Minocycline for Clinically Isolated Syndrome (CIS) FAQ

Updated May 2017

1. **What is minocycline?**

   Minocycline is in a class of medications called tetracycline antibiotics and is used to treat bacterial infections including acne; pneumonia and other respiratory tract infections; and infections of skin, genital, and urinary systems. Minocycline is an oral capsule and works by preventing the growth and spread of bacteria. Minocycline has also demonstrated anti-inflammatory and neuroprotective properties.

2. **What are the details of the clinical trial?**

   In 2008, MS neurologist Dr. Luanne Metz from the University of Calgary launched a phase III, double-blind, randomized, placebo-controlled clinical trial with funding from the Multiple Sclerosis Scientific Research Foundation. The goal of the study was to determine if minocycline, taken orally at a dose of 100mg twice a day, can reduce the proportion of participants with CIS who convert to MS over a 6-month follow-up period. The secondary objective was to determine whether the effect could last up to two years.

   The clinical trial followed 142 participants with CIS across 12 Canadian MS clinics:

   - Calgary Multiple Sclerosis Clinic, Calgary
   - MS Patient Care and Research Clinic, Edmonton
   - Fraser Health Multiple Sclerosis Clinic, Burnaby
   - UBC Hospital, Vancouver
   - MS Research Unit, Health Sciences Centre, Winnipeg
   - Dalhousie MS Research Unit, Halifax
   - London Health Sciences Centre, London
   - The Ottawa Hospital, Multiple Sclerosis Research Clinic, Ottawa
   - Sunnybrook Health Sciences Centre, Toronto
   - Clinique Neuro Rive-Sud, Greenfield Park
   - CHUM Notre-Dame, Montreal
   - CHAUQ Enfant-Jesus, Quebec City

   Participants were randomly selected to receive minocycline, or a mock treatment (placebo). The results of this trial are now published in the New England Journal of Medicine.

3. **Why did the clinical trial take as long as it did?**

   In Canada, clinical trials are highly regulated and very costly to implement. To understand the steps required for a clinical trial please see here. This trial took place in twelve sites across Canada, each site requiring ethics review board approval. Recruitment of participants can also

be a lengthy process. Every clinical trial is designed to answer a specific question in a specific group of people. In this trial the investigators were determining if minocycline reduces the conversion from CIS to confirmed MS so only people with CIS could be enrolled.

4. **How does minocycline work to decrease the conversion from CIS to Multiple Sclerosis?**
   Minocycline appears to have anti-inflammatory and neuroprotective properties that delay the conversion from a first neurological event suggestive of MS to clinically definite MS (CDMS). For details on mechanism, see Minocycline Fact Sheet.

5. **If minocycline – an antibiotic – is effective in decreasing the risk to conversion from CIS to CDMS, does that mean that MS is caused by a bacterial infection?**
   Although researchers continue to look at infection as playing a key role in the development of MS, no one bacterial or viral agent has been identified. In MS, it is believed that minocycline works in an anti-inflammatory and neuroprotective manner. It may also work by influencing the bacteria in the gastrointestinal tract, known as the microbiome. Minocycline is known to improve the balance of organisms in the microbiome to be more anti-inflammatory.

6. **Is minocycline more effective in decreasing the risk to conversion from CIS to CDMS than other treatments for CIS?**
   There are a number of other disease-modifying therapies that are indicated for treatment of CIS, however to date there have been no head-to-head clinical trials comparing minocycline with the other treatments. The treatment effect of minocycline over 6 months appears to be similar to the treatment effect of other therapies studied for CIS.

7. **What are the short and long term side effects of minocycline?**
   The most common short term side effects in people treated with minocycline include: diarrhea; dizziness or light-headedness; grey discoloration of the skin or tissue in the mouth including the teeth; sun sensitivity and secondary infection due to fungi which can cause itching of the rectum or vagina. Side effects reported during the clinical trial were comparable to those identified on the product monograph for minocycline. Minocycline is contraindicated in women who are pregnant or nursing. The Health Canada product monograph for minocycline also cautions that treatment with minocycline may reduce the effectiveness of oral contraceptives if taken at the same time. This is based on rare case reports and one study of antibiotics as a group. This concern should therefore be considered but unfortunately there is little evidence to guide decisions. Minocycline is not recommended for long term treatment in children under the age of 13. Antibiotic resistance is uncommon with minocycline.

