CRA/CanRIO Living Guidelines for the Management of Baseline Immunosuppression in Individuals with Pre-existing Rheumatic Diseases Initiating Immune Checkpoint Inhibitors: A Summary and Reflection

By Shahin Jamal, MD, FRCPC, MSc; and Carrie Ye, MD, FRCPC, MPH

Immune checkpoint inhibitors (ICIs) have revolutionized cancer treatment and outcomes by facilitating chronic activation of the immune system to target and destroy cancer cells. They are being used for multiple different types of cancers, and in different ways including for curative intent, palliative intent and as adjuvant therapy. In the US, patients with cancer eligible for ICI treatment increased from 1.54% in 2011 to 43.68% in 2018.[1] With the growing use of ICI (sometimes in combination with other ICI, chemotherapy, targeted therapies, hormone therapies, cancer vaccines, and other emerging therapies) and the aging population, ICI use is predicted to continue expanding in the coming years. The downside of chronic immune activation is the development of off-target inflammatory reactions, called immune-related adverse events (irAE), which can impact any body system.

Patients with pre-existing rheumatic diseases (PRD) were largely excluded from clinical trials studying ICI in cancer. Regardless, it is widely accepted that our patients with PRD should be offered ICI, if indicated, for their cancer. Our role as rheumatologists is to work with the oncologist, patient and other health care providers to optimize cancer outcomes in the safest way possible.[2] In clinical practice, patients with PRD have unique challenges including higher risk of developing de novo irAE, risk of flare of their underlying rheumatic diseases, and management of their baseline immunosuppression to optimize cancer outcomes without a flare in their underlying disease.

There are currently no clinical trials or other guidelines to help guide clinicians on best practices to manage rheumatic disease in patients who are being treated with ICI for their cancer. To this end, the Canadian Rheumatology Association (CRA) and Canadian Research Group of Rheumatologists in Immuno-Oncology (CanRIO) collaborated to develop living guidelines on optimal management of baseline immunosuppression in patients with PRD who are initiating ICI. The multidisciplinary panel (see photo) included clinical rheumatology experts from across Canada, along with an oncologist, methodologist and patient partner. The guidelines are divided into two parts, with part 1 focusing on patients with pre-existing inflammatory arthritis (including rheumatoid arthritis, polymyalgia rheumatica, psoriatic arthritis, and seronegative spondyloarthropathy) and part 2 focusing on patients with pre-existing systemic autoimmune rheumatic diseases (including systemic sclerosis, systemic lupus erythematosus, Sjogren's disease, myositis, sarcoidosis, vasculitis and Behcet's disease).[3,4] General good practice statements and specific statements regarding management of baseline immunosuppression by disease are summarized in the tables which accompany the published articles. In general, we recommended de-escalating baseline immunosuppression for those with pre-existing inflammatory arthritis, while recommending continuing the same level of immunosuppression for those with pre-existing systemic autoimmune rheumatic diseases, although nuances exist for each specific PRD. These guidelines have been made available as open access for wide distribution and use. As they are living guidelines, we will be able to update them as research evolves.

The development of these living guidelines has been a collaborative and rewarding experience, with a steep learning curve for us all. We would like to acknowledge the support of the CRA Guidelines Committee, especially Jordi Pardo and Glen Hazlewood, and our patient partner, Dirk Velthuizen, who provided invaluable insights. We hope that these guidelines will be useful for clinical care and advocacy and as a platform for further research.

Panel Members at the End of Two Days of Discussion and Voting:
Top row (from left to right): Alexandra Ladouceur, Marie Hudson, Faiza Khokhar, Janet Roberts, and Aurore Fifi-Mah.
Second row: Dirk Velthuizen, Carrie Ye, Nancy Maltez, Megan Himmel, and Shahin Jamal.
Third row: Roko Nikolic, Jordi Pardo, Janet Pope, Ines Colmegna, and Alexandra Saltman.
Bottom row: Sabrina Hoa, May Choi, and Lourdes Gonzalez Arreola.

CRA/CanRIO are working on two further guidelines, focusing on ICI-induced inflammatory arthritis and ICI-induced myositis, so stay tuned.

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2. Kostine M, Finckh A, Bingham CO, et al. EULAR points to consider for the diagnosis and management of rheumatic immune-related adverse events due to cancer immunotherapy with checkpoint inhibitors. *Ann Rheum Dis.* 2021;80(1):36-48.
3. Ye C, Nikolic RPA, Choi M, et al. Canadian Rheumatology Association/Canadian Research Group of Rheumatology in Immuno-Oncology Living Guidelines for Baseline Immunosuppression in Individuals With Preexisting Rheumatic Diseases Initiating Immune Checkpoint Inhibitors. Part 1: Preexisting Inflammatory Arthritides. *J Rheumatol.* 2025.
4. Ye C, Nikolic RPA, Choi M, et al. Canadian Rheumatology Association/Canadian Research Group of Rheumatology in Immuno-Oncology Living Guidelines for Baseline Immunosuppression in Individuals With Preexisting Rheumatic Diseases Initiating Immune Checkpoint Inhibitors. Part 2: Preexisting Systemic Autoimmune Rheumatic Diseases. *J Rheumatol.* 2025.