

The Microenvironment



THE CANADIAN
HEMATOLOGY
SOCIETY

SOCIÉTÉ
CANADIENNE
D'HÉMATOLOGIE

NEWSLETTER

JUNE 2020

MESSAGE FROM THE PRESIDENT

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CANADIAN HEMATOLOGY SOCIETY

199 — 435 St. Laurent Blvd.
Ottawa, ON K1K 2Z8 CANADA

Phone: 613-748-9613

Fax: 613-748-6392

Email:
office@canadianhematologysociety.org

Website:
canadianhematologysociety.org

DEAR COLLEAGUES

Over the last weeks, I have attempted to write a quarterly greeting to the CHS membership for the Microenvironment. The COVID-19 pandemic, however, gaining momentum and killing many thousands of people globally has eclipsed all thoughts. This pandemic has disrupted the provision of Health Care across the globe. Completing the daily COVID -19 screening survey and entering my familiar hospital is anything but business as usual. An empty cafeteria with scant tables placed to optimize social distancing is a rare event in the typical bustling hospital environment, a daily mask allocation an important provision. Every day, new guidance follows the emergence of more information gleaned from the early COVID-19 pandemic experiences including China, Italy and now North America. As Hematologists, we are familiar with the evaluation of infectious risk for our patients with immunodeficiency from underlying disease or treatments. The risk of a potentially fatal COVID-19 infection adds another dimension of oversight. Pandemic planning, risk stratifying patients, diseases, chemotherapy regimens; transitioning to Telehealth and telephone follow up visits is happening in real time. Today, the flow of our clinics is unrecognizable from even a month ago. Falling back on the principles of Public Health disease prevention, we continue to find our way through the pandemic. I admire the courage and dedication of our colleagues across the country. Our future as a country is lived one day at a time; we are moving towards more clarity in how best to provide care for our patients and each other. In these unprecedented times, it is important to be safe and kind. Please take care of yourself and stay safe. We will be together again.



Dr. Nicole Laferriere
President, CHS

Nicole

LE MESSAGE DE LA PRÉSIDENTE

CHERS COLLÈGUES

Au cours des dernières semaines, j'ai tenté d'écrire un message trimestriel aux membres du SHC pour le microenvironnement. La pandémie de la COVID-19, qui a pris de l'ampleur et a tué plusieurs milliers de personnes dans le monde, a monopolisé mon attention. Cette pandémie a perturbé la prestation des soins des services de santé à travers le monde. La réalisation de l'enquête de dépistage de la COVID-19 chaque jour et le fait d'entrer dans mon hôpital habituel n'a rien d'ordinaire. Il est rare de trouver une cafétéria vide avec des tables espacées pour optimiser la distanciation sociale dans le milieu hospitalier trépidant. Une quantité de masques suffisante pour toute la journée est une tâche importante.

Chaque jour, de nouvelles orientations suivent l'émergence d'informations supplémentaires tirées des premières expériences de pandémie de la COVID-19, notamment celles provenant de Chine, d'Italie et maintenant d'Amérique du Nord. En tant qu'hématologues, nous connaissons bien l'évaluation du risque infectieux pour nos patients atteints d'immunodéficience d'une maladie sous-jacente ou de traitements. Le risque d'une infection à la COVID-19 potentiellement mortelle ajoute une autre dimension à la surveillance. La planification en cas de pandémie, le classement des patients en fonction du risque, les maladies, les schémas de chimiothérapie; la transition vers la télésanté et les visites de suivi par téléphone se produisent en temps réel. Aujourd'hui, le flux de patients de nos cliniques n'est absolument pas comparable à ce qu'il était il y a un mois à peine.

Pour revenir sur les principes de santé publique de prévention des maladies, nous continuons malgré la pandémie. J'admire le courage et le dévouement de nos collègues à travers le pays. Notre avenir en tant que pays se vit un jour à la fois; nous comprenons de mieux en mieux quelle est la meilleure façon de prodiguer des soins à nos patients et aux autres.

