

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

Submission date 12/03/2011	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
Registration date 25/08/2011	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
Last Edited 25/08/2011	Condition category 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

Contact name

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Additional identifiers

EudraCT/CTIS number

2009-017793-20

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

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 intraportal 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

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

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: 2.000×10^6 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 measure

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: $\text{volume (cm}^3\text{)} = \text{Area (cm}^2\text{)} \times \text{reconstruction index (cm)}$
 - 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

Secondary outcome measures

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. Metanephries (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

Overall study start date

20/03/2011

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 + ligature 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 adhesion 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

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

60

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/m²
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)

Sponsor details

Hospital Universitario Virgen Del Rocio.
Fundacion Progreso Y Salud
Manuel Siurot S/N
Sevilla
Spain
41013

Sponsor type

Hospital/treatment centre

Website

<http://www.msps.es/en>

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**Publication and dissemination plan**

Not provided at time of registration

Intention to publish date**Individual participant data (IPD) sharing plan**

IPD sharing plan summary
Not provided at time of registration