



SCIENTIFIC ROUNDTABLE

MAKING MYELOMA MATTER

14th annual Myeloma Canada Scientific Roundtable

Meeting Summary

November 3- 4, 2023

Montreal, Quebec

Prepared by: David McMullen

Reviewed by: Gabriele Colasurdo

Introduction

The 14th annual Myeloma Canada Scientific Roundtable convened myeloma clinicians and researchers from the major myeloma treatment and research centres across Canada, internationally renowned myeloma researchers from the United States and Europe, clinical trial nurses, representatives from industry partners, and patient representatives, to:

- Exchange highlights of recent myeloma related research and treatment development work
- Review new myeloma treatments in the research pipeline
- Facilitate planning and collaboration of future Canadian myeloma research

This year's theme was "unmet need populations" and the focus was on novel concepts and innovative treatment approaches to address gaps in patient care. The meeting was ably chaired by Dr. Nizar Bahlis from Calgary and Dr. Keith Stewart from Toronto. The agenda consisted of academic presentations, industry presentations, clinical trial updates, and an update from Myeloma Canada. There was much opportunity for networking among attendees.

Sponsors

Thank you to the following sponsors for their generous support of the 14th annual Myeloma Canada Scientific Roundtable.

- **Gold:** Janssen, Pfizer
- **Silver:** AbbVie, Sanofi, Takeda
- **Bronze:** Amgen, FORUS Therapeutics, GlaxoSmithKline, Rapid Novor
- **Supporters:** Binding Site, Bristol Myers Squibb, JAMP Pharma, Sebia Diagnostics, Telo Genomics

Academic Presentations

Many of this year's topics were different from those of previous annual meetings. They included:

- Ultra High-risk Newly-diagnosed Multiple Myeloma
- Renal Failure in Multiple Myeloma
- The Very Elderly with Multiple Myeloma
- Advanced Stage IIIb AL Amyloidosis
- Waldenström Macroglobulinemia

Each topic comprised of 2-3 presentations, followed by a question and panel discussion session. There was much rich discussion. Below is a brief overview of the presentations.

Ultra High-Risk Newly Diagnosed Multiple Myeloma

Molecular Tools for Defining Ultra High-risk Disease

Dr Keith Stewart, Princess Margaret Cancer Centre, Toronto

- Treating ultra high-risk disease remains an unmet need.
- Dr Stewart reviewed:
 - Various methods and approaches for defining high-risk, including frailty, age, and the number of high-risk chromosomal abnormalities, in addition to the Revised International Staging System.
 - Gene expression profiling (e.g., SKY92; whole genome sequencing) methods are improving.
- Clinical care should be optimized based on risk and should use the best available therapies.

Managing Newly Diagnosed Multiple Myeloma in 2023

Dr Saad Usmani, Memorial Sloan Kettering Cancer Centre, New York

- Stratifying patients based on risk is important.
 - Standard risk patients generally do well.
 - Treating patients with high-risk disease remains challenging.
- Depth of response matters, especially for high-risk disease.
 - We are moving towards minimal residual disease (MRD) negativity and sustained MRD negativity.
- The future lies in genomic sequencing to examine the biology of the disease and optimize treatment based on the biology.
- Frailty is an important feature in organizing treatment.
- Transplant remains important for some patients, especially for high-risk disease.
 - In New York they use a four-drug combination for high-risk disease, and two-drug maintenance.
- Consider T cell therapy for high-risk disease, early in the disease.
- Using daratumumab in front-line treatment is beneficial.

Renal Failure in Multiple Myeloma

Novel Treatment of Myeloma in the Acute Kidney Injury Setting

Dr Meletios Dimopoulos, University of Athens, Greece

- In spite of earlier diagnoses, almost half of newly diagnosed patients still have renal impairment.
 - Severe renal impairment is a medical emergency.
 - 24-hour urine testing is still important to have at diagnosis, and at various times later.
- Renal impairment can be reversible.
 - Important factors include age, other health conditions, and myeloma treatment response.
- Dr. Dimopoulos reviewed various myeloma treatments and their impact on the kidneys.

Advances in Renal Care

Dr Adriana Rossi, Mount Sinai Health System, New York.

- Myeloma can damage any part of the kidney's nephrons (filters fluid and waste from the blood).
- Kidneys can also be damaged by dehydration, sepsis, or cytokine release syndrome.
- Dr Rossi reviewed two recent studies, EuLITE and MYRE, that examined myeloma patients on hemodialysis.
- Myeloma therapies are now so powerful that fewer severe kidney problems occur.
 - Patients are living longer and kidney transplants are now being conducted for some patients.
- Monoclonal gammopathy of renal significance (MGRS) is being studied more now than previously.
 - The International Kidney and Monoclonal Gammopathy Research Group is active in this area.

