | 31c | Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code | not applicable |
| **Appendices** | | | |
| Informed consent materials | 32 | Model consent form and other related documentation given to participants and authorised surrogates | 15 |
| Biological specimens | 33 | Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable | 15 |

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

# *PatientInneninformation[1] und Einwilligungserklärung zur Teilnahme an der klinischen Prüfung*

## *Obsidian® - ASG Autologe plättchenreiche Fibrinmatrix zur Vorbeugung einer postoperativen Pankreasfistel nach Pankreasresektion – Eine Machbarkeitsstudie*

Sehr geehrte Patientin, sehr geehrter Patient!

Wir laden Sie ein an der oben genannten klinischen Prüfung teilzunehmen. Die Aufklärung darüber erfolgt in einem ausführlichen ärztlichen Gespräch.

**Ihre Teilnahme an dieser klinischen Prüfung erfolgt freiwillig. Sie können jederzeit ohne Angabe von Gründen aus der Studie ausscheiden. Die Ablehnung der Teilnahme oder ein vorzeitiges Ausscheiden aus dieser Studie hat keine nachteiligen Folgen für Ihre medizinische Betreuung.**

Klinische Prüfungen sind notwendig, um verlässliche neue medizinische Forschungsergebnisse zu gewinnen. Unverzichtbare Voraussetzung für die Durchführung einer klinischen Prüfung ist jedoch, dass Sie Ihr Einverständnis zur Teilnahme an dieser klinischen Prüfung schriftlich erklären. Bitte lesen Sie den folgenden Text als Ergänzung zum Informationsgespräch mit Ihrem Prüfarzt sorgfältig durch und zögern Sie nicht Fragen zu stellen.

Bitte unterschreiben Sie die Einwilligungserklärung nur

- wenn Sie Art und Ablauf der klinischen Prüfung vollständig verstanden haben,
- wenn Sie bereit sind, der Teilnahme zuzustimmen und
- wenn Sie sich über Ihre Rechte als Teilnehmer an dieser klinischen Prüfung im Klaren sind.

Zu dieser klinischen Prüfung, sowie zur Patienteninformation und Einwilligungserklärung wurde von der zuständigen Ethikkommission eine befürwortende Stellungnahme abgegeben.

# 1. Was ist der Zweck der klinischen Prüfung?

Der Zweck dieser klinischen Prüfung ist die Überprüfung der Machbarkeit einer neuartigen Methode zur Vermeidung von Komplikationen nach Ihrer Operation. Sie werden in der Universitätsklinik für Allgemeinchirurgie (Klinische Abteilung für Viszeralchirurgie) der Medizinischen Universität Wien auf Grund einer Erkrankung der Bauchspeicheldrüse (Pankreas) aufgenommen, die durch eine Operation demnächst werden in der Universitätsklinik für Allgemeinchirurgie (Klinische Abteilung für Viszeralchirurgie) der Medizinischen Universität Wien auf behandelt werden soll. Ziel dieser Operation ist, den erkrankten Teil Ihrer Bauchspeicheldrüse zu entfernen. Im Rahmen dieser Operation muss die Bauchspeicheldrüse etwa in der Mitte durchtrennt werden. Ziel ist es, einen Teil der Drüse zu erhalten. Im Verlauf kommt es nach der Operation an der

[1] Wegen der besseren Lesbarkeit wird im weiteren Text zum Teil auf die gleichzeitige Verwendung weiblicher und männlicher Personenbegriffe verzichtet. Gemeint und angesprochen sind – sofern zutreffend – immer beide Geschlechter.

Stelle der Durchtrennung der Bauchspeicheldrüse häufig zu einer Undichtigkeit, sodass Bauchspeicheldrüsensaft in die Bauchhöhle austritt. Dies wird „Pankreasfistel“ genannt. Dies stellt auch gleichzeitig die häufigste Komplikation der Operation dar und erfordert eine – meist länger (evtl. mehrere Wochen) dauernde – Ableitung dieser Flüssigkeit nach außen. Hierzu ist oft auch die Einlage einer zusätzlichen Drainage von außen im Rahmen einer Röntgenuntersuchung (Computertomographie) erforderlich. Selten können auch schwerwiegendere Probleme (Blutungen, Infektionen) durch die Pankreasfistel verursacht werden. Ein wichtiges Ziel ist daher, das Auftreten einer solchen Pankreasfistel zu verhindern, was durch chirurgische Maßnahmen bei der Operation jedoch trotz größter Sorgfalt bei jedem vierten Patienten nicht gelingt.

