

## **Summary – CCSVI Working Group Meeting, November 4, 2010**

The CCSVI Working Group held its third meeting on November 4 by teleconference.

### Participants:

Linda Lumsden, Chair  
Shelley Black  
Anthony Feinstein (first hour)  
Marilyn Lenzen  
Samuel Ludwin  
Lindsay Machan (first hour)

Linda Molyneux  
T.J. (Jock) Murray  
Julian Spears (first hour)  
Brock Winterton  
Yves Savoie (ex officio)

Regrets: James Orr

Staff resource: Deanna Groetzinger

Before continuing its discussion of what is needed to move forward with pan-Canadian therapeutic clinical trials of chronic cerebrospinal venous insufficiency (CCSVI) and MS, the group reviewed a list of scientific meetings taking place in late 2010 and 2011 that are anticipated to have presentations of CCSVI and MS research. The purpose of the list is for the working group to have advance knowledge about scientific meetings to ensure that research findings about CCSVI can be made available to working group members as quickly as possible. Working group members were asked to provide information about any additional scientific meetings relating to CCSVI and MS so they can be added to the list.

### **Therapeutic clinical trial**

Returning to the discussion of how fast a therapeutic clinical trial could begin, if evidence warrants, the group reviewed the post-conference report of presentations relating to CCSVI and MS made at the October meeting of the European Committee on Treatment and Research in Multiple Sclerosis (ECTRIMS). It was noted the studies did not reach consensus in a number of important areas including the lack of a “gold standard” as to which methodology should be used for diagnosis, an issue the working group had discussed at its October meeting.

There was discussion about other studies and why some studies are considered to be more influential by those who make decisions about access to procedures and therapies. It was noted studies that use control groups carry more weight since there can be a direct comparison of those who have had a therapy and those who have not. The hierarchy of evidence was described by a group member as (in descending order of importance): meta-analysis, randomized clinical trials, open trials, case studies, expert opinion and anecdote. Another group member pointed out that perspectives other than clinical trial data should be brought into the discussion, and one perspective is the experiences of people who have had the procedure and the physicians who carry out the procedure.

One working group member stated a properly controlled treatment trial that has a sham (non-treatment) arm is the only way to resolve the question as to whether the CCSVI procedure works or not. The individual making the suggestion said the question isn't whether there are vein abnormalities, since they are known to exist, but whether they have an effect on MS and whether treating them improves the course of MS or of symptoms.

Members of the group responded to this suggestion with great interest. Some group members wondered if it would be possible to include a control (non-treatment) arm in a therapeutic clinical trial since most people would want the procedure. Several mentioned that typically people in control groups receive the actual treatment at the end of the study, if it is shown to work. There was disagreement as to how long a therapeutic clinical trial would need to last with some proposing six months and others saying 12 months would be the minimum length if more than symptoms were to be assessed. It was pointed out it would be important to agree on what "improvement" is before the study is started.

There was discussion as to whether the procedure would be considered useful if it relieves MS symptoms. Group members shared the view such an outcome would be considered a success. It was pointed out a short clinical trial would not answer the question of whether the procedure might have an impact on the level of disability or course of MS.

While there was some concurrence that a therapeutic clinical trial is needed as soon as possible and that a two-pronged approach would be useful (one trial to examine the impact of the procedure and a second trial to study the impact on the disease course on a longer-term basis), the group did not reach consensus as to when it should begin and what data should be in place prior to its beginning.

### **Establishment of a registry**

The group then turned to the discussion of whether a registry of those who have had the procedure for CCSVI could be established. One of the group members provided a brief overview of existing MS registries, noting there is considerable variance and none reach the goal of collecting relevant information from the population of people who have MS. Most current registries are based in MS clinics and thus do not capture information about the entire MS population.

It was pointed out that it would be unlikely to be able to establish the perfect registry and that it was important to launch one and start collecting information on people who have had the CCSVI procedure. One suggestion was to utilize the existing MS clinics to identify people who have had or are planning to have the procedure. There was discussion as to whether information about quality of life issues (e.g., fatigue, cognitive issues) could be captured and agreement that such information should be included. It was noted such information could be collected using standard tests that are used widely.

### **Recommendation**

There was consensus that a registry that is well designed as possible would facilitate the collection of information on those who have CCSVI procedure. It was agreed to recommend the MS Society take on the role as a funder and proponent of a registry and to seek the possible participation of external partners. The design of a registry would be undertaken by appropriate experts.

### **Provincial government activities**

Following up on commitments made by various provincial governments, the group was advised that the Saskatchewan government had committed to make members of its therapeutic trial advisory group public once it has been established. The Newfoundland observational study has preliminary ethics approval and will soon start to examine people with MS who plan to have the CCSVI procedure as well as a matched group of people who do not plan to have the procedure. In addition, the MS Society has asked for earmarking of funds toward a therapeutic clinical trial, so that such funds can be readily available if and when such trial is warranted, from British Columbia, Alberta, Ontario and Quebec.

### **Next steps**

The discussion and recommendation will be brought to the November 18 meeting of the national board of directors. It will be noted while consensus was reached relating to the establishment of a registry that consensus was not reached relating to the timing of a possible therapeutic clinical trial. The CCSVI Working Group will meet again in December.