The Very Elderly with Multiple Myeloma

Physiology of Aging and Novel Supportive Care Approaches

Dr Tanya Wildes, University of Nebraska, Omaha

- The biology of aging, including telomere length, cellular senescence, and mitochondrial dysfunction, translates into physiology of aging, with huge heterogeneity.
- Geriatric assessment profiling tools have been developed, with four domains: functional, physical, psychological, and social-economic.
- Studies show that application of these tools can result in better patient communication with the physician, and can help guide treatment and supportive care for older patients. It can result in medication adjustments, better quality of life, less toxicity, fewer severe adverse events, and fewer emergency hospital events, without compromising survival.
- Geriatric assessment may be the next frontier in improving care for patients.

Management of the Very Elderly Myeloma Patient

Dr Hira Mian, Juravinski Cancer Centre, Hamilton

- In the next decade, 2/3 of newly diagnosed patients will be over 70 years of age. In older adults with myeloma:
 - Early mortality is a problem and there is a wide spectrum of aging.
- There is benefit in conducting frailty assessment in older adults, at diagnosis and at other times.
 - There are various methods of frailty assessment.
 - Frailty assessment is being discussed more.
 - Frailty is dynamic and can change over time.
- It's important not to overtreat older adults with myeloma.
 - It's also important not to undertreat because myeloma is still their leading cause of mortality.
- Frailty assessment should be considered for bispecific antibody and CAR T-cell treatments, and in clinical trials.

Clonal Hematopoiesis in the Elderly Patient

Dr Aniket Bankar, Princess Margaret Cancer Centre, Toronto

- There is a condition called clonal hematopoiesis (CH), or clonal hemopoieses of indeterminate potential (CHIP) that has been studied recently, with significant studies in 2014 and more recently.
- Incidence of CH increases with age.
 - CH may impact on the likelihood of developing cancers, and other diseases.
- Significant proportions of myeloma and MGUS patients have CH.
 - Myeloma outcomes may be affected by presence of CH.
 - Lenalidomide can be beneficial.
- There are currently no interventions targeting CH.

Advanced Stage IIIB AL Amyloidosis

Emerging Treatment Approaches for Stage IIIB AL Amyloidosis

Dr Ashutosh Wechalekar, University College London, United Kingdom

- Dr Wechalekar reviewed both existing and newer practices for the treatment of this advanced stage of AL amyloidosis.
 - Various clinical trials are underway for stage IIIB AL amyloidosis.
- Many of the treatments are similar to those for myeloma.

Achieving Early Cardiac Response

Dr Victor Jimenez-Zepeda, Tom Baker Cancer Centre, Calgary

- Preventing early mortality in patients with significant cardiac damage from AL amyloidosis is an unmet need.
 - Dr Jimenez-Zepeda reviewed various tests and treatment approaches targeting early cardiac response.
 - Early diagnosis is important.
 - Daratumumab can be beneficial.
- The “Amyloidosis Program of Calgary” was created for treatment and research with the goal of improving outcomes for patients and families affected by amyloidosis.

Waldenström Macroglobulinemia (WM)

Understanding Neuropathy and Novel Approaches

Dr Shirley D'Sa, University College London, United Kingdom

- There are various types and causes of neuropathy in WM.
 - Various tests and clinical observations can be used to determine these.
- Dr. D'Sa reviewed treatments that might be used for WM associated neuropathy, based on type, cause, and severity of the neuropathy.
- Monoclonal gammopathy of neurological significance (MGNS) is being studied.

Novel Approaches for MYD88-neg Waldenström Macroglobulinemia

Dr Jorge Castillo, Dana-Farber Cancer Institute, Boston

- A minority subset of WM patients don't have the MYD88 gene mutation.
 - Diagnosis of this disease, called “wild type WM”, is more difficult and requires additional tests.
 - Prognosis is poorer.

Industry Presentations

There were nine sponsors that made brief presentations about their products, services, research, future plans and potential developments. Four of the presentations were “open” and are therefore reported on herein.

Forus Therapeutics

- Forus brings new products to Canadians, including selinexor (Xpovio) for myeloma.
- At that time, selinexor with bortezomib and dexamethasone (XVd) was covered in eight provinces.
- Gastrointestinal effects can be reduced by various measures, including dose reduction.
- Selinexor is being evaluated with other drug combinations.

Rapid Novor

- Their core business (based in Kitchener, Ontario) is antibody sequencing by mass spectrometry.
- EasyM is a mass spectrometry-based blood test for monoclonal protein that they developed.
 - It is a highly sensitive test used for MRD testing and monitoring for myeloma.
 - EasyM is certified and available for clinical use in the US and awaiting certification in Canada.