Wir wollen Sie daher einladen, an einer Studie teilzunehmen, mit der wir versuchen möchten, das Auftreten einer Pankreasfistel auf einem völlig neuartigen Weg zu verhindern. Es gibt die Möglichkeit, aus körpereigenem Blut eine Flüssigkeit herzustellen, welche während der Operation auf die Schnittstelle der Bauchspeicheldrüse aufgebracht wird und die Heilung und Dichtigkeit der Schnittstelle unterstützen soll. Diese Flüssigkeit wurde bereits erfolgreich bei Operationen am Darm angewandt. Bislang gibt es keine Untersuchungen zum Einsatz bei Bauchspeicheldrüsenoperationen. Wir nehmen an, dass sich durch die beschriebene Maßnahme die Häufigkeit und Schwere einer Pankreasfistel deutlich senken lässt und möchten zunächst die Machbarkeit der Verabreichung in einer klinischen Studie untersuchen.

## 2. Welche anderen Behandlungsmöglichkeiten gibt es?

Zur Behandlung Ihrer Erkrankung stehen **stattdessen auch** die folgenden Möglichkeiten zur Verfügung: wenn Sie an der Studie nicht teilnehmen möchten, findet die Operation ohne Anwendung der zusätzlichen Methode statt.

## 3. Wie läuft die klinische Prüfung ab?

Diese klinische Prüfung wird an der Klinik für Viszeralchirurgie durchgeführt, und es werden insgesamt ungefähr 25 Personen daran teilnehmen.

Vor Aufnahme in diese klinische Prüfung wird die Vorgeschichte Ihrer Krankheit erhoben, und Sie werden einer umfassenden ärztlichen Untersuchung unterzogen.

Ihre Teilnahme an dieser klinischen Prüfung wird voraussichtlich 12 Wochen dauern.

Eine Reihe von Untersuchungen und Eingriffen werden im Zuge Ihrer Behandlung durchgeführt, gleichgültig, ob Sie nun an dieser klinischen Prüfung teilnehmen oder nicht. Diese werden von Ihrem Prüfarzt im Rahmen des üblichen ärztlichen Aufklärungsgespräches mit Ihnen besprochen.

Folgende Maßnahmen werden ausschließlich aus Studiengründen durchgeführt:

Während dieser klinischen Prüfung werden Ihnen am Tag der Operation 120ml Blut abgenommen (dies entspricht etwa 8 Esslöffel). Mit diesem Blut wird dann die Flüssigkeit hergestellt, die bei Ihrer Operation zur Abdichtung der Schnittstelle der Bauchspeicheldrüse verwendet werden soll. Sie werden nach der Operation regelmäßig von Studienärzten besucht, damit wir Ihren Verlauf beobachten können. Nachdem Sie nach Hause entlassen werden, würden wir Sie am 30. und 90. Tag nach der Operation nochmals einbestellen bzw. telefonisch kontaktieren. Insgesamt sind 7 Studienbesuche angedacht, wobei die ersten 5 in jedem Fall stattfinden, während Sie ohnehin im Krankenhaus sind. Weitere Maßnahmen sind nicht studienspezifisch, sondern würden auch ohne Teilnahme an der Operation durchgeführt werden.

# 4. Was ist „Obsidian® - ASG Autologe plättchenreiche Fibrinmatrix“?

Obsidian®-ASG Autologe plättchenreiche Fibrinmatrix ist ein Medizinprodukt, welches bereits zugelassen ist für die Anwendung bei Operationen. Dieses Medizinprodukt wird gegenwärtig insbesondere bei der Behandlung von Darmerkrankungen verwendet. Es wurde bisher bei über 200 Patienten angewendet.

# 5. Worin liegt der Nutzen einer Teilnahme an der Klinischen Prüfung?

Mit der Anwendung von Obsidian®-ASG Autologe plättchenreiche Fibrinmatrix kann möglicherweise der Verlauf Ihrer Operation verbessert werden, indem Komplikationen gänzlich verhindert oder zumindest deren Schwergrad deutlich reduziert werden können. Es ist jedoch auch möglich, dass Sie durch Ihre Teilnahme an dieser klinischen Prüfung keinen direkten Nutzen für Ihre Gesundheit ziehen. Es ist jedoch ein Erkenntnisgewinn in der Wissenschaft und Nutzen für die zukünftige Behandlung von Patient:innen möglich.