Dans cette période sans précédent, il est important d'être prudents et gentils les uns envers les autres. Veuillez prendre soin de vous et rester en sécurité. Nous serons de nouveau ensemble.

Nicole

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Canadian Blood Services' response to COVID-19

Contributed by : Tanya Petrasko MD, Vancouver

The COVID-19 pandemic has impacted how we operate our blood donor centres and our ability to collect blood in our off-site mobile collection events. To ensure we meet physical distancing recommendations, we have reduced the number of donors we are able to welcome each day. We have also introduced numerous enhanced wellness measures to protect donors, staff and volunteers. At this time, we require all donors to book an appointment online at blood.ca, on the GiveBlood app, or by calling 1 888 2 DONATE (1-888-236-6283).

To enable us to open physical space in our donor centres, and to redeploy our employees to help collect blood and platelets, some plasma donation appointments were postponed. This was done to help us address the immediate need for blood and platelet collections. Plasma can be frozen and stored for up to one year, allowing us to maintain our inventory during this time. Red blood cells, however, have a shelf life of 42 days, and platelets have a shelf life of only seven days. This means we need to collect blood on a daily basis to ensure the platelet supply is consistently refreshed and given our reduction in mobile events are exploring ways to increase our operating ours at our donor centres.

These temporary adjustments have allowed us to optimize our full collections network during the COVID-19 pandemic. Thanks to the strength of our system, this temporary adjustment has allowed us to maintain optimal inventories for hospitals and other centres that receive blood and blood products — including plasma and plasma protein and related products. We continue preparing to open a new plasma donor centre in Sudbury, Ont. this summer, with two others opening in Lethbridge, Alta. and Kelowna, B.C. over the following year.

In addition to our efforts to optimize collections, the national blood inventory remains strong because the reduction in our operations has been mirrored by a reduction in demand. Canadian Blood Services is actively assessing information on how provinces are opening health services, such as surgeries and stem cell transplantation, in order to appropriately plan to meet an anticipated increase in demand in the coming weeks and months.

Canadian Blood Services is pleased to be collecting plasma from eligible donors who have recovered from COVID-19 and have been symptom-free for at least 28 days. This plasma will be used for national clinical trials approved by Health Canada to test the safety and effectiveness of COVID-19 convalescent plasma as a possible treatment to help patients with the virus. Caregivers of patients who have recovered from the virus can refer them to our registry at blood.ca/convalescentplasma if they would like to become donors. For the latest on our COVID-19 response, visit blood.ca/covid19.

NRBDO: Access to Innovative and Curative Therapies

Contributed by : Jennifer van Gennip Executive Director NRBDO

Many innovative and curative therapies for rare disorders are coming to market now and in the near future. Game-changing therapies are being developed for hemophilia, sickle cell disease, and aTTP patients to name just a few.

But while the science evolves rapidly, the NRBDO and its member patient groups have concerns about the review and reimbursement processes keeping up. New therapies are being developed, but will Canadian patients be able to access them?

In Canada, all plasma products and their replacements are to be distributed by Canadian Blood Services (CBS), funded by the provinces and territories collectively, and by Héma-Quebec in Quebec. But as some of these plasma protein replacements resemble less and less the originals in their mode of action while fulfilling the same function, questions arise about whether they should be on the formularies of the two blood agencies, or if they should instead be put on provincial and territorial drug formularies. These questions have, over the last two years, resulted in significant delays in new products coming to the Canadian market.

This is frustrating for patients and the physicians who treat them alike. The NRBDO is advocating to the provinces and territories for CBS to continue to distribute and provide universally and free of charge, all plasma products and their replacements, as described in the Memorandum of Understanding that the CBS was founded on.

On November 6, 2020, the NRBDO will hold a conference to explore the innovative and curative therapies coming to market for rare blood disorders, the barriers that patients and physicians face in accessing these therapies, and the role of patient organizations in improving access. Members of the Canadian Hematology Society who are interested in learning more and/or becoming champions for treatment access are invited to register by email at info@nrbd.ca.

