VOLUME 34 (SUPPLEMENT 1) MARCH 2007

A PEER-REVIEWED SUPPLEMENT TO

THE CANADIAN JOURNAL OF
NEUROLOGICAL SCIENCES

Canadian Guidelines for the Development of Antidementia Therapies (The Background Papers)

2nd Canadian Conference on Antidementia Drug Guidelines

Supplement Editor: Howard H. Feldman

https://doi.org/10.1017/S0317167100005473 Published online by Cambridge University Press

Volume 34 (Supplement 1) March 2007

THE CANADIAN JOURNAL OF
Neurological Sciences
LE JOURNAL CANADIEN DES
Sciences Neurologiques

1 Introduction
Howard H. Feldman

3 Canadian Drug Regulatory Framework
L. Kelly, M. Lazzaro, C. Petersen

11 Diagnostic Criteria of Dementia
Rémi W. Bouchard

19 Study Design in Dementia Drug Trials
Chris MacKnight

23 Outcomes for Assessment of Symptomatic and Stabilization/Disease Modifying Drugs
Serge Gauthier

27 Consent in Alzheimer's Disease Research: Risk/Benefit Factors
B. Lynn Beattie

32 Ethical Considerations for the Conduct of Antidementia Trials in Canada
John D. Fisk

37 Alternatives to Placebo-Controlled Trials
David L. Streiner

42 Target Symptoms and Outcome Measures: Cognition
Andrew Kirk

47 The Role of Functional Assessment as an Outcome Measure in Antidementia Treatment
Fadi Massoud

52 Global Assessment Measures for Assessing Efficacy in Dementia Drug Trials
Kenneth Rockwood

57 Quality of Life in Dementia
Gary Naglie

62 Disease Staging and Milestones
Kiran Rabheru

67 Assessment of Behavioural and Psychological Symptoms Associated with Dementia
David Conn, Lilian Thorpe

72 Biological Markers in Alzheimer's Disease
Peter Bailey

77 Imaging Biomarkers and their Role in Dementia Clinical Trials
Howard Chertkow, Sandra E. Black

84 Primary Prevention and Delay of Onset of AD/Dementia
Howard H. Feldman, Claudia Jacova

90 Is Mild Cognitive Impairment a Valid Target of Therapy
Kenneth Rockwood, Howard Chertkow, Howard H. Feldman

97 Improving Drug Trials for Mild to Moderate Alzheimer's Disease
David B. Hogan

103 Treatment of Moderate to Severe Alzheimer's Disease: Rationale and Trial Design
Nathan Herrmann

109 Clinical Trials in Parkinson's Disease Dementia and Dementia with Lewy Bodies
Richard Camicioli, Serge Gauthier

118 Frontotemporal Dementia: Recommendations for Therapeutic Studies, Designs, and Approaches
Morris Freedman

125 Therapeutic Issues in Vascular Dementia: Studies, Designs and Approaches
Sandra E. Black

Volume 34 (Supplement 1) March 2007

THE CANADIAN JOURNAL OF Neurological Sciences

LE JOURNAL CANADIEN DES Sciences Neurologiques

The official journal of: / La Revue officielle de:

The Canadian Neurological Society
La Société Canadienne de Neurologie

The Canadian Neurosurgical Society
La Société Canadienne de Neurochirurgie

The Canadian Society of Clinical Neurophysiologists
La Société Canadienne de Neurophysiologie Clinique

The Canadian Association of Child Neurology
L'Association Canadienne de Neurologie Pédiatrique

The permanent secretariat for the four societies and the Canadian Congress of Neurological Sciences is at:
Le secrétariat des quatre associations et du Congrès Canadien des Sciences Neurologiques est situe en permanence à:
7015 Macleod Trail SW, Suite 709, Calgary AB, Canada T2H 2K6.