# 6. Gibt es Risiken, Beschwerden und Begleiterscheinungen?

Die Behandlung mit Obsidian®-ASG Autologe plättchenreiche Fibrinmatrix kann zu Nebenwirkungen oder Beschwerden führen. Die bislang beobachteten Nebenwirkungen und Beschwerden umfassen Nachwirkungen der Blutabnahme wie Schmerzen im Bereich der Einstichstelle oder einem Bluterguss. Dies tritt häufig auf (bei mehr als der Hälfte der Patient:innen), heilt aber in aller Regel folgenlos und rasch ab. Sehr selten (bei 5 von 100 Patient:innen) kann bei der Blutabnahme auch ein kleiner Nerv verletzt werden. Es können sehr selten (bei 5 von 100 Patient:innen) allergische Reaktionen auf Inhaltsstoffe des Produktes auftreten. Wenn eine dementsprechende Allergie bekannt ist, dürfen Sie nicht an der Studie teilnehmen. Wie mit jeder neuen Substanz können auch bei der Anwendung von Obsidian®-ASG Autologe plättchenreiche Fibrinmatrix neue, bisher unbekannte Nebenwirkungen auftreten.

# 7. Zusätzliche Einnahme von Arzneimitteln?

Aufgrund der Teilnahme an der Studie ist keine Änderung Ihrer Medikation erforderlich.

# 8. Hat die Teilnahme an der klinischen Prüfung sonstige Auswirkungen auf die Lebensführung und welche Verpflichtungen ergeben sich daraus?

Nein.

# 9. Was ist zu tun beim Auftreten von Symptomen, Begleiterscheinungen und/oder Verletzungen?

Sollten im Verlauf der klinischen Prüfung irgendwelche Symptome, Begleiterscheinungen oder Verletzungen auftreten, müssen Sie diese Ihrem Prüfarzt mitteilen, bei schwerwiegenden Begleiterscheinungen umgehend, ggf. telefonisch (Telefonnummern, etc. siehe unten).

# 10. Versicherung

Als Teilnehmer an dieser klinischen Prüfung besteht für Sie der gesetzlich vorgeschriebene verschuldensunabhängige Versicherungsschutz (Personenschadenversicherung gemäß § 20 Medizinproduktegesetz, der alle Schäden abdeckt, die an Ihrem Leben oder Ihrer Gesundheit durch die an Ihnen durchgeführten Maßnahmen der klinischen Prüfung verursacht werden können, mit Ausnahme von Schäden auf Grund von Veränderungen des Erbmaterials in Zellen der Keimbahn.

Die Versicherung wurde für Sie bei der Zürich Versicherungs-Aktiengesellschaft im Rahmen einer Rahmenversicherung der Medizinischen Universität Wien für klinische Studien abgeschlossen (Polizze-Nr. 07229622-2).

Auf Wunsch können Sie in die Versicherungsunterlagen Einsicht nehmen.

Im Schadensfall können Sie sich direkt an den Versicherer wenden und Ihre Ansprüche selbständig geltend machen. Für den Versicherungsvertrag ist österreichisches Recht anwendbar, die Versicherungsansprüche sind in Österreich einklagbar.

Zur Unterstützung können Sie sich auch an die Patientenanwaltschaft, Patientenvertretung oder Patientenombudsschaft wenden.

Um den Versicherungsschutz nicht zu gefährden

- dürfen Sie sich während der Dauer der klinischen Prüfung einer anderen medizinischen Behandlung nur im Einvernehmen mit Ihrem behandelnden Prüfarzt unterziehen **(ausgenommen davon sind Notfälle).** Dies gilt auch für die zusätzliche Einnahme von Medikamenten oder die Teilnahme an einer anderen Studie.
- müssen Sie dem behandelnden Prüfarzt - oder der oben genannten Versicherungsgesellschaft - eine Gesundheitsschädigung, die als Folge der klinischen Prüfung eingetreten sein könnte, unverzüglich mitteilen.
- müssen Sie alles Zumutbare tun um Ursache, Hergang und Folgen des Versicherungsfalles aufzuklären und den entstandenen Schaden gering zu halten. Dazu gehört ggf. auch, dass Sie Ihre behandelnden Ärzte ermächtigen, vom Versicherer geforderte Auskünfte zu erteilen.

# 11. Informationen für gebärfähige Frauen – Schwangerschaftstest

Schwangere und stillende Frauen dürfen an dieser klinischen Prüfung NICHT teilnehmen.

Als gebärfähige Frau dürfen Sie an der klinischen Prüfung nur teilnehmen,

- wenn ein Arzt vor der klinischen Prüfung das Nichtvorliegen einer Schwangerschaft (Schwangerschaftstest) feststellt.
- wenn Sie sich verpflichten während der Dauer eine zuverlässige Art der Empfängnisverhütung (Pille, Spirale) zu praktizieren.

Sollten Sie dennoch während der klinischen Prüfung schwanger werden oder den Verdacht haben, dass Sie schwanger geworden sind, informieren Sie bitte umgehend Ihren Prüfarzt. Es wird dann umgehend Kontakt mit der Gynäkologie aufgenommen.

