

# The use of stem cells to assist in regenerating the liver before cancerous parts of the liver are removed

<b>Submission date</b> 12/03/2011	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
<b>Registration date</b> 25/08/2011	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
<b>Last Edited</b> 25/08/2011	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

**Plain English summary of protocol**  
Not provided at time of registration

## Contact information

**Type(s)**  
Scientific

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## Additional identifiers

**Clinical Trials Information System (CTIS)**  
2009-017793-20

**Protocol serial number**  
N/A

# Study information

## Scientific Title

Infusion of intraportal autologous mononuclear bone marrow cells as a liver regeneration enhancer prior to extended hepatectomy. A randomised, open-label multicentre phase II clinical trial

## Acronym

CMMo/RH

## Study objectives

Autotransplanting autologous mononuclear bone marrow cells might enhance hepatic regeneration, administered intraportally prior to surgery, in patients with a hepatic space occupying lesion (SOL) which need an extended hepatic resection (more than five segments) and in which the residual hepatic volume is insufficient to guarantee hepatic function and the necessary safety margins following the resection.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Autonomous Clinical Trials Committee of Andalusia  
Clinical Research Ethics Committee at University Hospital Virgen del Rocio  
Ethics Committee at University Hospital Valme, Seville

## Study design

Prospective multicentre open-label randomised and controlled phase II clinical trial

## Primary study design

Interventional

## Study type(s)

Treatment

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

Use of stem cells in hepatic resection due to hepatic space occupying lesions

## Interventions

1. Control group: right hepatic portal embolization
2. Study group: right hepatic portal embolization plus infusion of stem cells. Generic drug name: mononuclear bone marrow stem cells
3. Dosage given:  $2.000 \times 10^6$  cells
4. Method and frequency of administration: intraportal infusion in a single administration
5. Follow up for all treatment arms: 12 months

## Intervention Type

Other

## Phase

Phase II

## Primary outcome(s)

1. Adverse events and serious adverse events in the first 24 hours of administering the BM-MNCs, and observed in the follow ups at 2, 4 and 6 weeks following cell therapy administration
2. Assessment of the hepatic volume via computed tomography (CT) (10 mm thick axial helical CT with 10 mm reconstruction) at 2, 4 and 6 weeks following the administration of cell therapy (until 8 weeks in cyrrhotic patients):
  - 2.1. In each axial section: volume (cm<sup>3</sup>) = Area (cm<sup>2</sup>) x reconstruction index (cm)
  - 2.2. The volumes are calculated by totalling the areas of each cut
3. The following parameters are used:
  - 3.1. Total hepatic volume (THV)
  - 3.2. Residual hepatic volume (RHV)
  - 3.3. Percentage THV / RHV

## Key secondary outcome(s)

1. Duration of hepatic regeneration (days)
2. Percentage of patients that can be fully operated on
3. Time since [falling ill]
4. Assessment of the hepatic regeneration response:
  - 4.1. TNF-a, interleukina 2, interleukina 6
  - 4.2. Hepatocyte Growth Factor (HGF)
  - 4.3. Epidermal Growth Factor (EGF)
  - 4.4. Transforming Growth Factor Alpha (TGF-a)
  - 4.5. Insulinaemia
  - 4.6. Metanephrines (urine)
5. Inherent post-operative complications regarding the residual hepatic volume (degree of liver failure: Model fo End stage Liver Disease - MELD)
6. Resection margins free from tumours
7. Structured histological assessment of the regenerated hepatic tissue and of the degree of fibrosis

## Completion date

20/03/2013

## Eligibility

### Key inclusion criteria

1. Patients of both sexes aged between 18 and 70
2. Normal analytical parameters, defined by:
  - 2.1. Leukocytes higher than 3,000
  - 2.2. Neutrophils higher than 1,500
  - 2.3. Platelets higher than 100,000
  - 2.4. AST/ALT less than 1.5 standard institutional range
  - 2.5. Creatinine less than 1.5 mg/dl
3. Patients with a hepatic space occupying lesion (SOL) which need an extended hepatic resection (of more than five segments)
4. The selection must be careful and basically include 4 types of hepatic lesions which must previously be submitted to a hepatic volumetry:
  - 4.1. Metastatic disease susceptible to extended right hepatectomy in segment IV
  - 4.2. Metastatic disease susceptible to right hepatectomy with suspected liver disease (neoadjuvant chemotherapy) (when hepatic function is unclear, the indocyanine green test can

be used)