The Network of Rare Blood Disorder Organizations (NRBDO) is a pan-Canadian coalition of not-for-profit organizations representing people with rare blood disorders and/or people with a chronic condition who are recipients of blood or blood products or their alternatives. We were founded in 2004.

You can learn more about the NRBDO or connect with any of our member patient groups at www.nrbd.ca, or via email at info@nrbd.ca.

Old but New: Preliminary Results from the QUAZAR AML-001 Maintenance Trial

By Danielle Hammond, MD

Charles de Gaulle would have been better off acknowledging that winning the battle is necessary, but not sufficient, for winning the war. The most effective post remission therapy for intermediate- and unfavorable-risk acute myeloid leukemia (AML) remains allogeneic hematopoietic stem cell transplantation (alloHSCT). Even with the widespread adoption of reduced intensity conditioning regimens for patients ≥ 55 -60 years, only a minority of patients with AML in first complete remission (CR) will be allografted, largely due to anticipated non-relapse mortality.

With the exception of arsenic trioxide and retinoic acid in acute promyelocytic leukemia (APL), no allograft sparing maintenance strategy has demonstrated sufficient benefit in AML to become the standard of care. It is not for lack of trying—a review of the literature reveals a graveyard of maintenance studies dating back to the 1960s which had mixed results with respect to disease-free and event-free survival (DFS, EFS), and almost none demonstrating overall survival (OS) benefit. This was true regardless of the agent(s) employed: dose-attenuated chemotherapy, gemtuzumab ozogamicin, lenalidomide, interferon, interleukin-2, sorafenib, and parenteral hypomethylating agents (HMAs) have all been tried. One exception is a French study which demonstrated a survival benefit in patients aged ≥ 60 years with AML receiving 2 years of maintenance therapy with norethandrolone, an androgen analog.¹ However, this “*joie de vivre*” strategy has not been widely adopted.

In transplant-ineligible patients, the master UK NCRI AML16 trial included a maintenance phase in which 453 patients with AML for MDS with $>10\%$ blasts in CR1 were randomly assigned, stratified by induction regimen and baseline characteristics, to receive 9 cycles of azacitidine 75 mg/m² on days 1-5 per 6-week cycle versus observation. There was no difference in 5-year OS between the maintenance and observation groups (24% vs 20%; $P = 0.5$). However, the rich got richer: in an unplanned subset analysis, there was improved OS

with azacitidine maintenance when looking exclusively at the patients who were MRD negative by flow cytometry (5-year OS 40% maintenance vs 13% observation arm; $P = 0.003$).² Most recently, the HOVON97 azacitidine maintenance trial demonstrated a DFS benefit of 15.9 versus 10.3 months but no OS benefit in 116 patients ≥ 60 years in CR or CR with incomplete count recovery (CRi) following 2 cycles of intensive chemotherapy.³ Echoing the findings of the UK NCRI AML16 post-hoc analysis, the DFS benefit was limited to patients in CR or CRi with preserved platelet counts, inferred to reflect higher quality (i.e. MRD negative) remissions.

CC-486 is an oral formulation of azacitidine that allows for extended dosing schedules hypothesized to prolong drug exposure to malignant cells and thus maximize clinical activity. Preliminary results from the QUAZAR AML-001 phase III trial (NCT01757535), which employed CC-486 as post-remission maintenance therapy in a placebo-controlled and double-blind design, were presented at the ASH 2019 meeting.⁴ Included patients were ≥ 55 years with either de novo or secondary (to MDS or CMML) AML without a recurrent translocation [t(8;21), inv(16)/t(16;16), t(15;17), or t(9;22)] who were in first CR/CRi following intensive chemotherapy (ICT) but not planned to receive a consolidative alloHSCT. How patients were deemed unfit for alloHSCT is unclear. Critically, patients who reached a CR/CRi with a HMA or had prior therapy with a HMA for MDS within 4 months of developing AML were excluded. Within 4 months of reaching first CR/CRi, 472 patients were randomized 1:1 to receive either CC-486 300 mg po daily ($n = 238$) or placebo ($n = 234$) on days 1-14 of 28-day treatment cycles. If there was evidence of early relapse (5-15% peripheral or bone marrow blasts), the dosing schedule could be intensified to 21 instead of 14 consecutive days per cycle. Treatment could be continued indefinitely until progression to $>15\%$ blasts, unacceptable toxicity, or alloHSCT. Minimal residual disease (MRD) was evaluated at baseline and during maintenance treatment.

