Locally Advanced Pancreatic Cancer After Systemic Therapy: Ablative MR-guided Radiotherapy (LAPSTAR) - a Randomized Controlled Trial

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To improve survival and qualitity of life in patients with LAPC using ablative treatment with MRgRT (5x10Gy) in addition to standard of care.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Miscellaneous and site unspecified neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON56693

Source
ToetsingOnline

Brief title
LAPSTAR

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
locally advanced pancreatic carcinoma, pancreatic cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: KWF

Intervention

Keyword: Ablative MR guided radiotherapy, Home monitoring, Locally advanced pancreatic carcinoma, Quality of life

Outcome measures

Primary outcome

The primary outcome is health-related quality of life deterioration-free survival, defined as the Time Until Definitive Deterioration (TUDD) including death from any cause, calculated from the time of randomization.

HRQoL is primarily assessed using the EORTC QLQ-C30 (version 3.0) Summary Score. TUDD is defined as a definitive deterioration of >=10 points on Summary Score (with no further improvement of >=10 points afterwards) or death from any cause are considered an event. HRQoL is assessed longitudinally at inclusion (baseline, prior to MRgRT), after two weeks, after four weeks and every subsequent two months until end of study follow-up or death.

Secondary outcome

Secondary objectives in both study arms are:

- To assess individual components of the composite endpoint (HRQoL Summary Score, overall survival)

- To assess other HRQoL components from the EORTC QLQ-C30 and HRQoL according to the EORTC QLQ-PAN26 and EQ5D-5L questionnaires23-25

- To assess continuation of systemic therapy and/or administration of

subsequent treatments (e.g., surgery, second-line systemic treatment, experimental treatment in clinical studies etc.), recommendations from multidisciplinary team meetings, reasons for refraining from recommended therapy, and reasons for discontinuation of therapy (i.e., start of best supportive care)

- To assess tumor response on imaging according to RECIST criteria in patients who receive imaging procedures during follow-up (no part of the trial follow-up)26

- To assess the need for palliative interventions (pain medication, stent placement, bypass surgery)

- To assess the cost-effectiveness (early Health Technology Assessment)

- To assess serum CA 19-9 response in patients in whom serum CA 19-9 is measured (no part of the trial follow-up)

- To assess the feasibility of Trial@home monitoring devices for home monitoring of pancreatic cancer patients

- To quantify the correlation of the obtained digital data from Trial@home with clinical endpoints

- To exploratively generate new digital biomarkers from the data collected from Trial@home (e.g., early signs of adverse evernts, clinical deterioration and/or quality of life)

Secondary Objectives for the intervention arm only are:

• To assess acute (3 months) RT-related toxicity measured from the start of MRgRT, according to CTCAE v527

• To assess completion of therapy

• To assess correlation of diffusion weighted images at each treatment fraction

and the possible correlation with outcomes for patients treated on a 1.5T

MR-Linac

Exploratory endpoints in both study arms:

- To analyse tumor biopsies (fine-needle biopsies; FNB), tumor cytology

(fine-needle aspiration; FNA) and blood samples acquired in the diagnostic

work-up and follow-up, to identify subtypes that predict treatment response and

understand genetic, epigenetic, metabolic, and immune subtypes.

- To analyse medical imaging data acquired in the diagnostic work-up and

follow-up of patients to identify potential radiomics patterns / biomarkers,

and learn about the morphological changes in response to MRgRT and how those

related to response.

Study description

Background summary

About 40% of pancreatic cancer patients are diagnosed with locally advanced pancreatic cancer (LAPC). Recommended treatment consists of chemotherapy to prevent disease dissemination and prolong survival. Nevertheless, local tumor growth causes severe morbidity, including pain, gastrointestinal obstruction and malnutrition. This has a substantial negative impact on health-related quality of life (HRQoL). Eventually, one-third of patients die due to local tumor growth rather than from systemic disease spread. For palliation of symptoms and improved local tumor control, potentially prolonging survival, minimally-invasive ablative therapies are needed.
Online adaptive stereotactic Magnetic Resonance-guided radiotherapy (MRgRT) is an innovative treatment modality that enables high-precision ablative therapy for pancreatic tumors. This potentially improves radiotherapy efficacy without

increasing the risk of treatment-related toxicity. Consequently, MRgRT holds promise for treatment of pancreatic cancer.

Study objective

To improve survival and qualitity of life in patients with LAPC using ablative treatment with MRgRT (5x10Gy) in addition to standard of care.

Study design

LAPSTAR is a multicenter randomized trail. (RCT).
All patients in the Netherlands with LAPC who cannot undergo surgery after initial systemic therapy with (m)FOLFIRINOX or gemcitabine/nab-paclitaxel can be included.
Randomization will take place after obtaining informed concentrations. Patients will be randomized 1:1 into the intervention or control arm.
Patients in the intervention arm will be treated with 5x10Gy MRgRT in combination with standard treatment. MRgRT will be performed at one of the consortium centers (UMCU, AUMC, Radboudumc or Catharina Hospital).
Standard treatment may include chemotherapy ((m)FOLFIRINOX or gemcitabine/nab-paclitaxel) or other supportive therapies.
Patients in the control arm will receive the standard treatment and will not receive additional therapy.

During the study, patients will be asked to complete quality of life questionnaires (EORTC QLQ-C30, EORTC QLQ-PAN26, EQ5D-5L)).
Follow-up time is 18 months.

Intervention

Ablative MR-guided radiotherapy (MRgRT) in addition to standard of care, consitsting of 5x10 Gy MRgRT.

Study burden and risks

Patients in the interventional arm have minimal additional risks compared to patients in the control arm. There is a very small risk of harm due to MRgRT.
The most common side effects of radiation therapy are: fatigue, pain, diarrhoea, nausea, weight loss and intestinal discomfort. These side effects, however, often improve quickly in the period after radiotherapy.
Serious side effects such as obstruction perforation and bleeding of the gastrointestinal tract are rare.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Pathology proven pancreatic ductal adenocarcinoma (PDAC);
- At least two (preferably four) months systemic therapy with (m)FOLFIRINOX and/or gemcitabine + nab-paclitaxel; or eligibility for chemotherapy but no initiation of chemotherapy based on patients* wish;
- No option for surgical resection, either because anatomical irresectability based on the surgeon*s judgement (assessed on imaging or during explorative laparotomy) and/or frailty (unfit for surgery or chemotherapy) and/or no surgery based on patient's wish.
- No evidence of distant metastatic disease progression, evaluated by CT Thorax / Abdomen / Pelvis and/or PET-CT scan;
- Performance status WHO 0-2.

Exclusion criteria

- Contra-indications for MRI or CT with an intravenous contrast agent according to the protocol of the local radiology and/or radiotherapy departments
- Contraindications for MRgRT, as determined by the involved expert radiation oncologists of the Consortium
- <18 years old
- Pregnancy

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	06-06-2024
Enrollment:	156
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	11-04-2024
Application type:	First submission
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT06272162
CCMO	NL85622.041.24