4.3. Bilobar hepatic metastases with multiple nodules in the right lobe, and more than 3 nodules bigger than 30mm in the left hepatic lobe (LHL): tumourectomy of the LHL + ligation of the right portal branch (or post-operative percutaneous embolisation) with a view to carry out a right hepatectomy 4-6 weeks afterwards (two-stage surgery)

4.4. Hepatocarcinoma susceptible to extended right hepatectomy

4.5. Benign Hepatic Lesions (Haemangiomas, Hydatid Cysts, or Primary Hepatic Tumours /Hepatoblastoma), which because of their extension put the viability of the remaining hepatic tissue at risk

5. The pre-operative assessment of the residual hepatic volume should be, following the hepatectomy >30% (>40% in diseased livers)

6. The following definitions/measurements/factors should be included in the evaluation:

6.1. Total hepatic volume: residual hepatic volume (RHV) + resectable hepatic volume

6.2. Resectable hepatic volume: includes the volume of the tumoral lesions plus the surrounding hepatic parenchyma with compromised vascular structures

6.3. Functional hepatic volume: is the difference between the THV and the volume of the lesions

6.4. Residual Hepatic Volume: Terminal Hepatic Volume (THV) - Hepatic Volume (HV) to be resected

7. Patients who give their informed, written consent in order to participate in the study and offer sufficient guarantees regarding their adherence to the protocol, to be judged by the investigator in charge of patient services

8. Women of childbearing age must obtain negative results from a pregnancy test, following the habitual procedures of each hospital at the beginning of inclusion in the study and commit to using a medically approved contraceptive throughout the whole period of the study

### **Participant type(s)**

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Lower age limit**

18 years

### **Sex**

All

### **Key exclusion criteria**

1. Previous neoplastic history or haematological disease (Myeloproliferative disease, Myelodysplastic syndrome or Leukemia)

2. Patients with uncontrolled arterial hypertension (with arterial tension of more than 180/110 on more than one occasion)

3. Severe heart failure - New York Heart Association Class IV (NYHA IV)

4. Patients with malignant ventricular arrhythmias or unstable angina

5. Diagnosis of Deep Vein Thrombosis (DVT) within the last 3 months

6. An active infection or wet gangrene on the day of bone marrow-mononuclear cells (BM-MNCs) infusion

7. Concomitant therapy which includes hyperbaric oxygen, vaso-active substances, agents

- against angiogenesis, cyclooxygenase-II (COX-II) inhibitors
8. Body mass index (BMI) of more than 40 Kg/m<sup>2</sup>
  9. Patients diagnosed as alcoholics at the moment of inclusion
  10. Proliferative retinopathy
  11. A concomitant illness which reduces life expectancy to less than one year
  12. Difficulty in treatment
  13. Heart failure or ejection fraction (EF) < 30%
  14. Cerebrovascular disease or Myocardial infarction in the last 3 months
  15. Pregnant women or women of childbearing age who do not have an adequate method of contraception

**Date of first enrolment**

20/03/2011

**Date of final enrolment**

20/03/2013

## Locations

**Countries of recruitment**

Spain

**Study participating centre**

**Servicio De Cirugia General**

Sevilla

Spain

14013

## Sponsor information

**Organisation**

Department of Health and National Health Service [Ministerio De Sanidad and Consejeria De Salud] (Spain)

**ROR**

<https://ror.org/047pymx40>

## Funder(s)

**Funder type**

Hospital/treatment centre

**Funder Name**

Department of Health (Ministerio De Sanidad) (Spain)

**Funder Name**

National Health Service (Consejeria De Salud De Andalucia) (Spain)

**Results and Publications**

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

**IPD sharing plan summary**

Not provided at time of registration