Clinical trial TC02.

<table>
<tr><td>Title</td><td colspan="4">Infusion of mesenchymal stem cells as treatment for steroid resistant grade II to IV acute GVHD or poor graft function: a multicenter phase II study</td></tr>
<tr><td>Summary</td><td colspan="4"><u>Objective :</u> This clinical study aims at evaluating if an intravenous injection of mesenchymal stem cells could be employed after hematopoietic stem cell transplantation in order to treat acute graft-versus-host disease (GVHD) (1st part of the study), to enhance graft function (2nd part of the study), or to prevent graft rejection (3rd part of the study). This could improve the survival of patients affected by haematological malignancies that are currently treated with hematopoietic stem cell transplantation.

<u>Primary outcome :</u> To establish efficacy of infusions of MSC from mismatched unrelated donors :
(1) Efficacy on steroid-resistant grade II-IV acute GVHD
(2) Efficacy on poor graft function
(3) Efficacy on prevention of graft rejection in patients with low or failing donor T-cell chimerism after allogeneic HCT

<u>Disease :</u> After allogeneic hematopoietic stem cell transplantation :
(1) Steroid-resistant acute GVHD
(2) Poor graft function
(3) Poor chimerism

<u>Treatment :</u> Mesenchymal stem cells (MSC)

Mesenchymal stem cells (MSC) are stem cells that normally give rise to bone, cartilage and fat, but they also have immunosuppressive properties. They can be cultured from the bone marrow of normal volunteers, do not need to be HLA-matched with the patient and can be injected intravenously without significant side effects.</td></tr>
<tr><td>Principal inclusion criteria</td><td colspan="4">• Male or female.
• Any age.
• Previous allogeneic transplantation (related or unrelated donor, any degree of HLA matching) or autologous transplantation (for part 2 only) of HSC at any time before.
• Informed consent given by donor or his/her guardian if of minor age.
• Additional criteria for each part of the protocol.</td></tr>
<tr><td rowspan="4">Type of trial</td><td>Phase</td><td colspan="3">2</td></tr>
<tr><td>Number of patients</td><td colspan="3">(1) Steroid-resistant acute GVHD : 40
(2) Poor graft function : 40
(3) Poor chimerism : 20</td></tr>
<tr><td>Patient allocation</td><td colspan="3">All patients receive the treatment with mesenchymal stem cells</td></tr>
<tr><td>Blinding to treatment</td><td colspan="3">No</td></tr>
<tr><td rowspan="2">Protocol N°</td><td>BHS number</td><td>EC number</td><td>EUDRACT</td><td>ClinicalTrial.org</td></tr>
<tr><td>TC-02</td><td>TJB0703</td><td>2007-004310-14</td><td>NCT00603330</td></tr>
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<tr><td rowspan="3">Principal investigator and sponsor</td><td colspan="2">Principal investigator</td><td>Sponsor</td></tr>
<tr><td>Name</td><td>Institution</td><td rowspan="2">CHU de Liège</td></tr>
<tr><td>Pr Frédéric Baron</td><td>CHU de Liège</td></tr>
<tr><td>Participating centres</td><td colspan="3">• AZ Sint-Jan, Brugge (<u>Dr Selleslag, Dr Lodewyck</u>)
• CHU de liège (<u>Dr Beguin, Dr Baron, Dr Willems</u>)
• Cliniques universitaires de Mont-Godinne, Yvoir (<u>Dr Graux</u>)
• Cliniques universitaires St Luc UCL, Bruxelles (<u>Dr Poiré</u>)
• Hôpital de Jolimont, Haine-St-Paul (<u>Dr Straetmans</u>)
• Hôpital Reine Fabiola, Bruxelles (<u>Dr Ferster</u>)
• UZ Antwerpen, Antwerpen (<u>Dr Berneman, Dr Schroyens</u>)
• UZ Brussel, Brussel (<u>Dr Schots, Dr De Becker</u>)
• UZ Gasthuisberg KUL, Leuven (<u>Dr Maertens</u>)
• UZ Gent, Gent (<u>Dr Noens, Dr Kerre</u>)
• ZNA Stuivenberg, Antwerpen (<u>Dr Zachée</u>)</td></tr>
<tr><td rowspan="2">Status</td><td colspan="2">Start of study</td><td>January 2008</td></tr>
<tr><td colspan="2">Approximate duration</td><td>4 years</td></tr>
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