Sebia Diagnostics

- Sebia provides equipment for serum protein electrophoreses (SPEP) and immunofixation (IFE) testing.
- They've developed:
 - A new test for serum free light chain testing.
 - A method to eliminate interference from daratumumab and isatuximab in SPEP and IFE testing.
 - M-InSight, a very sensitive blood-based mass spectrometry test for monoclonal proteins.

Binding Site

- Binding Site are developing a sensitive, easy to use mass spectrometry method for monoclonal proteins, called EXENT.
- It has been launched in Europe, and submitted to the US FDA. Submission to Health Canada is anticipated in 2024.

Myeloma Canada 2023 Updates and Announcements

Martine Elias, Executive Director, Myeloma Canada

Martine reviewed:

- Myeloma Canada's [Promise](#) and the importance of patients in everything they do;
- the [Myeloma Priority Setting Partnership \(PSP\)](#) and the [Myeloma Top 10 Priorities](#) for research that is engrained in all the research that MC funds. The focus of the top 10 priorities is on supporting clinical research, improving quality of life, and health care delivery. Myeloma Canada Research Strategy is based on these priorities.
- Myeloma Canada's 2023 science and research impact.
 - **Clinical research:** Myeloma Canada committed \$450k over four years (\$300k in 2023) to support aspects of the [Canadian Clinical Trials Group MY.13 Clinical Trial](#) (an important Canadian Clinical Trials Group trial evaluating duration of daratumumab use).
 - **Aldo Del Col Research Grant program:** There were 13 project applications. A very structured process was used by an Independent Research Review Committee. This included: 1) individual review and ranking based on scoring criteria; 2) committee review; 3) Final ranking and selection of projects to fund. The Leukemia and Lymphoma Society of Canada partnered with Myeloma Canada to equally co-fund four research grants totalling \$400k.
 - **Défi Everest Challenge Research Grant in partnership with Myeloma Foundation 8849M:** The purpose of the grant was to improve diagnosis ([click here to see PSP priority #3](#)). There were four applicants; \$59.5k was awarded for a project led by Dr Alissa Visram and Dr Julie Stakiw.
 - **Pfizer Quality Improvement Grant partnership:** Four out of six applicants were awarded grants (approximately \$266k) to support quality improvement projects to advance the quality of care and best practices around treatment for patients with relapsed/refractory myeloma receiving bispecific antibody treatment. Myeloma Canada was the lead organization for the review and evaluation of the grant proposals.
 - **Dr. Andrew Belch Grant:** Eight young investigators were awarded grants of \$4k each for registration and travel expenses to attend a conference where they had an approved abstract.
 - **Research Fund-sharing Grants:** These involved partnering with hospital or university foundations for select Multiple Myeloma Marches, where a portion of the proceeds fund a project led by a myeloma researcher. Six researchers from across Canada received this award in 2023.
 - **Continuing Medical Education:** Myeloma Canada sponsored an educational program for primary care providers that is in development by Queen's University.

All of this work would not be possible without the Canadian myeloma community's involvement in fundraising marches and bike rides. Patients want to see their money used wisely, and that there is accountability. As such, Myeloma Canada produces yearly [Impact Reports](#). A target for 2030 is to have at least \$10 million invested annually in myeloma research, through fundraising and through partnerships with other organizations that fund myeloma research. Myeloma Canada has recently:

- joined the Canadian Cancer Research Alliance, enabling networking for funding partnerships with many other funding organizations;
- achieved Imagine Canada Level 2 Accreditation.
 - This enhances Myeloma Canada's governance and credibility among patients, and other funding organizations. It opens doors for other funding opportunities, including from large corporations. Myeloma Canada is one of the first small cancer organizations to achieve this accreditation;
- developed a business case for developing Canadian made CAR T-cell therapy.

Some of Myeloma Canada's plans for 2024 include:

- Launch of a new redesigned website with a section for healthcare professionals.
 - Upcoming projects (pending partner funding) include:
 - Developing Patient-Reported Outcome Measures (PROMs) for myeloma.
 - Incorporation of Minimal Residual Testing Infrastructure for Myeloma in Canada.
 - Continuation of work on the [Myeloma Consensus Guidelines](#).
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Writer's Comment

The high calibre of talent, dedication and passion of myeloma researchers in Canada is most impressive. We owe them huge appreciation and gratitude. Very much credit is also due to Myeloma Canada for organizing the 2023 Myeloma Canada Scientific Roundtable, facilitating collaboration of the Canadian myeloma researchers, to stimulate research, and to help maximize the potential of the Canadian myeloma research community. This research work will greatly benefit Canadian myeloma patients.