

## Trial Description

### Title

**Laparoscopic Split-PVE vs. PVE alone for Generation of Hypertrophy Before Major Liver Resection - A randomized controlled trial**

### Trial Acronym

**LAS VEGAS**

### URL of the trial

[---]\*

### Brief Summary in Lay Language

**Liver failure following liver surgery is a life-threatening complication. The risk of liver failure is directly linked to the liver volume following surgery. Therefore, various strategies were developed to increase the liver volume before surgery for safety reasons. The current standard of care is portal vein embolization (PVE) that blocks the blood flow to the liver sections which are planned to be removed and redirects the blood flow to the future liver remnant resulting in liver growth (=hypertrophy). An alternative approach is to divide the liver tissue surgically by a minimally-invasive approach (laparoscopic in-situ split) while the vessels remain intact and supplement the procedure with PVE. The liver surgery with removal of the affected liver sections will be performed subsequently if the desired volume of the future liver remnant is achieved. The present study is the first prospective study investigating which one of these two techniques is more efficient and safer for the patients. The study is planned as a randomized trial comparing laparoscopic in-situ split with PVE (=Split-PVE) to PVE alone with reference to the level of liver growth (=hypertrophy rate) at 10 days after PVE. Patients will be followed up for 24 months and surgical, oncological as well as outcomes of the quality of life will be assessed. In addition, blood and liver tissues will be collected during the study to evaluate the effect of liver growth in the study groups.**

### Brief Summary in Scientific Language

**Portal vein embolization (PVE) is the standard of care for preoperative induction of liver hypertrophy and generates up to 43% hypertrophy rates of the future liver remnant (FLR) within 4 to 8 weeks. However, during the waiting period for hypertrophy, up to 40% of patients develop tumor progression and are no longer candidates for curative resections. An alternative approach to PVE is Associating Liver Partition and Portal vein Ligation for Staged hepatectomy (ALPPS) - a combination of hepatic transection with portal vein ligation. Although the FLR hypertrophy is higher with ALPPS compared to PVE, this technique is associated with significant postoperative morbidity and mortality rates. Recently, minimally-invasive partial liver partitioning in combination with PVE (Split-PVE) was found to be an alternative technique to ALPPS by avoiding surgical dissection of the hepatic hilum in the first stage with potentially lower postoperative morbidity rates. Furthermore, Split-PVE is probably associated with a more pronounced liver hypertrophy compared to PVE alone due to occlusion of intrahepatic shunts. To date, no prospective trial has been performed evaluating the efficacy and safety**

**of Split-PVE vs. PVE, as well as a laparoscopic approach of liver partitioning. Although there is rising evidence for a plateau of liver hypertrophy after 3-weeks of PVE, liver hypertrophy assessments following PVE are made typically 4-6 weeks following intervention with an increased risk of tumor progression. The present study was designed on the assumption that a minimum difference of 5% liver hypertrophy at 10 days is clinically relevant between the study groups.**

**Do you plan to share individual participant data with other researchers?**

**No**

**Description IPD sharing plan**

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## Organizational Data

- DRKS-ID: **DRKS00021607**
- Date of Registration in DRKS: **2020/04/29**
- 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.: **2020-531N , Medizinische Ethik-Kommission II Medizinische Fakultät Mannheim der Universität Heidelberg**

## Secondary IDs

- Universal Trial Number (UTN): **U1111-1251-0557**

## Health condition or Problem studied

- ICD10: **C22 - Malignant neoplasm of liver and intrahepatic bile ducts**

## Interventions/Observational Groups

- Arm 1: **Split-PVE: Patients randomized to the experimental group will undergo laparoscopic partial in-situ split in a standardized approach. Partial transection of the parenchyma (~50-60%) will be carried out without ligation of the portal vein. Subsequent PVE is carried out within 5±2 days after the liver partitioning.**
- Arm 2: **PVE: Patients randomized to the control group will undergo a portal vein embolization (PVE) in a standardized approach**

## Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: [---]\*
- Allocation: **Randomized controlled trial**
- Blinding: [---]\*
- Who is blinded: [---]\*
- Control: **Active control (effective treatment of control group)**
- Purpose: **Treatment**
- Assignment: **Parallel**
- Phase: **N/A**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **N/A**

## Primary Outcome

**The degree of contralateral hypertrophy at 10 days following PVE is the primary endpoint. The FLR volume will be calculated in percentage as following:  $FLR (ml) / \text{total liver volume (ml)} \times 100 = FLR (\%)$ . The degree of contralateral liver lobe hypertrophy (DH) is defined as the relative increase in volume of the FLR after PVE in both study groups calculated as following:  $FLR_{\text{post-PVE}} - FLR_{\text{pre-PVE}}$ .**

## Secondary Outcome

- **Resectability rate**
- **Postoperative morbidity and mortality**
- **Timing of completion hepatic resection and delayed hepatic resection (days/weeks)**
- **Disease-free and overall survival at 24 months**
- **Differences in circulating biomarkers**
- **Differences in tissue-related biomarkers**
- **Patient-reported outcome**

## Countries of recruitment

- **DE Germany**

## Locations of Recruitment

- University Medical Center **Chirurgische Klinik (Department of Surgery), Mannheim**

## Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2020/07/27**
- Target Sample Size: **60**
- Monocenter/Multicenter trial: **Monocenter trial**
- National/International: **National**

## Inclusion Criteria

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

## Additional Inclusion Criteria

- 1) Indication for major hepatectomy confirmed by multi-disciplinary tumor conference
- 2) Insufficient future liver remnant of total liver volume, defined as:
  - < 30% in patients with healthy liver parenchyma
  - < 40% in patients with diseased liver parenchyma (e.g. chemotherapy-associated steatohepatitis, non-alcoholic steatohepatitis, Child-A liver cirrhosis)
- 3) Age equal to or greater than 18 years
- 4) WHO/ECOG 0-2
- 5) Written informed consent

## Exclusion criteria

- 1) Child B or C liver cirrhosis
- 2) Portal vein thrombosis with complete luminal obstruction affecting the main trunk
- 3) Impaired mental state or language problems
- 4) Expected lack of compliance

## Addresses

### ■ Primary Sponsor

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## Sources of Monetary or Material Support

#### ■ **Institutional budget, no external funding (budget of sponsor/PI)**

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## Status

#### ■ Recruitment Status: **Recruiting ongoing**

#### ■ Reason, if "Recruitment stopped after recruiting started" or "Recruiting withdrawn before recruiting started": [---]\*

#### ■ Reason, if Reason for Recruiting Stop "Other": [---]\*

DRKS-ID: **DRKS00021607**

Date of Registration in DRKS: **2020/04/29**

Date of Registration in Partner Registry or other Primary Registry: [---]\*

- Study Closing (LPLV): [---]\*
- Number of Participants in Germany after Recruiting complete: [---]\*
- Total Number of Participants (all Sites worldwide) after Recruiting complete: [---]\*

## 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.