# 12. Wann wird die klinische Prüfung vorzeitig beendet?

Sie können jederzeit auch ohne Angabe von Gründen, Ihre Teilnahmebereitschaft widerrufen und aus der klinischen Prüfung ausscheiden ohne dass Ihnen dadurch irgendwelche Nachteile für Ihre weitere medizinische Betreuung entstehen.

Ihr Prüfarzt wird Sie über alle neuen Erkenntnisse, die in Bezug auf diese klinische Prüfung bekannt werden, und für Sie wesentlich werden könnten, umgehend informieren. Auf dieser Basis können Sie dann Ihre Entscheidung zur **weiteren** Teilnahme an dieser klinischen Prüfung neu überdenken.

Es ist aber auch möglich, dass Ihr Prüfarzt (oder gegebenenfalls der Auftraggeber dieser klinischen Prüfung) entscheidet, Ihre Teilnahme an der klinischen Prüfung vorzeitig zu beenden, ohne vorher Ihr Einverständnis einzuholen. Die Gründe hierfür können sein:

a) Sie können den Erfordernissen der Klinischen Prüfung nicht entsprechen;

b) Ihr Prüfarzt hat den Eindruck, dass eine weitere Teilnahme an der klinischen Prüfung nicht in Ihrem Interesse ist;

c) der Auftraggeber trifft die Entscheidung, die gesamte klinische Prüfung abzubrechen, oder lediglich Ihre Teilnahme vorzeitig zu beenden.

Sofern Sie sich dazu entschließen, vorzeitig aus der klinischen Prüfung auszuscheiden, oder Ihre Teilnahme aus einem der oben genannten Gründe vorzeitig beendet wird, ist es für Ihre eigene Sicherheit wichtig, dass Sie sich einer normalen Kontrolluntersuchung unterziehen. Diese besteht meistens aus einer körperlichen Untersuchung sowie aus Laboruntersuchungen.

# 13. Datenschutz

Im Rahmen dieser klinischen Prüfung werden Daten über Sie erhoben und verarbeitet. Es ist grundsätzlich zu unterscheiden zwischen

1) jenen personenbezogenen Daten, anhand derer eine Person direkt identifizierbar ist (z.B. Name, Geburtsdatum, Adresse, Sozialversicherungsnummer, Bildaufnahmen...),
2) pseudonymisierten personenbezogenen Daten, das sind Daten, bei denen alle Informationen, die direkte Rückschlüsse auf die konkrete Person zulassen, entweder entfernt, durch einen Code (z. B. eine Zahl) ersetzt oder (z.B. im Fall von Bildaufnahmen) unkenntlich gemacht werden. Es kann jedoch trotz Einhaltung dieser Maßnahmen nicht vollkommen ausgeschlossen werden, dass es unzulässigerweise zu einer Re-Identifizierung kommt.
3) anonymisierten Daten, bei denen eine Rückführung auf die konkrete Person ausgeschlossen werden kann.

Zugang zu den Daten, anhand derer Sie direkt identifizierbar sind (siehe Punkt 1), haben der Prüfarzt und andere Mitarbeiter des Prüfzentrums, die an der klinischen Prüfung oder Ihrer medizinischen Versorgung mitwirken. Zusätzlich können autorisierte und zur Verschwiegenheit verpflichtete Beauftragte des Sponsors, der Medizinischen Universität Wien, sowie Beauftragte von in- und/ oder ausländischen Gesundheitsbehörden und jeweils zuständige Ethikkommissionen in diese Daten Einsicht nehmen, soweit dies für die Überprüfung der ordnungsgemäßen Durchführung der klinischen Prüfung notwendig ist. Sämtliche Personen, die Zugang zu diesen Daten erhalten, unterliegen im Umgang mit den Daten den jeweils geltenden nationalen Datenschutzbestimmungen und/oder der EU-Datenschutz-Grundverordnung (DSGVO).

Der Code, der eine Zuordnung der pseudonymisierten Daten zu Ihrer Person ermöglicht, wird nur an Ihrem Prüfzentrum aufbewahrt.

Eine Weitergabe der Daten erfolgt nur in pseudonymisierter oder anonymisierter Form.

Für etwaige Veröffentlichungen werden nur die pseudonymisierten oder anonymisierten Daten verwendet.

Im Rahmen dieser klinischen Prüfung ist keine Weitergabe von Daten in Länder außerhalb der EU (Drittland) vorgesehen.

Ihre Einwilligung bildet die Rechtsgrundlage für die Verarbeitung Ihrer personenbezogenen Daten. Sie können die Einwilligung zur Erhebung und Verarbeitung Ihrer Daten jederzeit ohne Begründung widerrufen. Nach Ihrem Widerruf werden

keine weiteren Daten mehr über Sie erhoben. Die bis zum Widerruf erhobenen Daten können allerdings weiter im Rahmen dieser klinischen Prüfung verarbeitet werden.