The median age was 68 years (range 55-86). The vast majority (91%) had de novo AML, likely as a consequence of the HMA exclusion criteria. In turn

related to the lack of secondary AML cases, only 14% of patients had adverse-risk cytogenetics. Eighty percent of patient had received at least one cycle of consolidation chemotherapy prior to starting maintenance. Of note, 43% of patients randomized to the CC-486 arm and 50% randomized to the placebo arm were MRD positive prior to maintenance therapy, which presumably is an important source of relapse. The median number of cycles received in the CC-486 versus placebo arm was 12 (1-80) versus 6 (1-73). After a median follow-up of 41 months, the primary endpoint was met given that there was an almost 10-month improvement in OS favoring the CC-486 arm (24.7 vs 14.8 months; $P = 0.0009$) with a stratified hazard ratio of 0.69. There was a concordant improvement in RFS of ~5 months with a 1-year relapse rate of 53% in the CC-486 arm versus 71% in the placebo arm. Outcomes by baseline MRD status have not yet been reported. While the toxicity profile was described as “comparable” to parenteral azacitidine, in my opinion there were increased gastrointestinal side effects with a resulting difference in drug discontinuation in the CC-486 (5%) versus placebo (0.4%) groups. However, there was also a surprisingly high incidence of Grade 1 or 2 adverse GI effects reported even in the placebo group – nausea (64% CC-486 vs 23% placebo), vomiting (59% vs 10%), and diarrhea (49% vs 21%). From a myelosuppression perspective, there was only a notable increase in neutropenia <1.0 (41% CC-486 vs 21% placebo). This did translate into a modest difference in infections (17% CC-486 vs 8% placebo). Importantly, there was no disparate decline in health-related quality of life from baseline between the two groups.

While the QUAZAR AML-001 study represents a conceptional breakthrough in the management of AML, there are cautions to widespread dissemination of HMAs in the post-remission setting. The first is that the oldest patients are most in need of an allograft-sparing strategy, yet they are also the ones enriched for secondary AML and mostly excluded in this study on the basis of HMA exposure. Second, the clinical scenario studied here is anticipated to become increasingly rare. While performance status can deteriorate due to complications arising from induction chemotherapy, a population of patients deemed “fit” for induction with ICT yet “unfit” for a subsequent reduced intensity alloHSCT has always been an awkward concept that is rife with subjectivity. Furthermore, pending full results of the phase III VIALE-A study—which reportedly demonstrates (at least statically) superior remission rates and OS—venetoclax in combination with a HMA is anticipated to become the “non-intensive” standard of care induction regimen for non-APL AML. The line between induction and post-remission therapy with venetoclax plus HMA

regimens become blurred as one or both of these agents on attenuated schedules can be used for prolonged periods. Third, clinicians should not immediately extrapolate to using the widely-available parenteral HMAs with the expectation of similar survival benefit. CC-486 is believed to have succeeded where parenteral azacitidine has failed because of its convenient oral route enabling an altered pharmacokinetic profile. Lastly, the field is converging on tailoring post-remission therapy to MRD status. MRD status post chemotherapy appears to identify chemo-sensitive patients who are likely to benefit from additional similar treatments, such as HMAs, whereas the chemo-insensitive do not. It remains to be seen if CC-486 maintenance can eradicate MRD and overcome its adverse impact. In the likely event it cannot, such patients will be better served by small molecule inhibitors targeting persistent driver mutations, such as IDH and FLT3-ITD mutations, either alone or in synergistic pairings. Putting aside the vast differences in disease biology, the AML treatment paradigm is encouragingly inching closer to that employed in multiple myeloma: short periods of intensive treatment for active disease followed by intervals of non-toxic, rational maintenance therapy that reduces the rate of relapse, hopefully translating into improved survival without sacrificing quality of life.

