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

Submission date	Recruitment status	[ ] Prospectively registered
12/03/2011	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
25/08/2011	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
25/08/2011	Cancer	[ ] 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

Study information

Scientific Title

Infusion of intraportal autologus 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 x 106 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 (cm3) = Area (cm2) 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 + 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

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, Myelodyplastic 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 arrythmias 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)

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