Nach der DSGVO stehen Ihnen grundsätzlich die Rechte auf Auskunft, Berichtigung, Löschung, Einschränkung der Verarbeitung, Datenübertragbarkeit und Widerspruch zu, soweit dies die Ziele der klinischen Prüfung nicht unmöglich macht oder ernsthaft beeinträchtigt und soweit dem nicht andere gesetzliche Vorschriften widersprechen.

Das gemäß DSGVO vorgesehene Recht auf Löschung Ihrer im Rahmen dieser klinischen Prüfung verarbeiteten Daten steht Ihnen aufgrund von Regelungen nach dem Arzneimittelgesetz und Medizinproduktegesetz nicht zu. Zusätzlich ist bei einer klinischen Prüfung nach dem Arzneimittelgesetz das Recht auf Datenübertragbarkeit außer Kraft gesetzt.

Die voraussichtliche Dauer der klinischen Prüfung ist 12 Monate. Die Dauer der Speicherung Ihrer Daten über das Ende oder den Abbruch der klinischen Prüfung hinaus ist durch Rechtsvorschriften geregelt.

Falls Sie Fragen zum Umgang mit Ihren Daten in dieser klinischen Prüfung haben, wenden Sie sich zunächst an Ihren Prüfarzt. Dieser kann Ihr Anliegen ggf. an die Personen, die für den Datenschutz verantwortlich sind, weiterleiten.

Kontaktdaten der Datenschutzbeauftragten der an dieser klinischen Prüfung beteiligten Institutionen:

Datenschutzbeauftragte/r der MedUni Wien: datenschutz@meduniwien.ac.at

Datenschutzverantwortliche/r des AKH: datenschutz@akhwien.at

Sie haben das Recht, bei der österreichischen Datenschutzbehörde eine Beschwerde über den Umgang mit Ihren Daten einzubringen (www.dsb.gv.at; E-Mail: dsb@dsb.gv.at ).

## 14. Entstehen für die Teilnehmer Kosten? Gibt es einen Kostenersatz oder eine Vergütung?

Durch Ihre Teilnahme an dieser klinischen Prüfung entstehen für Sie keine zusätzlichen Kosten mit Ausnahme der Fahrtkosten für die Verlaufskontrolle 30 Tage nach der Operation. Allerdings ist zu diesem Zeitpunkt auch unabhängig von der Teilnahme an der Studie eine Kontrolle empfohlen. Es ist keine Vergütung vorgesehen.

## 15. Möglichkeit zur Diskussion weiterer Fragen

Für weitere Fragen im Zusammenhang mit dieser klinischen Prüfung stehen Ihnen Ihr Prüfarzt und seine Mitarbeiter gern zur Verfügung. Auch Fragen, die Ihre Rechte als Patient und Teilnehmer an dieser klinischen Prüfung betreffen, werden Ihnen gerne beantwortet.

I. Name der Kontaktperson: Priv.-Doz. Dr. Ulla Klaiber

Ständig erreichbar unter: .Mobil: +43 67764384772

II. Name der Kontaktperson: Dr. Charlotte Gustorff

Ständig erreichbar unter: Mobil: +43 6703501743

# 19. Einwilligungserklärung

Name des Patienten:

Geb.Datum:

Ich erkläre mich bereit, an der klinischen Prüfung Obsidian zur Reduktion der Pankreasfistel teilzunehmen. Ich bin darüber aufgeklärt worden, dass ich die Teilnahme ohne nachteilige Folgen, insbesondere für meine medizinische Betreuung, ablehnen kann.

Ich bin von Frau/Herrn (Dr.med.) .....ausführlich und verständlich über die klinische Prüfung, mögliche Belastungen und Risiken, sowie über Wesen, Bedeutung und Tragweite der klinischen Prüfung, die bestehende Versicherung sowie die sich für mich daraus ergebenden Anforderungen aufgeklärt worden. Ich habe darüber hinaus den Text dieser Patientenaufklärung und Einwilligungserklärung, die insgesamt 7 Seiten umfasst, gelesen. Aufgetretene Fragen wurden mir vom Prüfarzt verständlich und zufriedenstellend beantwortet. Ich hatte ausreichend Zeit, mich zu entscheiden. Ich habe zurzeit keine weiteren Fragen mehr.

Ich werde den ärztlichen Anordnungen, die für die Durchführung der klinischen Prüfung erforderlich sind, Folge leisten, behalte mir jedoch das Recht vor, meine freiwillige Mitwirkung jederzeit zu beenden, ohne dass mir daraus Nachteile, insbesondere für meine medizinische Betreuung, entstehen.

