Trial Description

Title

Multicenter, randomized, controlled, open-label, phase-III clinical trial of PREoperative endoscopic injection of BOTulinum toxin in the sphincter of Oddi to reduce postoperative pancreatic fistula after distal pancreatectomy (PREBOT trial)

Trial Acronym

PREBOT

URL of the trial

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Brief Summary in Lay Language

After pancreatic resections, leckage of pancreatic fluid from the resection margin of the pancreas is the most important complication, especially after the resection of the tail of the pancreas (pancreatic left resection). This complication is called pancreatic fistula. To date, numerous surgical efforts to solve this problem have been ineffective. Naturally, the pancreatic fluid flows through the pancreatic duct towards the small intestine. Studies with the aim to promote this way by insertion of a tube into the pancreatic duct have shown promising results. However, because of prosthesis-associated disadvantages and risks a tube-free approach would be more favorable. To control the outflow of pancreatic juice into the small intestine, there is a special muscle, the so called sphincter of Oddi. By reducing sphincter pressure, injection of a muscle relaxant, botulinum toxin, in the sphincter of Oddi represents a safe and effective treatment option in patients with dysfunction of the sphincter of Oddi. A drug-induced sphincter relaxation to reduce sphincter pressure may improve the outflow of pancreatic fluid into the small intestine and thereby lower back pressure on the resection margin of the pancreas, so that pancreatic fistula will be prevented. First experiences from a current trial (DRKS00007885) indicate that this really works. The aim of this randomized-controlled trial is to investigate the injection of botulinum toxin in the sphincter of Oddi before resection of the pancreatic tail to reduce postoperative pancreatic fistula.

Brief Summary in Scientific Language

Postoperative pancreatic fistula (POPF) is the most important complication after distal pancreatectomy. Numerous recent surgical efforts to reduce POPF rate by special closure techniques of the pancreatic stump have been ineffective. In contrast, studies investigating endoscopic stenting with the aim to improve drainage of pancreatic fluid into the duodenum have shown promising results. However, because of prosthesis-associated disadvantages and risks a stent-free approach would be more favorable. By reducing sphincter pressure, endoscopic injection of botulinum toxin in the sphincter of Oddi represents a safe and effective treatment option in patients with sphincter of Oddi dysfunction. In the setting of distal pancreatectomy, a pharmacologically induced sphincter relaxation to improve drainage and thereby lower back pressure on the resection margin of the pancreas may prevent POPF successfully. First experiences from a current trial

(DRKS00007885) indicate that this really works, whereby feasibility and safety are given. The aim of this trial is to prove these data in a randomized-controlled study design.

Organizational Data

- DRKS-ID: **DRKS00010080**
- Date of Registration in DRKS: **2016/02/24**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **AFmu-423/2016 , Ethik-Kommission I der Medizinischen Fakultät Heidelberg**

Secondary IDs

- EudraCT-No.
(for studies acc. to Drug Law): **2016-000799-11**

Health condition or Problem studied

- ICD10: **K86.8 - Other specified diseases of pancreas**

Interventions/Observational Groups

- Arm 1: **Single endoscopic injection of botulinum toxin in the sphincter of Oddi before distal pancreatectomy**
- Arm 2: **No preoperative endoscopic intervention**

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Randomized controlled trial**
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Control group receives no treatment**
- Purpose: **Prevention**
- Assignment: **Parallel**
- Phase: **III**
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Phase: **III**

Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **Yes**

Primary Outcome

Clinically relevant postoperative pancreatic fistula (POPF) and/or death within 30 days after the index operation

Secondary Outcome

Ovarall POPF rate and severity of POPF, Post-interventional pancreatitis, Perioperative sepsis, Delayed gastric emptying (DGE), Post-pancreatectomy hemorrhage (PPH), Intra-abdominal infection/abscess, Lymphatic fistula, Wound infection, Burst abdomen, Re-interventions/-operations, Mortality within 6 months after the index operation, Quality of life (EORTC QLQ C30 und PAN26) after 1 and 6 months, Intensive care unit/intermediate care unit/total hospital stay, Readmission to hospital

Countries of recruitment

- DE **Germany**
- UK **United Kingdom**
- IT **Italy**

Locations of Recruitment

- University Medical Center **Klinik für Allgemein-, Viszeral- und Transplantationschirurgie/Department of General, Visceral and Transplantation Surgery, Heidelberg**

Recruitment

- Planned/Actual: **Planned**
- (Anticipated or Actual) Date of First Enrollment: **2017/02/01**
- Target Sample Size: **254**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **International**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **no maximum age**

Additional Inclusion Criteria

Patients scheduled for elective DP, ≥18 years of age, Ability of subject to understand character and individual consequences of the clinical trial, Written informed consent, For women with childbearing potential, presence of negative urine or blood pregnancy test, and adequate contraception for the first 5 days after trial intervention

Exclusion criteria

Serious cardiovascular disease (e.g. myocardial infarction in the last 12 months; congestive heart failure NYHA III/IV, unstable angina pectoris); Renal insufficiency, i.e. creatinine clearance <30 mL/min; Liver cirrhosis of any Child-Pugh grade; American Society of Anaesthesiologists (ASA) score >III; Hypersensitivity to any botulinum toxin preparation or to any of the components in the formulation; Neuromuscular disorder, e.g. peripheral motor neuropathic disease, amyotrophic lateral sclerosis or neuromuscular junction disorders (e.g. myasthenia gravis or Lambert-Eaton syndrome), or any other neurological disorder with associated increased risk for the patient undergoing botulinum toxin injection; Any condition in which duodenoscopy and/or the trial intervention is not possible, e.g. for anatomical reasons, or obsolete in the actual situation, e.g. in patients with acute pancreatitis; History of botulinum toxin application and either positive test or missing test for neutralising antibodies to botulinum Toxin; Understanding or language problems; Inability to comply with study and/or follow-up procedures; Pregnancy or lactation; Concurrent participation in another interventional clinical trial, or participation within the previous 30 days before study enrollment (or longer exclusion period, if required by national or local regulations); Legally incapacitated patients; Patients held in an institution by legal or official order; Any condition or situation which could result in an undue risk for the patient and/or influence outcome measures in the opinion of the investigator

Addresses

- **Primary Sponsor**

  Ruprecht-Karls-University Heidelberg, Medical Faculty represented by

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Sources of Monetary or Material Support

- **Public funding institutions financed by tax money/Government funding body (German Research Foundation (DFG), Federal Ministry of Education and Research (BMBF), etc.)**

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URL: **[---]***

Status

- Recruitment Status: **Recruiting withdrawn before recruiting started**
- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

** This entry means the parameter is not applicable or has not been set.*
**** This entry means that data is not displayed due to insufficient data privacy clearing.*