1. Pigneux A, Béné MC, Guardiola P, et al. Addition of androgens improves survival in elderly patients with acute myeloid leukemia: a GOELAMS study. *J Clin Oncol*. 2017;35(4):387-393.
2. Burnett A, Russell N, Freeman S, et al. A comparison of limited consolidation chemotherapy therapy or not, and demethylation maintenance or not in older patients with AML and high risk MDS: Long term results of the UK NCRI AML16 trial [abstract]. *Haematologica*. 2015; 100(S1). Abstract 513.
3. Huls G, Chitu DA, Havelange V, et al. Azacitidine maintenance after intensive chemotherapy improves DFS in older AML patients. *Blood*. 2019;133(13):1457-1464.
4. Wei AH, Döhner H, Pocock C, et al. The QUAZAR AML-001 Maintenance Trial: Results of a phase III international, randomized, double-blind, placebo-controlled study of CC-486 (oral formulation of azacitidine) in patients with acute myeloid leukemia (AML) in first remission. Abstract #LBA-3. Presented at the 2019 ASH Annual Meeting, December 10, 2019; Orlando, FL.



Hope to see you at ASH Dec 5-8, in San Diego! Dr. Nicole Laferriere President, CHS

2019 CHS AWARDS



Ryan Rys 2019 PhD and Post-Doctoral Abstract Award



Dr. Victor Blanchette 2019 Lifetime Achievement Award



Elysha VanderVeer 2019 Stephen Couban Award

CHS Executive:

**From left to right -
Nicole Laferriere, President,
Gail Rock, Exec. Vice-President,
Chris Hillis, Secretary,
Caroline Malcolmson, Chief
Resident,
Lynn Savoie, Past-President.
(Missing, Hassan Sibai, Treasurer,
and Jason Berman,
Vice-President)**



Aaron Schimmer 2019 Paper of the Year Award



Josheph. R. Shaw 2019 John Crookston Award



Dr. Gail Rock and Dr. Blanchette

Dr. Victor Blanchette Recipient of the CHS Lifetime Achievement Award 2019

Dr. Victor Blanchette was awarded the CHS Lifetime Achievement Award at the CHS Members Annual Reception, Awards, Presentations and Dinner on December 6, 2019 for his outstanding contributions in the field of Hematology and Oncology. Dr. Blanchette is Professor of Pediatrics, at the University of Toronto; a Staff Pediatric Hematologist in the Division of Hematology/Oncology and a Senior Associate Scientist (Emeritus) in the Research Institute at the Hospital for Sick Children, Toronto. He is the McCaig Magee Family Medical Director of the SickKids-Caribbean Cancer and Blood Disorders Initiative in the Centre for Global Child Health at the Hospital for Sick Children.

After completing his medical training at the University of Cambridge and St Bartholomew's Hospital in the United Kingdom, Dr Blanchette pursued subspecialty training in pediatrics at Johns Hopkins Hospital in Baltimore, USA followed by fellowship training in pediatric hematology/oncology at McMaster University Medical Centre in Hamilton, Canada.

Dr Blanchette's research interests are in the area of the congenital and acquired bleeding disorders of children. He is Co-Director of the Pediatric Comprehensive Care Hemophilia Program at the Hospital for Sick Children, and Chair of the International Prophylaxis Study Group (IPSG). Dr. Blanchette is recipient of the Canadian Pediatric Society 2009 Alan Ross Award, the Canadian Blood Services 2010 Lifetime Achievement Award, the American Society of Pediatric Hematology/Oncology 2012 Distinguished Career Award and the 2019 Hemostasis and Thrombosis Research Society (HTRS) Lifetime Achievement Award. In 2018 Dr. Blanchette was awarded the Order of Barbados (Silver Crown of Merit), the country of his birth, for his contributions to the field of medicine. Dr Blanchette is an elected Fellow of the Royal College of Physicians and Surgeons of the United Kingdom.

