Webinar Report

RESEARCH Spotlight

#LetsTalkNMD

Current State of Spinal Muscular Atrophy in Canada
04-21/2020
NMD4C (Neuromuscular Disease Network For Canada)

NMD4C launched in January 2020, is a Canadian network that is funded by Muscular Dystrophy Canada and the Canadian Institutes for Health Research.

NMD4C brings together the country’s leading clinical, scientific, technical, and patient expertise on neuromuscular disease. The rarity and diversity of neuromuscular diseases make interdisciplinary collaboration and networking essential to future progress.
NMD4C strives to train and educate neuromuscular disease stakeholders

Muscular Dystrophy Canada and NMD4C launched a new joint educational initiative under the #LetsTalkNMD webinar series.

The goal is to share knowledge on best practices, current issues, disease diagnosis and management and possible therapeutic interventions. Our target audience are neurologists, scientists, physicians, medical trainees/students and other allied healthcare professionals involved in the care of patients with neuromuscular disease.
COVID-19 & Neuromuscular: Resources

COVID-19 Ask The Experts

COVID-19 and Neuromuscular Patients

COVID-19: Care Recommendations for Home-Based Ventilation Patients

Pulmonary Support for Myotonic Dystrophy Patients During COVID-19 Pandemic
SMA Clinical Care in the Era of COVID-19:
Jodi Warman Chardon

Newborn Screening in Ontario:
Kristin Kernohan, Alex Mackenzie, Hugh McMillan

Update on Zolgensma for Canada:
Hugh McMillan

Update on Risdiplam for Canada:
Craig Campbell

Adult Outcome Measures:
Colleen O’Connell

Update on CNDR-SMA Project:
Lawrence Korngut, Victoria Hodgkinson

Disclaimer: Please note the speakers in this webinar have involvement in the subject matter with real or perceived relationships.
SMA CLINICAL CARE IN THE ERA OF COVID-19

Jodi Warman-Chardon, MD, MSc

NEUROMUSCULAR CENTRE. THE OTTAWA HOSPITAL (OTTAWA, ONTARIO)
COVID-19 has potential to disproportionately and severely affect individuals with SMA.

Patients with SMA are at a risk of severe COVID-19 infection because of respiratory insufficiency from neuromuscular weakness or musculoskeletal limitations (e.g., kyphoscoliosis), weak cough or airway secretion, baseline use of ventilation, bulbar weakness or comorbid conditions (e.g., obesity).
COVID-19 may put patients with SMA at increased risk for muscle weakness and pain.

There is no clinical evidence that COVID-19 virus directly affects motor neurons. However, patients with SMA are at significantly increased risk of acute weakness because COVID-19 is associated with elevated muscle enzyme levels.
COVID-19 has contributed to drastic changes in neuromuscular care and practice. COVID-19 has necessitated major changes to the manner in which we deliver and organize healthcare.

Our best practices for patients with SMA has changed from only a month ago.
Canadian clinicians are worried about delivery of Spinraza if closures continue.

A survey of 25 clinicians who manage patients with SMA in Canada indicated that 58% have had no delays in delivery of Spinraza (Nusinersen) in spite of COVID-19 closures. Of those with delays, 4% were related to patient preference, 12% was mediated by the physician and 12% was radiology or hospital administration.
Physical distancing has forced a rapid and unprecedented transition to telemedicine.

Care for SMA can be transferred to virtual care such as symptom verification, physical therapy and occupational therapy, diet assessments and multi-disciplinary evaluations. The challenges are with swallowing assessments, coordinating local laboratory or imaging evaluations and pulmonary function testing etc.
Modelling data tells us that delaying a Spinraza (nusinersen) maintenance dose by a short delay (i.e. weeks) should not have a huge impact but longer delays (i.e. months) might require greater time to return to central nervous system steady-state levels.

Schedule as close to regular dosing while balancing risk of infection with functional decline.
COVID-19 has contributed to significant delays to basic and translational SMA research.
NEWBORN SCREENING IN ONTARIO

Kristin Kernohan, PhD, FCCMG
Alex MacKenzie, MD, PhD
Hugh McMillan, MD, MSc

CHILDREN'S HOSPITAL EASTERN ONTARIO
NEWBORN SCREENING ONTARIO
People have two copies of the survival motor neuron-1 (SMN1) gene. When a baby is born with no working copies of SMN1 gene, they will develop SMA. SMA can be caused by deletions (~97% of cases) or other genetics changes (~3%).

Newborn screening will only detect cases of SMA caused by deletions and conversions in the SMN1 gene.
Babies with a deletion of both their copies of SMN1, and with SMN-2 (SMN2) copy numbers of 1, 2, 3 or 4 will be reported as having a screen positive result and referred for more testing. This means that greater than 99% of SMA type 1 and 2 cases and greater than 97% of SMA type 3 cases caused by a deletion in the SMN1 gene will be picked up by screening. SMA type 4 will also be detected if caused by SMN2 copy numbers of 4 or less. For the new pilot project in Ontario, the screening target is early onset disease, with the goal of treatment to prevent symptoms.

As of mid-January 2020, all infants in Ontario are screened for SMA.
By two weeks of life, an infant can have a confirmed SMA diagnosis.
Early diagnosis of SMA has allowed for very early access to treatment options.

Once a genetic diagnosis is confirmed, and before the onset of symptoms, there can be initiation of treatment as early as 1 month of life.
Data shows prolonged event-free survival and motor milestone achievement.

Zolgensma is an investigational therapy designed to deliver a working copy of the SMN1 gene to motor neurons in SMA patients by a one-time intravenous infusion. These modified genes live in the cell nucleus and make SMN protein, so motor neurons keep firing.
Risdiplam is an investigational SMN2 splicing modifier for SMA and is an orally administered liquid. It is designed to increase and sustain SMN protein levels both throughout the central nervous system and in peripheral tissues of the body. It is being evaluated for its potential ability to help the SMN2 gene produce more functional SMN protein throughout the body.

Risdiplam shows benefit on motor outcomes in a wide range of children and young adults with SMA.
ADULT OUTCOME MEASURES IN SMA

Colleen O'Connell. MD

DALHOUSIE UNIVERSITY FACULTY OF MEDICINE
(FREDRICTON, NEW BRUNSWICK)
There is a project underway currently to identify outcome measures that clinicians should use across Canada when evaluating adults with SMA. Agreement of which measures to use helps to: (1) understand natural progression and treatment outcomes in adults; (2) assist in clinical decisions (e.g., anticipatory care and managing expectations); (3) advocate for supports in clinics.

Agreement on how to measure clinical outcomes for adults is important.
Consensus was reached on how best to measure respiratory, motor and function abilities for adult with SMA in the following groups; 'sitters', 'non-sitters' and 'ambulatory'. There are also measures being considered for assessing quality of life, patient-specific goals and patient-reported outcome measures for adults with SMA.
UPDATE ON CANADIAN NEUROMUSCULAR DISEASE REGISTRY (CNDR) SMA PROJECT

Lawrence Korngut, MD
Victoria Hodgkinson, PhD

CANADIAN NEUROMUSCULAR DISEASE REGISTRY
CNDR is a Canada-wide registry of people diagnosed with a neuromuscular disease with over 30 clinics involved. Currently there are ~200 patients with SMA with baseline data and over a 100 patients with motor outcomes information. There are ongoing and future research projects through the registry available.

National registry helps to organize information for clinical and research purposes
research@muscle.ca
muscle.ca/webinars
neuromuscularnetwork.ca