Ich stimme ausdrücklich zu, dass meine im Rahmen dieser klinischen Prüfung erhobenen Daten wie im Abschnitt „Datenschutz“ dieses Dokuments beschrieben verarbeitet werden.

Eine Kopie dieser Patienteninformation und Einwilligungserklärung habe ich erhalten. Das Original verbleibt beim Prüfarzt.

.....
(Datum und Unterschrift des Patienten)

.....
(Datum, Name und Unterschrift des verantwortlichen Prüfarztes)

(Der Patient erhält eine unterschriebene Kopie der Patienteninformation und Einwilligungserklärung, das Original verbleibt im Studienordner des Prüfarztes.)

# *Patient information[1] and declaration of consent for participation in the clinical trial*

## *Obsidian® - ASG Autologous platelet-rich fibrin matrix for the prevention of postoperative pancreatic fistula after pancreatic resection - A feasibility study*



Dear Patient!

We invite you to take part in the above-mentioned clinical trial. You will be informed about this in a detailed medical consultation.

**Your participation in this clinical trial is voluntary. You can withdraw from the trial at any time without giving reasons. Refusal to participate or early withdrawal from this trial will have no adverse consequences for your medical care.**

Clinical trials are necessary in order to obtain reliable new medical research results. However, an essential prerequisite for conducting a clinical trial is that you give your written consent to participate in this clinical trial. Please read the following text carefully as a supplement to the information meeting with your investigator and do not hesitate to ask questions.

Please sign the declaration of consent only

- if you have fully understood the nature and procedure of the clinical trial,
- if you are willing to agree to participate and
- if you are aware of your rights as a participant in this clinical trial.

The responsible ethics committee issued a favourable opinion on this clinical trial, as well as on the patient information and consent form.

# 1. What is the purpose of the clinical trial?

The purpose of this clinical trial is to test the feasibility of a new method to avoid complications after your operation. You are admitted to the Department of General Surgery (Division of Visceral Surgery) of the Medical University of Vienna due to a disease of the pancreas, which is to be treated by surgery in the near future at the Department of General Surgery (Division of Visceral Surgery) of the Medical University of Vienna. The aim of this operation is to remove the diseased part of your pancreas. As part of this operation, the pancreas must be cut approximately in the centre. The aim is to preserve part of the gland. In the course of the operation on the

[1] For the sake of readability, the use of the masculine and feminine forms in the following text is omitted in some cases. The use of personal terms is avoided. Where applicable, both genders are always meant and addressed.

The pancreas often leaks at the point where the pancreas is severed, causing pancreatic juice to leak into the abdominal cavity. This is called a "pancreatic fistula". This is also the most common complication of the operation and requires this fluid to be drained to the outside - usually for a longer period of time (possibly several weeks). This often requires the insertion of an additional drainage tube from the outside as part of an X-ray examination (computerised tomography). In rare cases, more serious problems (bleeding, infections) can also be caused by the pancreatic fistula. An important goal is therefore to prevent the occurrence of such a pancreatic fistula, but despite the greatest care, surgical measures during the operation do not succeed in every fourth patient.

We would therefore like to invite you to take part in a study in which we would like to try to prevent the occurrence of a pancreatic fistula in a completely new way. It is possible to produce a fluid from the body's own blood, which is applied to the incision site of the pancreas during the operation and is intended to support the healing and sealing of the incision site. This fluid has already been used successfully in intestinal surgery. To date, there have been no studies on its use in pancreatic surgery. We assume that the described measure can significantly reduce the frequency and severity of pancreatic fistula and would first like to investigate the feasibility of administration in a clinical trial.

## 2. What other treatment options are there?

The following options are **also** available to treat your condition **instead**: if you do not wish to take part in the study, the operation will take place without using the additional method.

## 3. How does the clinical trial work?

This clinical trial will be conducted at the Department of Visceral Surgery and will involve a total of approximately 25 participants.

Before being admitted to this clinical trial, your medical history will be taken and you will undergo a comprehensive medical examination.

Your participation in this clinical trial is expected to last 12 weeks.

A number of examinations and procedures will be carried out as part of your treatment, regardless of whether you are taking part in this clinical trial or not. These will be discussed with you by your investigator as part of the usual medical consultation.

The following measures are carried out exclusively for study reasons:

During this clinical trial, 120ml of blood will be taken from you on the day of the operation (equivalent to about 8 tablespoons). This blood will then be used to prepare the fluid that will be used during your operation to seal the incision in the pancreas. You will be visited regularly by study doctors after the operation so that we can monitor your progress. After you are discharged home, we will visit you again on the 30th and 90th day after the operation or contact you by telephone. A total of 7 study visits are planned, with the first 5 taking place while you are in hospital anyway. Further measures are not specific to the study, but would also be carried out without participation in the operation.