Dr. Blanchette is well known for his desire to provide the same level of medical care for all children in need no matter where they are in the world. In 2012 Dr. Blanchette spearheaded the SickKids- Caribbean Initiative (SCI) to give back to his home country of Barbados. With his philosophy of every child deserves



the same level of medical care no matter what their socioeconomic background is or their location in the world he was able to identify the disadvantageous of children living with cancer or blood disorders in six Caribbean countries and was instrumental in laying the ground work for the SCI.

Over the years the SCI was able to establish six working groups, made up of a cross -section of individuals from the Caribbean sites and SickKids: Clinical Care, Diagnostic Services, Local Oncology Databases, Nursing, Sickle Cell Disease and Research, Scholarly Activities and Advocacy. The SCI went on to install seven telemedicine sites in hospitals in the six SCI participating countries and trained three hematology/oncology Caribbean doctors. The SCI was also able to train 27 nurses from five countries in the first post-basic haematology/oncology diploma program at the University of the West Indies School of nursing. All of these measures have profoundly impacted the lives of children living with cancer and sickle-cell disease in the Caribbean.



Canadian Hematology Society (CHS)
 Annual Reception, Dinner & Awards Evening
 Sunday December 6, 2020.
 San Diego, California, USA
 Contact:
office@canadianhematologysociety.org

Jerry Scott Day
 to be held virtually
 July 18, 2020.
 For more
 information please
 email: heme.prg.utoronto.ca

American Society for Apheresis (ASFA)
 2020 Annual Meeting Cancelled due
 to COVID-19
 Contact for updates:
<http://www.apheresis.org/page/ASFA2020>

**38th World Congress
 of the International
 Society
 of Hematology
 (ISH)**
 Postponed until
 March 8-10, 2021
 Bangkok, Thailand.
 For more
 information
 please visit:
ish2020.org



**European Hematology
 Association (EHA) Annual
 June 11-14, 2020**
 Virtual Congress
 For more information
 please visit:
annual.congress@ehaweb.org



YOUR CHS NEWSLETTER The Microenvironment

**Member
 submissions
 welcome!**



Contact: office@canadianhematologysociety.org

RK SMILEY WINNERS 2020

Dr. Courtney Jones, University Health Network

Dr. Courtney
Jones



Identification of Glutathionylated Proteins in the Mitochondria of Leukemia Stem Cells

The long-term objective of this project is to target glutathione (GSH) regulated energy metabolism in leukemia stem cells (LSCs) with the overall goal of improving outcomes for AML patients. This goal fulfills an important clinical need, as current therapies do not fully eradicate the LSC population. Our preliminary data suggests that GSH metabolism supports oxidative phosphorylation (OXPHOS), an Achilles heel of LSCs, through a process called glutathionylation. Therefore, the goal of this project is to identify OXPHOS related proteins that are glutathionylated in LSCs. Upon successful completion of this project we will have identified a novel mechanism by which GSH metabolism regulates OXPHOS in LSCs which may lead to the identification of new therapeutic targets in AML.

Andrew Leber, BHSc and Dr. Clinton Campbell, MD, PhD, FRCPC, McMaster University

Marrow: A deep learning platform to improve diagnosis in hematology.

The future of diagnostic pathology is digital, and the need for digital and remote workflows is more evident now than ever. Consequently, there is great interest in applying a type of artificial intelligence (AI) called deep learning to support pathology diagnostic workflows through digital whole slide image (WSI) analysis. Deep learning has shown success in pathology image classification tasks in several non-hematological pathology specialties, but there are few applications of deep learning to hematopathology. The current paradigm in computational WSI analysis uses supervised deep learning approaches, where pathologists manually annotate cells or tissues to train AI models.



