The DRAGON-PLC trial: An international multicentre randomised controlled trial to compare combined Portal and Hepatic Vein Embolisation (PVE/HVE) with PVE alone in patients with primary liver cancers.

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To evaluate the effect of combined PVE/HVE compared to PVE alone on resectability and overall survival in patients with primary liver cancers.

Ethical review	Approved WMO
Status	Pending
Health condition type	Hepatobiliary neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON57347

Source
ToetsingOnline

Brief title
The DRAGON-PLC trial

Condition

- Hepatobiliary neoplasms malignant and unspecified
- Hepatobiliary neoplasms malignant and unspecified
- Hepatobiliary therapeutic procedures

Synonym
hepatocellular carcinoma / cholangiocarcinoma, primary liver cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: ZonMw;KCE,KWF en mogelijk de NIHR (voor financiering in het VK).

Intervention

Keyword: Combined Portal and Hepatic Vein Embolization (PVE/HVE), Future Liver Remnant (FLR), Hypertrophy, Primary Liver Cancer (PLC)

Outcome measures

Primary outcome

A split primary endpoint will be evaluated: resectability and overall survival.

* The FLR is considered sufficient for resection 3 weeks after embolisation.

Definition resectable: Patients are deemed resectable if the FLR is >=30% in normally functioning livers, >=40% in livers with potentially impaired function (e.g. resulting from prior systemic therapy or bile duct colonization / transpapillary biliary drainage), or >=50% in livers with severely impaired function resulting from liver cirrhosis (max. Child Pugh A5) OR for any FLR volume, function on hepatobiliary scintigraphy is > 2.67 %/min/m2

* 5-year overall survival

Secondary outcome

Additional outcomes will be assessed in order to compare PVE/HVE to PVE embolisation. These endpoints entail several read-outs regarding liver growth, complications and 90-day survival after embolization and resection, clinical resection rates, composites of resectability and 90-day survival, QoL of the patient, costs, salvage procedures in case of insufficient FLR growth after

embolization, recurrence and oncological interventions during follow-up. A

detailed overview of all secondary endpoints is given in Section 4.

Study description

Background summary

Primary liver cancer (PLC) is the third most common cause of cancer death worldwide. Surgical resection is the mainstay for a curative approach as contemporary chemotherapy and immune-based therapies only lead to a median survival of 10-14 months. A complete surgical resection increases the median survival to 42 months (range 32-52 months). However, PLC is mainly diagnosed at an advanced stage and >70% of PLC patients are ineligible for an immediate surgical approach. There are different reasons that make a patient ineligible for surgery, one important reason is the risk of liver failure after the surgery due to a small remnant liver.
This study aims to improve the oncological, radiological and surgical strategy to allow more patients to undergo liver resection safely, to improve quality of life and to extend overall survival at acceptable costs.
Adequate function of the future liver remnant (FLR) is a prerequisite for surgical resectability. This is necessary in order to avoid liver failure after surgery, a major cause of morbidity (38%) and mortality (27%). To mitigate this risk, regenerative strategies based on preoperative calculation of the FLR volume and function are essential. Patients with technically resectable disease but predicted insufficient FLR volume or function are referred to as primarily unresectable or potentially resectable (PU/PR). These patients can undergo strategies that capitalize on the regenerative capacity of the liver which aim to preoperatively increase the FLR volume and function in order to allow surgery. Many of the patients that are primarily unresectable due to an insufficient FLR can become ultimately and safely resectable after the induction of adequate FLR-hypertrophy by the current standard, portal vein embolisation (PVE). However, 25% of patients do not show sufficient FLR growth after PVE and are unable to safely undergo resection. A new approach has been developed to improve this. Combined portal and hepatic vein embolisation (PVE/HVE) has great promise in terms of increasing FLR growth, resection rate (RR), safety and potentially, overall survival. Establishing PVE/HVE as the new standard could result in increased survival and a better quality of life (QoL) for patients.

Study objective

To evaluate the effect of combined PVE/HVE compared to PVE alone on

resectability and overall survival in patients with primary liver cancers.

Study design

An international multicentre randomised controlled trial (see appendix A for an overview of all participating centres) in which patients will be randomised (1:1) in centre and cancer type-stratified blocks into two arms: combined PVE/HVE and PVE alone. In total 358 patients will be included (n=179 patients per arm).

Intervention

The study interventions consist of a combined Portal Vein and Hepatic Vein Embolisation (PVE/HVE) in the intervention group and PVE only in the control group. After the intervention, patients will have follow-up visits with computed tomography (CT) liver volumetry scans at 1 week, 3 weeks and 6 weeks after embolisation. If a sufficient FLR volume is already reached after 1 week or 3 weeks, the subsequent visits are no longer necessary.

Study burden and risks

There are no trial-specific risks expected for the group receiving PVE/HVE treatment. Based on a previous safety study (DRAGON 1) and retrospective analyses, no increased risk of adverse outcomes is expected between groups. Hospital visits, admissions and number of follow-up appointments do not differ between the intervention group and the standard care. On average, the procedure of the intervention group will be one hour longer. Patients will be asked to fill out questionnaires at six time points during the first year after inclusion, twice in the second year and third year, and once a year in year 4 and 5. Overall, the additional burden of patients receiving the planned intervention compared to standard treatment is limited.
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Contacts

Public
Universiteit Maastricht

Universiteitssingel 50
Maastricht 6229 ER
NL
Scientific
Universiteit Maastricht

Universiteitssingel 50
Maastricht 6229 ER
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- PLC diagnosis, specifically intrahepatic cholangiocarcinoma (iCCC), perihilar cholangiocarcinoma (pCCC), and hepatocellulair carcinoma (HCC);
- Requiring PVE due to an FLR volume is <30% in normally functioning livers, <40% in livers with potentially impaired function e.g. resulting from prior systemic therapy induction or bile duct colonization / transpapillary biliary drainage, or <50% in livers with severely impaired function resulting from liver cirrhosis (max. Child Pugh A5) OR function on hepatobiliary scintigraphy (HEBIS) is < 2.67 %/min/m2;
- Age >= 18 years;
- Able to understand the trial and provide informed consent.

Exclusion criteria

- Liver cirrhosis with a Child-Pugh score of B or C;
- Presence of portal hypertension;
- Presence of cholangitis;
- Pregnant women;
- Premenopausal females not able/willing to commit to contraception (specifically long-acting reversible contraception or hormonal contraception);
- Patients unresectable due to prohibitive comorbidities (decision made by local multidisciplinary team);
- Patients with hepatic malignancies other than iCCC, pCCC or HCC;
- PVE/HVE anatomically not feasible;

- Any patient with non-resectable or non-ablatable extrahepatic metastatic disease.
- Unable to understand the study information, study instructions and give informed consent.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	03-03-2025
Enrollment:	72
Type:	Anticipated

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	14-03-2025
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
CCMO	NL87590.068.24