

# Distal pancreatectomy, minimally invasive or open, for malignancy

<b>Submission date</b> 16/04/2018	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 19/04/2018	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 28/05/2024	<b>Condition category</b> Surgery	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Cancer of the body or tail (or distal part) of the pancreas is a devastating disease with a 5-year survival of 20% after intended curative treatment. Surgery is the only potentially curative treatment for pancreatic cancer but the postoperative morbidity (30%) and mortality rates (3-5%) are high. Minimally invasive (keyhole) surgery is on the rise worldwide. These procedures are performed through tiny incisions instead of one large opening. Several studies suggest that minimally invasive surgery is superior to conventional open surgery in terms of post-operative pain, morbidity and length of hospital stay. The introduction of minimally invasive pancreatic surgery has been much slower than for other surgical procedures, although the number of minimally invasive pancreatic resections performed has increased significantly in the past decade. Minimally invasive distal pancreatectomy (MIDP) has been shown in recent systematic reviews to have excellent outcomes in benign or premalignant disease concerning intraoperative and postoperative outcomes (i.e. blood loss, spleen preservation, postoperative morbidity, postoperative recovery) when compared to open distal pancreatectomy (ODP). However high-quality comparative studies of minimally invasive versus open surgery for distal pancreatic malignancies are scarce. Surgeons are faced with the decision to perform a MIDP or ODP in a patient with pancreatic cancer without clear evidence to support them. Especially oncological safety is not clearly demonstrated. At this moment a substantial amount of pancreatic cancer patients do not receive minimally invasive surgery and consequently may not benefit from possible shorter time to recovery and better quality of life after surgery, which especially for these patients with poor prognosis could be of substantial value. The aim of this study is to provide evidence on the potential benefits of minimally invasive surgery in patients with cancer of the body or tail of pancreas.

### Who can participate?

Patients aged 18 or over who require resection of their distal pancreas for pancreatic ductal adenocarcinoma (PDAC), a type of pancreatic cancer

### What does the study involve?

Participants are randomly allocated to either open or minimally invasive surgery. They receive a large abdominal dressing directly after surgery to mask their treatment (minimally invasive or open) by covering all incisions. This abdominal dressing is removed when recovery is complete,

at day 5 after the operation or for medical reasons, such as for example suspicion of a wound infection. Participants complete quality of life questionnaires at the start of the study, and 1, 3 and 6 months after their surgery. Survival rates are calculated for 1, 2 and 3 year after the surgery.

What are the possible benefits and risks of participating?

Minimally invasive surgery may reduce the length of the hospital stay and improve postoperative morbidity and mortality. There are no added risks.

Where is the study run from?

This study is led by the University Hospital Southampton NHS Foundation Trust (UK) and Amsterdam UMC (The Netherlands). Patients are recruited by 38 centres from 12 countries.

When is the study starting and how long is it expected to run for?

January 2018 to May 2024

Who is funding the study?

1. The Dutch Digestive Foundation (The Netherlands)
2. Academic Medical Center, Amsterdam (The Netherlands)
3. Ethicon Endo-surgery Inc.
4. Medtronic

Who is the main contact?

1. Prof. Mohammed Abu Hilal
2. Prof. Marc Besselink

### **Study website**

<http://www.e-mips.org/diploma-trial>

## **Contact information**

### **Type(s)**

Scientific

### **Contact name**

Prof Mohammed Abu Hilal

### **Contact details**

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**Additional identifiers****EudraCT/CTIS number**

Nil known

**IRAS number****ClinicalTrials.gov number**

NCT04483726

**Secondary identifying numbers**

The United Kingdom: RHMGSU0230, CPMS ID 37581; The Netherlands: NL63299.018.17

**Study information****Scientific Title**

Distal pancreatectomy, minimally invasive or open, for malignancy (DIPLOMA): a pan-European, randomized controlled, multicenter, patient blinded, non-inferiority trial