# 4. What is "Obsidian® - ASG Autologous Platelet Rich Fibrin Matrix"?

Obsidian®-ASG Autologous Platelet Rich Fibrin Matrix is a medical device that is already authorised for use in surgery. This medical device is currently used in particular for the treatment of intestinal diseases. It has been used in over 200 patients to date.

# 5. What are the benefits of participating in the clinical trial?

The use of Obsidian®-ASG Autologous Platelet Rich Fibrin Matrix may improve the outcome of your surgery by preventing complications altogether or at least significantly reducing their severity. However, it is also possible that your participation in this clinical trial will not directly benefit your health. However, it is possible that you will gain scientific knowledge and benefit the future treatment of patients.

# 6. Are there risks, complaints and side effects?

Treatment with Obsidian®-ASG Autologous Platelet Rich Fibrin Matrix may cause side effects or discomfort. The side effects and discomfort observed to date include after-effects of blood collection such as pain at the puncture site or bruising. This occurs frequently (in more than half of patients), but usually heals quickly and without consequences. Very rarely (in 5 out of 100 patients), a small nerve can also be injured when blood is drawn. Very rarely (in 5 out of 100 patients) allergic reactions to the ingredients of the product may occur. If you have a known allergy, you must not take part in the study. As with any new substance, the use of Obsidian®-ASG Autologous Platelet Rich Fibrin Matrix may cause new, previously unknown side effects.

# 7. Taking additional medication?

You do not need to change your medication as a result of participating in the study.

# 8. Does participation in the clinical trial have any other effects on your lifestyle and what obligations does this entail?

No.

# 9. What should I do if symptoms, side effects and/or injuries occur?

If any symptoms, side effects or injuries occur during the course of the clinical trial, you must report them to your investigator, in the case of serious side effects immediately, if necessary by telephone (see below for telephone numbers, etc.).

# 10. Insurance

As a participant in this clinical trial, you have the statutory no-fault insurance cover (personal injury insurance in accordance with Section 20 of the Medical Devices Act, which covers all damage that may be caused to your life or health by the clinical trial measures carried out on you, with the exception of damage due to changes in the genetic material in germline cells.

The insurance was taken out for you with Zurich Insurance Company as part of a framework insurance policy of the Medical University of Vienna for clinical studies (policy no. 07229622-2).

You can inspect the insurance documents on request.

In the event of a claim, you can contact the insurer directly and assert your claims independently. The insurance contract is governed by Austrian law and insurance claims are enforceable in Austria.

For support, you can also contact the patient advocacy organisation, patient representative body or patient ombudsman.

In order not to jeopardise the insurance cover

- you may only undergo other medical treatment for the duration of the clinical trial with the agreement of your treating investigator **(with the exception of emergencies).** This also applies to the additional intake of medication or participation in another study.
- you must immediately notify the treating investigator - or the insurance company mentioned above - of any damage to your health that may have occurred as a result of the clinical trial.
- you must do everything reasonable to clarify the cause, course and consequences of the insured event and minimise the damage incurred. This may also include authorising your attending physicians to provide information requested by the insurer.

# 11. Information for women of childbearing age - Pregnancy test

Pregnant and breastfeeding women are NOT allowed to participate in this clinical trial.

As a woman of childbearing potential, you may only participate in the clinical trial,

- if a doctor determines the absence of pregnancy (pregnancy test) before the clinical trial.
- if you undertake to use a reliable form of contraception (pill, coil) for the duration of the treatment.

Should you nevertheless become pregnant during the clinical trial or suspect that you have become pregnant, please inform your investigator immediately. The gynaecology department will then be contacted immediately.

# 12. When is the clinical trial terminated prematurely?

You can withdraw your willingness to participate at any time without giving reasons and withdraw from the clinical trial without any disadvantages for your further medical care.

Your investigator will inform you immediately of any new findings that become known in relation to this clinical trial that could be significant for you. On this basis, you can then reconsider your decision to **continue** participating in this clinical trial.

However, it is also possible that your investigator (or, if applicable, the sponsor of this clinical trial) may decide to terminate your participation in the clinical trial prematurely without first obtaining your consent. The reasons for this may be

a) They cannot fulfil the requirements of the clinical trial;

b) Your investigator has the impression that further participation in the clinical trial is not in your interest;

c) the sponsor makes the decision to cancel the entire clinical trial or only to terminate your participation prematurely.

If you decide to withdraw from the clinical trial prematurely, or if your participation is terminated prematurely for one of the reasons mentioned above, it is important for your own safety that you undergo a normal check-up. This usually consists of a physical examination and laboratory tests.