The Canadian Journal of Neurological Sciences is published quarterly. The annual subscription rate for Individuals are: C$90 (Canada), US$90 (USA), and US$95 (elsewhere). Subscription rates for Institutions are: C$100 (Canada), US$100 (USA), and US$105 (elsewhere). Resident, intern and student rates are available. See www.cjns.org for details. Single copies C$25 each plus postage and handling. All manuscripts and communications should be sent to: Canadian Journal of Neurological Sciences, 709 - 7015 Macleod Trail SW, Calgary, AB Canada T2H 2K6. Telephone (403) 229-9575; Fax (403) 229-1661. E-mail: journal@cjns.org; Website: www.cjns.org

Mailed under Publications Mail Agreement no: 40007777; PAP Registration no: 09824. Postage paid at Calgary, Alberta. This journal is indexed by *Abstracts on Hygiene and Communicable Diseases, Aquatic Sciences and Fisheries Abstracts, ASCA-Automatic Subject Citation Alert, Biological Abstracts, BIOBASE, BIOSIS, Chemical Abstracts Current Awareness in Biological Sciences, Current Contents (Clinical Medicine and Life Sciences), Dental Index, e-psyche, Excerpta Medica, Index Medicus, Index to Scientific Reviews, Journal Watch Neurology, Laboratory Hazards Bulletin, Leisure, Recreation and Tourism Abstracts, MEDLINE, Neurosciences Citation Index, Nutrition Abstracts and Reviews, Nutrition Research Newsletter, Pharmaeconomics and Outcome News, PsycInfo, Psychological Abstracts, Reactions Weekly, Referativnyi Zhurnal, Review of Medical and Veterinary Mycology, Science Citation Index, Weed Abstracts.*

Le Journal Canadien des Sciences Neurologiques est publié trimestriellement. L'abonnement annuel est de 90 $C (non-membres au Canada); 90 $É-U (Etats Unis) et 95 $É-U (ailleurs); l'abonnement annuel for pour les institutions est de 100 $C (non-membres au Canada); 100 $É-U (Etats Unis) et 105 $É-U (ailleurs); Internes, résidents, fellows pré et post doctoral voir www.cjns.org pour détails. Copie simple: 25 $C plus affranchissement et manutention. Toutes les communications et les manuscrits doivent être adressés à Journal Canadien des Sciences Neurologiques, 709 - 7015 Macleod Trail SW, Calgary, AB Canada T2H 2K6. Téléphone (403) 229-9575; Fax (403) 229-1661. E-mail journal@cjns.org; Website: www.cjns.org

Posté sous poste-publications: numéro de convention: 40007777; numéro d'enregistrement PAP 09824. Port payé à Calgary, Alberta. Le Journal est cité et indexé dans *Abstracts on Hygiene and Communicable Diseases, Aquatic Sciences and Fisheries Abstracts, ASCA-Automatic Subject Citation Alert, Biological Abstracts, BIOBASE, BIOSIS, Chemical Abstracts Current Awareness in Biological Sciences, Current Contents (Clinical Medicine and Life Sciences), Dental Index, e-psyche, Excerpta Medica, Index Medicus, Index to Scientific Reviews, Journal Watch Neurology, Laboratory Hazards Bullentin, Leisure, Recreation and Tourism Abstracts, MEDLINE, Neurosciences Citation Index, Nutrition Abstracts and Reviews, Nutrition Research Newsletter, Pharmaeconomics and Outcome News, PsycInfo, Psychological Abstracts, Reactions Weekly, Referativnyi Zhurnal, Review of Medical and Veterinary Mycology, Science Citation Index, Weed Abstracts.*

Advertising representative/Représentant de publicité:
Brett Windle, *Corporate Development Coordinator*
Tel (403) 229-9575 Fax (403) 229-1661
E-mail: brett-windle@cnsfederation.org

Printer/Imprimeur:
Sundog Printing Limited, 1311 Ninth Avenue SW
Calgary, Alberta T3C 0H9