**Acronym**

DIPLOMA

**Study objectives**

The trialists hypothesise that minimally invasive (laparoscopic and robot-assisted) distal pancreatectomy (MIDP) provides similar oncologic efficacy (i.e. microscopically radical resection margins (R0)) to open distal pancreatectomy (ODP) when performed in patients affected by PDAC.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

1. The United Kingdom: South West - Frenchay Research Ethics Committee, 08/03/2018, ref: 18/SW/0047

2. The Netherlands: Medical Ethics Review Committee of Amsterdam UMC, location Academic Medical Center, 25/01/2018, ref: NL63299.018.17

For the following countries, separate ethical approvals have been obtained: Belgium, France, Germany, Italy, Norway, Russia, Slovenia, Spain, Sweden, Finland and the USA.

**Study design**

Multicenter; Randomized 1:1 ratio; Interventional; Patient-blinded

**Primary study design**

Interventional

**Secondary study design**

Randomised controlled trial

**Study setting(s)**

Hospital

**Study type(s)**

Treatment

**Participant information sheet**

The Patient Information Sheet (English and Dutch) will be available on the following website:  
<http://www.e-mips.org/diploma/>

**Health condition(s) or problem(s) studied**

Proven or suspected pancreatic ductal adenocarcinoma (PDAC) in the pancreatic body or tail suitable for elective upfront distal pancreatectomy

**Interventions**

This study is designed for patients with an indication for distal pancreatectomy because of proven or suspected PDAC in the pancreatic body or tail. After inclusion, patients are randomly allocated in a 1:1 ratio to Minimally Invasive Distal Pancreatectomy or Open Distal Pancreatectomy, stratified by hospital volume and tumor involvement of other organs besides the pancreas and spleen. Randomization will take place as soon as the distal pancreatectomy can be planned. Patients will have a pre-surgery assessment conform local protocol.

Patients are blinded for the type of surgery they will receive. Patients will receive a large 40cm x 40cm abdominal dressing directly after surgery to mask their treatment (minimally invasive or open) by covering all incisions. This abdominal dressing will be removed when all criteria for functional recovery are met, and may be removed earlier when it's day 5 postoperatively or for medical reasons, such as for example suspicion of a wound infection. If earlier inspection is required, attempts are made to maintain patient blinding. This blinding has been proven successfully in previous multicentre (European) trials. A complete double-blinding, including medical and nursing ward staff, is considered not feasible.

Patients are asked to complete QoL questionnaires at baseline, 1 month, 3 months and 6 months after their surgery. Survival rates will be calculated for 1, 2 and 3 year postoperative.

**Intervention Type**

Procedure/Surgery

**Primary outcome measure**

Microscopically radical resection margin (R0) (these can be in the transection margin of the pancreas but also in the anterior, superior, posterior, inferior margins, i.e. circumferential margins); Timepoint: postoperative

## Secondary outcome measures

1. Intraoperative parameters (operative time, blood loss, blood transfusion and conversion)
2. Postoperative parameters (complications, mortality, re-interventions)
3. Pathology parameters (tumor size, lymph node retrieval, positive nodes, invasion, grading and staging)
4. Hospitalization parameters (time to functional recovery [measured daily using the functional recovery checklist], total hospital stay, readmission, intensive care admission)
5. Oncology parameters (use of (neo-)adjuvant chemotherapy, survival at 1, 2 and 3 years postoperative)
6. Quality of life, measured using the EORTC QLQ-30 and PAN-26 and EQ-5D-5L questionnaires at baseline and 1, 3 and 6 months postoperative
7. Costs

## Overall study start date

04/01/2018

## Completion date

05/05/2024

# Eligibility

## Key inclusion criteria

In order to be eligible to participate in this study, a patient must meet all of the following criteria:

1. Age  $\geq 18$  years
2. Elective indication for distal pancreatectomy for proven or suspected\* PDAC
3. Upfront (without induction/downsizing radio- or chemotherapy) resectable PDAC in the pancreatic body or tail\*\*
4. The tumor can be radically resected via both minimally invasive or open surgery according to the local treating team\*\*\*
5. The patient is fit to undergo both open and minimally invasive distal pancreatectomy

