

Stem cell therapy in radiotherapy from bench to Clinical Trial Evaluating Efficacy of Mesenchymal Stromal Cell Injections for Treatment of Chronic Pelvic Complications Induced by Radiation Therapy

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Abstract

The late adverse effects of pelvic radiotherapy concern 5 to 10% of patients, which could be life threatening. However, a clear medical consensus concerning the clinical management of such healthy tissue sequelae does not exist. Our group has demonstrated in preclinical animal models that systemic mesenchymal stromal stem cells (MSCs) injection is a promising approach for the medical management of gastrointestinal disorder after irradiation.

In a phase 1 clinical trial, we have shown that the clinical status of four first patients suffering from severe pelvic side effects (Epinal accident) was improved following MSC injection (figure). Two patients revealed a substantiated clinical response for pain and hemorrhage after MSC therapy. The frequency of painful diarrhea diminished from 6/d to 3/d after the first and 2/d after the 2nd MSC injection in one patient. A beginning fistulization process could be stopped in one patient resulting in a stable remission for more than 3 years of follow-up. A modulation of the lymphocyte subsets towards a regulatory pattern and diminution of activated T cells accompanies the clinical response. MSC therapy was effective on pain, diarrhea, hemorrhage, inflammation, fibrosis and limited fistulization. No toxicity was observed.

We are now starting a clinical research protocol for patients with post-radiation abdominal and pelvic complications who have not seen their symptoms improve after conventional treatments (NCT02814864, Trial evaluating the efficacy of systemic MSC injections for the treatment of severe and chronic radiotherapy-induced abdomino-pelvic complications refractory to standard therapy (PRISME). It involves the participation of 6 radiotherapy services for the recruitment of 12 patients. They will all be treated and followed up in the hematology department of Saint Antoine Hospital.

Biography

For 25 years, he has been developing gene and cell therapy using non-human primates, immune-tolerant mice and rats to protect against the side effects of radiation. He collaborates with clinicians to develop strategies for treatment of patients after radiotherapy overexposures. He has participated in the first establishment of proof of concept of the therapeutic efficacy of Mesenchymal stem cells (MSCs) for the treatment of hematopoietic deficit, radiodermatitis and over dosages of radiotherapy. He has contributed to the

first reported correction of deficient hematopoiesis in patients (graft failure and aplastic anemia) thanks to intravenous injection of MSCs restoring the bone marrow microenvironment, mandatory to sustain hematopoiesis after total body irradiation. He is scientific investigator of Clinical phase II trial evaluating the efficacy of systemic MSC injections for the treatment of severe and chronic radiotherapy-induced abdomino-pelvic complications refractory to standard therapy.