Dr. Clinton
Campbell

This approach has several important problems:

- 1) it instills human bias into the AI model (it assumes pathologists are the correct reference standard);
- 2) it is unfeasible to manually label the immense image datasets required for robust network training;
- 3) these models usually fail to generalize.

To address these challenges, we propose Marrow, a set of novel deep learning solutions specifically designed for bone marrow cell and tissue analysis. Marrow uses unsupervised deep learning methods, where AI algorithms learn morphological features without extensive labelling, allowing an unbiased assessment of bone marrow histomorphology. Furthermore, our technology will yield new representations of the information in bone marrow cells and tissue that may be different from those seen by the human brain. This technology will lay the foundation for further larger studies that may eventually help redefine the field of diagnostic hematology and transition it into the era of precision diagnostics.

THE RK SMILEY RESEARCH GRANT — 2020

Established in 2011 to mark the Fortieth Anniversary of the Canadian Hematology Society's service and to support hematology practitioners in Canada, this award is named in honour of the CHS Founding President, Dr. R.K. Smiley. Many impressive submissions from across Canada have been funded under the previous invitations to submit applications to this research grant program since its inception.

Dr. R.K. Smiley
1922 - 2010 • CHS Founding President



PROGRESS REPORTS FROM THE 2019 RECIPIENTS OF THE RK SMILEY AWARD

Kevin H. M. Kuo
(Principal Investigator)
University of Toronto
Denis Soulières,
Stéphanie Forté,
Véronique Naessens,
Sébastien Béland
and Melanie Cohn



Kevin H. M. Kuo

Background:

Sickle cell disease (SCD) patients are at significant risk for neurologic complications. At least 33% of adults have cognitive dysfunction. However, access to specialized assessments is limited, but is a pre-requisite for neurorehabilitation. As such, there is an unmet need for a validated screening tool for mild cognitive impairment (MCI) in SCD. The Rowland Universal Dementia Assessment Scale (RUDAS) is not biased by education and has been validated in many cultures. Hypotheses: RUDAS is a reliable and valid measure of MCI.

Methods: Study design: cross-sectional, multicentre (University Health Network (UHN), Centre Hospitalier de l'Université de Montréal (CHUM), and McGill University Health Centre (MUHC)). Inclusion criteria: Out-patients ≥ 18 ; all SCD phenotypes.

Exclusion criteria: inability to obtain informed consent and/or follow study instructions. Intervention: RUDAS is administered twice, 2-4 months apart, in French or English. Questionnaires on demographics and patient-reported outcomes (PROMIS® tools for Depression, Anxiety and Cognitive Function Abilities) will be completed. UHN, CHUM and MUHC will recruit 125, 92 and 38 participants respectively.¹

Statistical plan: Characteristics of the lowest and highest-performing quartile will be compared using Chi-squared test. Overall test generalizability, test-retest reliability and internal consistency will be calculated using G-theory. Multivariable regression will be applied to identify predictors of RUDAS (age, sex, educational attainment, household annual income, occupational status, genotype, symptoms of depression or anxiety, SCD severity score, disease-modifying therapy, hematocrit, evidence of ischemic injury and/or vasculopathy on MRI, and PROMIS® scores).

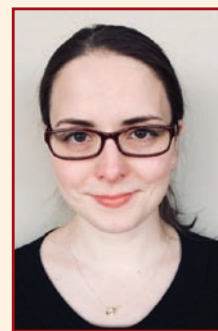
Preliminary Results: In the CHUM cohort, RUDAS declines with age and unemployment but is independent of sex, language and educational attainment. 9/92 participants (9.8 %) scored $< 23/30$ and were referred to appropriate resources.

Implications/Future directions: RUDAS may be a promising tool to identify the patients at highest risk for MCI who need access to specialized neurocognitive, educational and social interventions. Successful application of the CHS grant will provide the necessary funding to complete this pilot study. If

reliability of the RUDAS score is established in the SCD cohort, we will leverage these results to apply for a CIHR grant and compare the performance of the RUDAS to formal neurocognitive testing.