\*Pathology proof is not mandatory for two reasons, first it is not common practice in distal cancers to have this proof, so the decision for minimally invasive or open surgery will after the trial also depend on the 'suspected' diagnosis and second, there are even some concerns about the safety of endoscopic fine needle aspiration of distal pancreatic cancers with theoretical risk of peritoneal seeding

\*\*Malignant degenerated cysts are not allowed in the study. Neoadjuvant chemotherapy is only allowed in case of an upfront resectable tumor (neoadjuvant)

\*\*Multivisceral resections are allowed if, according to the local treating team, feasible with both, a minimally invasive and open approach

## Participant type(s)

Patient

## Age group

Adult

## Lower age limit

18 Years

**Sex**

Both

**Target number of participants**

258 (129 per arm). The trialists expect every site to include 5-10 patients annually.

**Total final enrolment**

258

**Key exclusion criteria**

Current exclusion criteria as of 19/05/2020:

Patients that meet any of the following criteria will be excluded from participation in this study:

1. American Society of Anesthesiologists classification >3
2. A medical history of chronic pancreatitis (according to the M-ANNHEIM criteria)
3. Second malignancy necessitating resection during the same procedure
4. Distant metastases (M1) including involved distant lymph nodes
5. Tumor involvement or abutment of major vessels (celiac trunk\*, mesenteric artery or portomesenteric vein);
6. Pregnancy
7. Participation in another study with interference of study outcomes

\*The celiac trunk should be 5mm clear from tumor

Previous exclusion criteria:

Patients that meet any of the following criteria will be excluded from participation in this study:

1. ASA >3 (see appendix 17.3.2)
2. A medical history of chronic pancreatitis (according to the M-ANNHEIM criteria, see Appendix for detailed definition)
3. Second malignancy necessitating resection during the same procedure
4. Radiotherapy because of pancreatic cancer prior to distal pancreatectomy
5. Distant metastases (M1) including involved distant lymph nodes
6. Tumor involvement or abutment of major vessels (celiac trunk\*, mesenteric artery or portomesenteric vein);
7. Pregnancy
8. Participation in another study with interference of study outcomes