8. **Will I benefit from taking minocycline if I have relapsing-remitting MS or progressive MS?**
   Two pilot studies have been done to look at the safety and efficacy of minocycline in people with relapsing-remitting MS (RRMS). Results from these studies were encouraging, but the data is preliminary and too limited to recommend minocycline as a stand-alone treatment for relapsing-remitting MS beyond the time of the initial attack. Minocycline has also been studied

as an add-on therapy for RRMS (see Q15). To date there have not been any studies of minocycline as a treatment for progressive MS.

9. **Can minocycline affect the transition from relapsing-remitting MS to secondary progressive MS?**
   The current trial looked only at conversion from CIS to MS and did not investigate the safety and efficacy of minocycline in other types of MS, including relapsing-remitting MS or progressive MS. Additional research would be necessary to provide clarity on the role of minocycline on the disease course of relapsing-remitting MS and secondary-progressive MS.

10. **Will there be other clinical trials in the future looking at the safety and efficacy of minocycline for other types of MS?**
    Researchers are interested in exploring the effects of minocycline on the course of relapsing-remitting MS, however at this time, it is not known if there will be additional studies. The MS Society will continue to follow and report on this area of research.

11. **Will Health Canada be required to approve minocycline for CIS before it can be prescribed for CIS and covered?**
    It is not expected that the Health Canada status of this drug will change with regards to treatment of CIS. Many medications are prescribed "off-label" to treat various conditions, which means that they may be prescribed for use in conditions other than what the drug was initially approved by Health Canada to treat.

12. **I have CIS and have not started treatment, can I begin treatment with minocycline now?**
    It is important to discuss your treatment options with your health care team, as this decision is based on a number of factors and your doctor will need to review the published clinical trial data to fully understand the risks and benefits of treatment and discuss them with you.

13. **I have CIS and am taking a disease modifying therapy, can I switch from my current therapy to minocycline?**
    To date there have been no clinical trials evaluating the safety and benefit of switching from another MS treatment to minocycline, nor studies to compare their effectiveness. It is important to discuss your treatment options with your health care team.

14. **I am taking a disease modifying therapy for CIS, can I take minocycline at the same time as my current therapy to further decrease my risk of conversion to MS?**
    Two clinical trials have been conducted to study the safety and efficacy of minocycline as taken in combination with another MS treatment. In one trial, Dr. Metz and colleagues randomly assigned 44 patients with RRMS who were taking glatiramer acetate to receive either minocycline at a dose of 100mg twice a day or a placebo, as an add-on therapy. They found that participants who took both glatiramer acetate and minocycline tended towards having fewer new MRI lesions than patients who took glatiramer acetate and placebo. In a separate trial, the safety and efficacy of taking interferon beta-1a in combination with minocycline was investigated, however the study was terminated early; in the smaller incomplete study the

investigators reported that there was no demonstrated therapeutic benefit. More research and larger clinical trials are required to determine the safety and benefit of taking minocycline in addition to other treatments. It is important to discuss your treatment options with your health care team, as this decision is based on a number of factors.

15. What is the cost of minocycline?

In Canada, the generic form of minocycline costs approximately $1 per dose. Based on two doses a day, this works out to approximately $500-600/year. The cost of minocycline will vary depending on the manufacturer, pharmacy fees and province.

16. What does this study mean for people living with MS moving forward?

The results of the clinical trial position minocycline as an affordable and accessible treatment option for those who have experienced initial symptoms, which are suggestive of MS. The results of these efforts will help to mobilize more options for people living with MS, and contribute to the growing movement to treat as early in the disease as possible.