¹Sample size calculation: assuming an AUC of 0.9, and a conservative standard error (SE) estimate of 0.02348 derived from all previous studies on RUDAS, 255 participants is required, of which 85 (33.3%) is estimated to have MCI.^a

Miriam Kimpton
(Principal Investigator)
Ottawa University
Marc Carrier,
Aurelien Delluc



Miriam Kimpton

Polycythemia vera (PV) and essential thrombocythemia (ET) patients are at an elevated risk of both arterial and venous thromboembolic events.

Guidelines recommend thromboprophylaxis with low-dose aspirin for all PV patients and for ET patients with the JAK2 mutation (JAK2ET), who do not have a contraindication for this therapy. The rate of thromboembolic events, however, remains unacceptably elevated with this thromboprophylactic strategy. Apixaban is a direct oral Xa inhibitor, which has shown good efficacy and safety as a thromboprophylactic agent in various patient populations.

The aim of this pilot project is to assess the feasibility of a randomized controlled trial (RCT) comparing apixaban 2.5mg BID to low-dose aspirin in decreasing the risk of thromboembolic complications.

We propose to conduct a prospective, randomized, open label, blinded endpoints trial of 20 patients at The Ottawa Hospital (Ottawa, Ontario). All PV and JAK2ET patients over the age of 18, without a contraindication for thromboprophylaxis or a need for a particular anticoagulation or antiplatelet therapy, will be asked to participate.

The primary outcome will be the monthly rate of recruitment. Secondary outcomes will include additional feasibility measures (retention and adherence proportions) as well as clinically meaningful outcomes (rates of arterial thrombotic events, venous thrombotic events, and major bleeding).

The pilot project provided us with the opportunity to gather invaluable information for the planning of the full-size RCT, and will form the basis for additional peer-review funding applications, such as Canadian Institutes of Health Research grants.



Membership Matters



The Canadian Hematology Society has represented all physicians and scientists with an interest in the discipline in Canada since it was founded in 1971, and currently has over 500 members.

1. Active Members

- Physicians and researchers in the practice of clinical or laboratory hematology in Canada, or
- Canadian physicians engaged in such practice, or
- Persons with university degrees making continuing contributions to research in hematology physiology or pathology in Canada

Active members only shall:

- vote
- hold office
- receive CHS grants, and
- pay dues.

2. Allied Health Members

- Health care workers engaged in the practice of clinical or laboratory hematology in Canada

3. Members-in-Training (Associate Members)

- Residents and fellows engaged in hematology training
- Masters and PhD graduate students
- Post-doctoral fellows engaged in hematology research
- The Program Director shall sponsor membership
- Shall hold all privileges of the Corporation except payment of dues or voting at the AGM
- Expected to become Active Members upon completion of training

4. Emeritus Members

- All individuals who have retired from full time hematology practice or research, or those who were active members and request a transfer of status with adequate reason.

5. Honourary Members

- Non-members may be invited to become Honourary Members of the corporation by virtue of their outstanding contributions to any discipline which is of importance to hematology.

CHS members are reminded... If you have not sent in your dues payment for **2020** it is now past due. The CHS annual dues are **\$125** for Active members and **\$75** for Allied Health. Payable on **January 1, 2020**; due on **March 1, 2020**

Annual dues payments may be made online at the CHS website: www.canadianhematologysociety.org Or by mail to: Canadian Hematology Society, 199-435 St. Laurent Blvd., Ottawa, Ontario K1K 2Z8

Please provide the following information with your payment:



2020 Membership Renewal / Address Change: Canadian Hematology Society

Membership Status

- Active
- Associate
- Allied
- Emeritus

Name: _____

Title: _____

Email: _____

Work Address: _____

Has your status changed?

- Yes
- No

Work Phone: _____

Work Fax: _____