DRAGON 1 - training, accreditation, implementation and safety evaluation of Portal and Hepatic Vein Embolization (PVE/HVE) to accelerate Future Liver Rem-nant (FLR) hypertrophy

Published: 26-03-2020
Last updated: 21-09-2024

DRAGON I is a pre-trial that aims to introduce PVE/HVE in liver surgery centers worldwide in a controlled fashion to ensuring patient safety, proper data monitoring and a critical assessment of efficacy. The goal of DRAGON 1 is to assemble the...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Observational invasive

Summary

ID

NL-OMON54956

Source
ToetsingOnline

Brief title
DRAGON 1 trial

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC
- Hepatobiliary neoplasms malignant and unspecified

Synonym
1. Colorectal cancer liver metastases (CRLM) 2.

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: Koninklijk Wilhelmina Fonds

Intervention

Keyword: CRLM- colorectal cancer liver metastases, FLR- Futrure liver remnant, HVE- Hepatic vein embolisation, PVE- portaal vene embolisatie

Outcome measures

Primary outcome

• Demonstrate ability of center to enroll 3 patients in 12 months safely

Secondary outcome

• Efficacy assessment of hypertrophy induced

• Assessment of variety of techniques

- LVD vs. Double vein embolization vs. staged PVE/HVE

• Feasibility assessment (proceeding to resection)

• Safety of PVE/HVE (mortality/ morbidity)

• Oncological effectiveness of PVE/HVE (recurrence/progression

Study description

Background summary

Extended hemi-hepatectomies are sometimes used to render initially nonresectable patients with colorectal cancer liver metastases (CRLM) resectable after conversion chemotherapy. In order to prevent post hepatectomy liver failure (PHLF), these resections should only be performed if FLR volume is at least 30% - 40% of the total volume of the liver, excluding the volume of the metastases themselves. If FLR volume is not sufficient to allow liver resection, portal vein embolization (PVE) is now standard treatment to increase the FLR volume. The downside of PVE is that only between 60-70% of patients end up with complete tumor resections, largely due to the slow hypertrophy induced, hesitancy to resect when volume cut-offs are not met and oncological selection

due to early recurrence.
Recently, an alternative method has been introduced to accelerate FLR hypertrophy. This method became known as Associating Liver Partition and Portal vein Ligation for staged hepatectomy (ALPPS). It has been shown in a randomized controlled trial (LIGRO trial) that resection rate in ALPPS is higher than in PVE. In ALPPS, rapid hypertrophy is induced by transection of the parenchyma between the FLR and the deportalized lobe and abrogation of collateral flow. However, functional transection by radiofrequency ablation or banding is also effective. Recently it was demonstrated that abrogation of the venous outflow of the deportalized lobe also induces rapid hypertrophy, a method that has been propagated as *Liver venous deprivation/ Portal and Hepatic vein embolization*. Such deprivation can be performed by embolizing the portal vein on one side of the liver and also occlude the outflow veins with umbrellas and glue at the same side. This simultaneous combination of portal vein embolization and embolization of the hepatic veins (right and/or middle) has been shown in patients to accelerate FLR hypertrophy similarly to ALPPS.
In contrast to ALPPS however, the first stage is a radiology intervention only, similarly to PVE.

Study objective

DRAGON I is a pre-trial that aims to introduce PVE/HVE in liver surgery centers worldwide in a controlled fashion to ensuring patient safety, proper data monitoring and a critical assessment of efficacy. The goal of DRAGON 1 is to assemble the participating centers for DRAGON 2, a future randomized trial of PVE/DVE vs. PVE.

Study design

Multicenter, international, prospective, multi-center trial to test enrolment capacity of participants and safety of Portal and Hepatic Vein Embolization (PVE/HVE): DRAGON 1 will form the basis of a planned subsequent trial (*DRAGON 2*) that will compare PVE with PVE/HVE.

Study burden and risks

We have no evidence that the novel procedure of occluding both portal and hepatic vein is associated with more risks than the conventional procedure of occluding only the portal vein. In both procedures, low-grade fevers, pain over the liver and general exhaustion for a few days have been described.

The new methods of portal vein and hepatic vein occlusion promises to accelerate growth of the healthy liver. This may result in reducing the waiting time to surgery. The new method may also the likelihood for participating patients to have a curative resection to start with.

Contacts

Public
Universiteit Maastricht

Universiteitssingel 40
Maastricht 6229 ER
NL
Scientific
Universiteit Maastricht

Universiteitssingel 40
Maastricht 6229 ER
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Inclusion criteria
• Patients with primarily unresectable/potentially resectable CRLM after conversion chemotherapy with a FLR <30% in normal livers or 40% in livers chemotherapy damaged livers. We trust the clinical judgement of teams in the participating centers to only include those patients who require regenerative liver surgery and not those that are primarily resectable
• 18 Years and older
• Patients up to ECOG 3 (not more than 50% bedbound)
• Patients with non-resected primary colorectal cancer (CRC) may be included if and only if there is an intent to remove the CRC after the liver treatment (liver first approach)
• Staging CT chest and (if symptomatic) CT/MRI brain needs to exclude

unresectable extrahepatic disease, while metastatic disease that may be cured in the future, is included
• Patients with resectable lung metastases or lung metastases that and be ablated can be included only after statement about resectability/ablatability by tumor board
• Patients have to be to understand the trial and provide informed consent.

Exclusion criteria

Exclusion criteria
• Patients with extrahepatic disease other than lung metastases
• Patients with metastatic disease to the lung that cannot be ablated or resected will be excluded
• Patients with intrahepatic Cholangiocarcinoma (IHCC)
• Patients with Perihilar Cholangiocarcinoma (PHCC)
• Patients with Hepatocellular Carcinoma (HCC)
• Pregnant or lactating women will be excluded. Women in conceiving age are required to take contraceptives or have to provide documentation of other means of contraception to be enrolled.
• Progression by modified RECIST criteria on cross-sectional imaging after conversion chemotherapy is an exclusion criterion.
• Complete response in cross-sectional imaging after conversion chemotherapy, which is certainly a rare event

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-05-2020
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO Date:	26-03-2020
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	13-08-2021
Application type:	Amendment
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	NL71535.068.19