

## **PROPHYLAXIS SUB-COMMITTEE REPORT: 2007/2008**

### *ASSOCIATION OF HEMOPHILIA CLINIC DIRECTORS OF CANADA*

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The major activity of the Prophylaxis Subcommittee during 2007/2008 continues to be the Canadian hemophilia dose-escalation prophylaxis study (CHPS 2) and the extension study CHPS 3. Co-Principal Investigators for the study are Dr. Victor Blanchette and Dr. Brian Feldman.

### **CHPS 1 and CHPS 2**

CHPS is a multicentre Canadian study of escalating dose prophylaxis. Participants are being followed in 11 centres across Canada. The study has given a rich data set on bleeding, factor usage, joint scores based on physiotherapy assessments and imaging in this cohort of boys.

The investigators recommended continuation of follow up of boys enrolled on CHPS 2 but patient enrollment has closed. Funding is available from Bayer until the end of 2009. There are currently a total of 55 boys now enrolled (CHPS 1 and CHPS 2) from the 11 centres. The boys have been followed an average of 76 months (range: 15-130 months).

Abstracts on the CHPS physiotherapy data were presented at the WFH musculoskeletal conference in Stresa, Italy in May 2007 (ref enclosure). Another abstract on the physiotherapy data was accepted as an oral presentation at the 2008 WFH World Congress in Istanbul, Turkey (reference enclosed).

### **CHPS 3**

In order to continue follow up of boys enrolled on CHPS 1 and CHPS 2 the investigators applied for, and received another cycle funding from Bayer, Canada (length of funding 2007-2009).

We have developed a new strength score (Daniel and Worthingham's score, range 0-5) for the physiotherapy assessments that will better capture changes as the boys get older. Other major changes are with the Research Ethics board awaiting approval.

Major changes are:

- MRIs and Xrays at ages 6 and 12
- Additional questionnaire to capture physical activity (3 Day Previous Activity Recall)
- Genetic assays and intrinsic markers (Prothrombin gene, Factor V leiden, vWD factor, blood group)

In CHPS 3 we will continue to record bleeding frequency; serial physiotherapy and imaging assessments will be performed.

Study aims are as follows:

- To determine risk factors for bleeding in boys with severe hemophilia A
- To compare the costs and benefits of the Canadian dose-escalation (“tailored”) prophylaxis regimen with intermediate dose prophylaxis (as practiced in the Netherlands), aggressive on demand therapy and full-dose prophylaxis (eg the Malmö prophylaxis model as practiced in the USA randomized joint outcome study).

## **Prophylaxis Use Survey**

The purpose of this survey was to determine current use of factor prophylaxis in all patients with hemophilia A or B in Canada. Data was collected on patients of all ages. The study has been completed and an abstract was accepted as a poster for WFH World Congress in Istanbul (ref enclosure). A manuscript has also been submitted to Hemophilia.

## **National Study of Prophylaxis in Adolescents and Young Adults with Inherited Severe Bleeding Disorders**

A new study initiative headed by Dr. Carcao has been funded by the CHS/Hema-Quebec – Bayer Partnership fund. It will examine treatment patterns for Inherited Bleeding disorders, including all severities of hemophilia, von Willebrand’s disease and other rare inherited bleeding disorders. The Case Report forms have been submitted to all participating centres for review and the study protocol has been submitted to the Division of Hematology/Oncology Internal Science review at the Hospital for Sick Children. Once this review is completed, the protocol will be submitted to the Hospital for Sick Children Research Ethics Board (REB) for review and approval.

## **Once a Day Prophylaxis Pilot Study**

A new prophylaxis study has been funded by the CHS/Hema-Québec – Bayer Partnership fund to examine the feasibility of studying once a day prophylaxis in adolescents and young adults with severe hemophilia. The study has been submitted to the Research Ethics Board at the Hospital for Sick Children and will then be forwarded to Health Canada for Clinical Trials Application (CTA) approval. This project is being conducted at L’Hôpital Ste-Justine in Montreal and in Toronto at the Hospital for Sick Children and St Michael’s Hospital. The study is expected to start in July, 2008.

## **International Prophylaxis Study Group (IPSG)**

Members of the Prophylaxis Subcommittee, Dr. Blanchette Dr. Rivard, Dr. Carcao and Pam Hilliard are actively involved in activities of the IPSG. This group continues to work in the area of Prophylaxis.

- On behalf of the IPSG the Imaging Expert Working Group is developing a single MRI scoring scale.
- The PT Expert Working Group has completed a validation study of the Hemophilia Joint Health Score (HJHS) that was developed by the expert working group. Results are being presented at WFH in Istanbul, Turkey.
- The Outcome Measures Expert Working Group is working to develop guidelines for the Quality of Life and Economic tools for use in prophylaxis clinical trials. A manuscript on recommendations for reporting economic evaluations of hemophilia prophylaxis was

published in Haemophilia (ref enclosure). Manuscripts are being preparation by both the HRQoL and Economic Analysis groups.

## Abstracts

P. Hilliard, M. McLimont, K. Mulder, K. Christie, H. Secord, C. Van Neste, N. Zourikian, B. Elliott, J. Nilson, C. Jarock, D. Langen, B. Feldman. **Musculoskeletal status of the Canadian Hemophilia Prophylaxis Study cohort after 10 years.** Abstract and oral presentation at WFH MSK Congress, May 3-6 2007

Victor S Blanchette, Georges E Rivard, Mohan K Pai, Sara J Israels, Marjorie McLimont and Brian M Feldman. **10 Year Musculoskeletal Outcomes with Tailored Primary Prophylaxis: the Canadian Hemophilia Prophylaxis Study.** Abstract and oral presentation at ASH, December 2007

Feldman BF, Funk S, Hilliard P, van der Net J, Zourikian N, Bergstrom B-M, Engel-bert RHH, Abad A, Petrini P and Manco-Johnson M on behalf of the International Prophylaxis Study Group. **The Haemophilia Joint Health Score (HJHS) International Validation Study.** The XXVIII World Federation of Hemophilia Congress (June 1 – 5, 2008 – Istanbul, Turkey)

Hilliard, Pamela; Blanchette, Victor\*; McLimont, Marjorie; Mulder, Kathy; Christie, Karen; Brooks, Julia; Van Neste, Catherine; Zourikian, Nichan; Elliott, Brenda; Nilson, JoAnn; Jarock, Carolyn; Langen, Donna; Feldman, Brian \*for the AHCDC. **The Canadian Hemophilia Prophylaxis Study cohort: musculoskeletal status by age.** The XXVIII World Federation of Hemophilia Congress (June 1-5, 2008 – Istanbul, Turkey)

Biss TT, Chan AK, Blanchette VS, Iwenofu LN, McLimont M, Carcao MD For the Association of Hemophilia Centre Directors of Canada (AHCDC) and the Canadian Association of Nurses in Hemophilia Care (CANHC). **A Survey of Factor Prophylaxis in Canadian Patients with Hemophilia.** The XXVIII World Federation of Hemophilia Congress (June 1-5, 2008 – Istanbul, Turkey)

## Publications

Nicholson A, Feldman BM, Berger K, Bohn R, Carcao M, Gringeri A, Hoots K, Mantovani L, Fischer K, Schramm W, Van Hout BA, Willan A. **Recommendations for reporting economics evaluations of hemophilia prophylaxis: a nominal group consensus statement on behalf of the economics expert working group of the International Prophylaxis Study Group.** Haemophilia 2008 Jan; 14 (1):127 -132.

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