FAQ: MEsenchymal **S**tem cell therapy for **CA**nadian **MS** patients **(MESCAMS)**

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What are mesenchymal stem cells?
Mesenchymal stem cells (MSC) – found in many places in the body including the bone marrow, skin and fat – have been demonstrated to suppress inflammation and repair nerve tissue, positioning them as promising candidates for the treatment of multiple sclerosis (MS).

What is the MESCAMS study?
MEsenchymal **S**tem cell therapy for **CA**nadian **MS** patients **(or MESCAMS)** is the name of the Canadian arm of an international clinical study called MESEMS investigating the safety and efficacy of MSC therapy for MS. MESCAMS is a phase II, randomized, double-blind, placebo-controlled cross-over study with two Canadian sites – The Ottawa Hospital and Health Sciences Centre (HSC) Winnipeg. MESCAMS is led by Dr. Mark S. Freedman (Ottawa Hospital Research Institute, University of Ottawa), the Principal Investigator (PI) at the Ottawa site and Dr. James J. Marriott (University of Manitoba) the PI at the Manitoba site.

Study participants received either an early intravenous treatment of their own MSC extracted from their bone marrow, or a mock solution (placebo). At 24 weeks the reverse will occur, meaning that those who received MSC initially will get the mock solution and those who started with the mock solution will get MSC. Treatment safety and ability to reduce inflammation as measured by MRI among other parameters will be observed at 24 weeks, and all participants will be followed for a total of 48 weeks.

What does the MESCAMS treatment entail?
Participants had 20 ml of bone marrow extracted from the hip bone under local anesthesia. MSCs are isolated from the bone marrow of the person undergoing the treatment and multiplied over a period of approximately three weeks at highly specialized laboratories in Ottawa and Winnipeg. Participants were randomly assigned to receive a single infusion of either their own MSCs or a mock solution at week zero. At 24 weeks, participants cross over to the opposite treatment arm (i.e., at the end of week 24, those who initially received MSC then receive the mock solution and vice versa).

What are the risks of MESCAMS treatment?
Only minimal risks have been identified by the principal investigators as being associated with this treatment. Common complications that may occur from the removal of bone marrow, including pain during and after the procedure as well as bleeding and infection at the puncture site (where the needle goes in). With the IV infusion of MSC or placebo, individuals may experience fever, chills and shivering. In order to preserve the integrity of the MSC, a chemical preservative called dimethylsulfoxide (DMSO) is used. When individuals undergo the MSC or mock infusion they will receive a small amount of DMSO. The most common side effects associated with DMSO administration is a mild drop or rise in heart rate and headache.

How is MESCAMS different from the previously conducted stem cell trial in Canada?
This is the first Phase II study evaluating the safety and benefit of mesenchymal stem cell therapy for multiple sclerosis. Unlike previous studies involving transplantation of hematopoietic stem cells, chemotherapy (which carry serious side effects) is not required.

Who was included in the MESCAMS study (inclusion criteria)?

- Male and female adults aged 18-50 diagnosed with multiple sclerosis:
    - Relapsing-remitting MS
        - Who have not responded to at least 1 year of therapy with one or more of the approved disease-modifying therapies as evidenced by at least **one** of the following:
            - One or more clinically documented relapse in the past 12 months
            - Two or more clinically documented relapses in past 24 months
            - One or more gadolinium-enhancing lesion as seen on MRI within the past 12 months

    - Secondary-progressive MS:
        - Who have not responded to at least one year of therapy with one or more of the approved disease-modifying therapies and **all** of the following:
        - an increase of one or more EDSS point in the past 12 months
        - one or more clinically documented relapse or one or more gadolinium-enhancing lesion as seen on MRI within the past 12 months

    - Primary progressive MS with **all** of the following:
        - an increase of one or more EDSS point in the past 12 months
        - one or more gadolinium-enhancing lesion as seen on MRI within the past 12 months
        - positive cerebrospinal fluid (CSF) (detection of oligoclonal banding)
- Diagnosed with multiple sclerosis for **2-15** years.
- EDSS score of **2.5 to 6.5**.

For full inclusion and exclusion information regarding this study, please visit ClinicalTrials.gov

What if I want to be considered as a participant in MESCAMS study?
The MESCAMS study is closed and no longer accepting participants.

Why did the study take place at only two sites in Canada, Ottawa and Winnipeg?
These two research facilities have been specifically constructed to harvest and manufacture stem cells and have been approved by the government to perform the procedure as outlined in the study protocol. In Canada, research sites must meet all government safety and design protocols as well as research ethics board criteria before moving forward with a clinical trial.

Is MESCAMS treatment now available for people living with MS?
MSC is not yet a proven effective treatment for MS. Early data from the study demonstrates that mesenchymal stem cells are safe for people with MS. While the study was unable to detect an effect on decreasing cell inflammation, researchers are continuing to analyze the data to understand other possible implications of the treatment across additional parameters (i.e. relapse rates, effects on neuroprotection and repair). Researchers expect to learn more in the coming months.