\*The celiac trunk should be 5mm clear from tumor

**Date of first enrolment**

01/05/2018

**Date of final enrolment**

07/05/2021

**Locations****Countries of recruitment**

Belgium

England

France

Germany

Italy

Netherlands

Norway

Russian Federation

Slovenia

Spain

Sweden

United Kingdom

United States of America

Wales

**Study participating centre**

**Amsterdam UMC**

Amsterdam

Netherlands

-

**Study participating centre**

**Erasmus Medical Center**

Rotterdam

Netherlands

-

**Study participating centre**

**Radboud University Medical Center**

Nijmegen

Netherlands

-

**Study participating centre**

**Catharina Hospital**

Eindhoven  
Netherlands

-

**Study participating centre**

**Utrecht Medical Center**

Utrecht  
Netherlands

-

**Study participating centre**

**St Antonius Hospital**

Nieuwegein  
Netherlands

-

**Study participating centre**

**University Hospital Southampton**

Southampton  
United Kingdom  
SO16 6YD

**Study participating centre**

**Morrison Hospital**

Swansea  
United Kingdom  
SA6 6NL

**Study participating centre**

**Oxford University Hospital**

Oxford  
United Kingdom  
OX3 9DU

**Study participating centre**



**King's College Hospital**

London

United Kingdom

SE5 9RS

**Study participating centre**

**University Hospital Birmingham**

Birmingham

United Kingdom

B15 2TH

**Study participating centre**

**The Freeman Hospital**

Newcastle Upon Tyne

United Kingdom

NE7 7DN

**Study participating centre**

**Lübeck University Hospital**

Lübeck

Germany

-

**Study participating centre**

**Universitätsklinikum Freiburg**

Freiburg

Germany

-

**Study participating centre**

**Universitätsklinikum Erlangen**

Erlangen

Germany

-

**Study participating centre**

**Heidelberg University Hospital**

Heidelberg

Germany

-

**Study participating centre**

**Oslo University Hospital and Institute for Clinical Medicine**

Oslo

Norway

-

**Study participating centre**

**Linköping University**

Linköping

Sweden

-

**Study participating centre**

**Verona University Hospital**

Verona

Italy

-

**Study participating centre**

**Università de Pisa**

Pisa

Italy

-

**Study participating centre**

**Pederzoli Hospital**

Peschiera

Italy

-

**Study participating centre**

**S. Orsola-Malpighi Hospital**

Bologna

Italy

-

**Study participating centre**

**San Raffaele Hospital IRCCS**

Milan

Italy

-

**Study participating centre**

**Niguarda Ca' Granda Hospital**

Milan

Italy

-

**Study participating centre**

**Humanitas University Hospital**

Milan

Italy

-

**Study participating centre**

**University Hospital Pavia**

Pavia

Italy

-

**Study participating centre**

**Hospital of Beaujon**

Beaujon

France

-

**Study participating centre**

**Centre Hospitalier Regional D'Orleans**  
Orleans  
France  
-

**Study participating centre**  
**Hopital Saint Eloi**  
Montpellier  
France  
-

**Study participating centre**  
**Institut Mutualiste Montsouris**  
Paris  
France  
-

**Study participating centre**  
**Hospital del Mar**  
Barcelona  
Spain  
-

**Study participating centre**  
**Hospital Clínic de Barcelona**  
Barcelona  
Spain  
-

**Study participating centre**  
**Hospital Josep Trueta**  
Girona  
Spain  
-

**Study participating centre**

**Hospital Universitari Vall d'Hebron**  
Barcelona  
Spain  
-

**Study participating centre**  
**Ghent University Hospital**  
Ghent  
Belgium  
-

**Study participating centre**  
**University Medical Center Ljubljana**  
Ljubljana  
Slovenia  
-

**Study participating centre**  
**Moscow Clinical Scientific Center**  
Moscow  
Russian Federation  
-

**Study participating centre**  
**Virginia Mason Medical Center**  
Seattle  
United States of America  
-

**Study participating centre**  
**Poliambulanza Foundation Hospital**  
Brescia  
Italy  
-

**Sponsor information**

**Organisation**

University Hospital Southampton NHS Foundation Trust

**Sponsor details**

Mailpoint 18  
Southampton General Hospital  
Tremona Road  
Southampton  
England  
United Kingdom  
SO16 6YD

**Sponsor type**

Hospital/treatment centre

**Organisation**

Academic Medical Center

**Sponsor details**

Meibergdreef 9  
Amsterdam  
Netherlands  
1105 AZ

**Sponsor type**

Hospital/treatment centre

**Website**

<https://www.amc.nl/web/Zorg.htm>

**ROR**

<https://ror.org/03t4gr691>

**Funder(s)****Funder type**

Charity

**Funder Name**

Maag Lever Darm Stichting; Grant Codes: I 17-08

**Alternative Name(s)**

Dutch Liver Foundation, Stomach Liver Bowel Foundation, MLDS

**Funding Body Type**

Private sector organisation

### **Funding Body Subtype**

Trusts, charities, foundations (both public and private)

### **Location**

Netherlands

### **Funder Name**

Academisch Medisch Centrum

### **Alternative Name(s)**

Academic Medical Center, AMC

### **Funding Body Type**

Private sector organisation

### **Funding Body Subtype**

Universities (academic only)

### **Location**

Netherlands

## **Results and Publications**

### **Publication and dissemination plan**

The results of this study will be submitted to a high-impact peer-reviewed medical journal regardless of the study outcome.

### **Intention to publish date**

01/11/2024

### **Individual participant data (IPD) sharing plan**

The data sharing plans for the current study are unknown and will be made available at a later date.

### **IPD sharing plan summary**

Data sharing statement to be made available at a later date

### **Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol article</a>		09/09/2021	13/09/2021	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Results article</a>		06/07/2023	17/07/2023	Yes	No