# 13. Data protection

Data about you will be collected and processed as part of this clinical trial. A basic distinction must be made between

1) personal data by which a person can be directly identified (e.g. name, date of birth, address, national insurance number, photographs, etc.),
2) pseudonymised personal data, i.e. data in which all information that allows direct conclusions to be drawn about the specific person is either removed, replaced by a code (e.g. a number) or (e.g. in the case of image recordings) made unrecognisable. However, despite compliance with these measures, the possibility of unauthorised re-identification cannot be completely ruled out.
3) anonymised data that cannot be traced back to a specific person.

The investigator and other employees of the trial centre who are involved in the clinical trial or your medical care have access to the data by which you can be directly identified (see point 1). In addition, authorised representatives of the sponsor, the Medical University of Vienna, as well as representatives of domestic and/or foreign health authorities and the relevant ethics committees, who are bound to confidentiality, may inspect this data insofar as this is necessary to verify the proper conduct of the clinical trial. All persons who have access to this data are subject to the applicable national data protection regulations and/or the EU General Data Protection Regulation (GDPR) when handling the data.

The code that makes it possible to assign the pseudonymised data to your person is only stored at your test centre.

The data will only be passed on in pseudonymised or anonymised form.

Only pseudonymised or anonymised data will be used for any publications.

No transfer of data to countries outside the EU (third country) is planned as part of this clinical trial.

Your consent forms the legal basis for the processing of your personal data. You can withdraw your consent to the collection and processing of your data at any time without giving reasons. After your revocation

no further data will be collected about you. However, the data collected up to the point of cancellation may continue to be processed in the context of this clinical trial.

According to the GDPR, you are generally entitled to the rights of access, rectification, erasure, restriction of processing, data portability and objection, provided that this does not render impossible or seriously impair the objectives of the clinical trial and provided that this does not conflict with other statutory provisions.

You do not have the right to erasure of your data processed in the context of this clinical trial as provided for in the GDPR due to regulations under the German Drug Law and Medical Devices Law. In addition, the right to data portability is overridden in the case of a clinical trial under the Medicinal Products Act.

The expected duration of the clinical trial is 12 months. The duration of the storage of your data beyond the end or cancellation of the clinical trial is regulated by legal provisions.

If you have any questions about the handling of your data in this clinical trial, please contact your investigator first. If necessary, they can forward your request to the persons responsible for data protection.

Contact details of the data protection officers of the institutions involved in this clinical trial: Data

Protection Officer of the MedUni Vienna: datenschutz@meduniwien.ac.at Data Protection Officer of the

AKH: datenschutz@akhwien.at

You have the right to lodge a complaint with the Austrian data protection authority about the handling of your data (www.dsb.gv.at; e-mail: dsb@dsb.gv.at ).

# 14. Are there any costs for the participants? Is there a reimbursement of costs or remuneration?

Your participation in this clinical trial will not incur any additional costs for you, with the exception of the travelling costs for the follow-up 30 days after the operation. However, a check-up is also recommended at this time regardless of participation in the trial. No compensation is provided.

# 15. Possibility to discuss further questions

Your investigator and his staff will be happy to answer any further questions you may have in connection with this clinical trial. They will also be happy to answer any questions concerning your rights as a patient and participant in this clinical trial.

I. Name of contact person: Priv.-Doz. Dr Ulla Klaiber

Always available at : Mobile: +43 67764384772

II. Name of contact person: Dr Charlotte Gustorff

Always available under: Mobile: +43 6703501743

# 19. declaration of consent

Name of the patient:

Date of birth:

I agree to participate in the Obsidian clinical trial for the reduction of pancreatic fistula. I have been informed that I can refuse to participate without adverse consequences, in particular for my medical care.

I was informed by Mrs/Mr (Dr.med.) .....in detail and comprehensibly about the I have been informed about the nature, significance and scope of the clinical trial, the existing insurance and the resulting requirements for me. I have also read the text of this patient information and consent form, which comprises a total of 7 pages. Any questions that arose were answered clearly and satisfactorily by the investigator. I had sufficient time to make a decision. I currently have no further questions.

I will follow the medical instructions necessary for the conduct of the clinical trial, but I reserve the right to terminate my voluntary co-operation at any time without any disadvantages, in particular for my medical care.

I expressly consent to the processing of my data collected in the course of this clinical trial as described in the "Data Protection" section of this document.

I have received a copy of this patient information and consent form. The original remains with the investigator.

.....
(Date and signature of the patient)

.....
(Date, name and signature of the responsible investigator)

(The patient receives a signed copy of the patient information and consent form, the original remains in the investigator's study folder).