ISSN 0317 - 1671

Canadian Guidelines for the Development of Antidementia Therapies

2nd Canadian Conference on Antidementia Drug Guidelines

March 2007

Can. J. Neurol. Sci. 2007; 34: Suppl. 1 - S1-2

INTRODUCTION

The dementias are recognized to be one of the most important challenges to our aging Canadian society in the 21st century. Scientific progress in understanding of the dementias has been advancing at an unprecedented rate, in turn suggesting that therapies will be developed to prevent, symptomatically treat, and modify their course. This rapid growth of research possibilities brings with it a range of ethical challenges, changing perspectives of risk/benefit and the need for discussion/debate on the best ways to advance the development of antidementia therapies.

Canada is well positioned to address these challenges. There is an integrated network of investigators doing clinical trials within the Consortium of the Canadian Centers for Clinical Cognitive Research (C5R), the Canadian Neurological Society, the Canadian Academy of Geriatric Psychiatry (CAGP) and the Canadian Geriatrics Society (CGS).

In turn, representatives of this network of societies came together for the 2nd Canadian Conference on Antidementia Drug Guidelines in Montreal on October 28-29, 2004 with the goal of developing guidelines to serve as a reference for those involved in developing antidementia therapies.

The overall result of this Conference was published in 2006 as Progress in Clinical Neurosciences: Canadian Guidelines for the Development of Antidementia Therapies: A Conceptual Summary.[1] This supplement now presents the background papers that were developed by participants of the Conference. Each paper was initially presented for discussion and later finalized through peer review to their current state. Many topics reflect the early days of therapeutic development and much more will need to be said about them over time. In turn, it can be anticipated that updating of these Guidelines will be required. These Guidelines are unique. Prior to their peer review they had received active input from representatives of the respective clinical and research groups: the regulatory authorities of the Central Nervous System (CNS) Division of the Therapeutic Products Directorate (TPD of Health Canada), the Alzheimer Society of Canada and the pharmaceutical industry.

On behalf of the contributors I trust that you will find the supplement stimulating and worthy of further discussion and feedback as we face the need to develop treatments for this burgeoning problem of dementia.

Howard H. Feldman
Division of Neurology
University of British Columbia
Vancouver, BC, Canada

Acknowledgements

The 2nd Canadian Conference on Guidelines for the Development of Antidementia Therapies gratefully acknowledges funding support through a workshop grant of the Canadian Institutes of Health Research Institute on Aging, by a workshop grant from the Canadian Consortium of Clinical Cognitive Research Centers (C5R) and by an unrestricted grant-in-aid from the following pharmaceutical companies: Astra-Zeneca Canada Inc., Aventis Pharma Inc., Boehringer Ingelheim Canada Ltd., GlaxoSmithKline Inc, Janssen Ortho Inc., Lundbeck Canada Inc., Myriad Genetics Inc., Novartis Pharmaceuticals Inc., ONO Pharma USA Inc., Pfizer Canada Inc., Sanofi-Synthelabo Canada Inc., Institute de Recherches Internationales Servier.

The Conference gratefully acknowledges the role of MedPlan in assisting in the planning, logistics, and organization of this Conference and in assisting in the editing and formatting of this publication.

Disclosure

Within the past 2 years Dr. Feldman has had operating grant funding from the Canadian Institutes of Health Research (CIHR), as well as having served as consultant, received grant funding or participated in CME programs sponsored by Astra Zeneca, Pfizer, Eisai, Novartis, Janssen, Servier, Sanofi Synthelabo, Lilly, GlaxoSmithKline, Myriad, Targacept, Forest, Lundbeck and Axonyx.

References

1. Feldman HH, Gauthier S, Chertkow H, Conn DK, Freedman M, MacKnight C. on behalf of the 2nd Canadian Conference on Antidementia Guidelines Committee. Canadian Guidelines for the Development of Antidementia Therapies: a conceptual summary. Can J Neurol Sci. 2006; 33(1): 6-26.