Immune checkpoint inhibitors in cancer immunotherapy

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1 Immune checkpoint inhibitors (ICIs) are novel therapeutic agents increasingly used in cancer therapy

Tumour cells can evade destruction by the immune system by triggering immune checkpoint receptors, such as cytotoxic T-lymphocyte–associated protein 4 (CTLA-4), programmed cell death protein 1 (PD-1) or programmed death-ligand 1 (PD-L1), that are expressed on T-cells and whose engagement inhibit T-lymphocyte function.[1] Immune checkpoint inhibitors are monoclonal antibodies that prevent this immunosuppression by blocking the engagement of these checkpoint molecules, thereby reinvigorating the antitumour immune response.

2 ICIs have shown unprecedented, durable survival benefits in the treatment of some cancers with historically poor prognoses and limited therapeutic options[2]

At present, 7 ICIs have been approved by Health Canada for first- and second-line use for treatment of several advanced malignant diseases including non-small–cell lung cancer, renal cell carcinoma and melanoma (Appendix 1, available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.191231/-/DC1).[2] Combination ICI therapy with ipilimumab and nivolumab in metastatic melanoma has led to a 5-year survival rate of 52%, compared with less than 25% before the availability of ICIs.[3,4]

3 Enhancing the immune response using ICIs can result in immune-related adverse events that can affect nearly every organ system[5]

Toxicities are common and occur in as many as 72% of patients who are treated with ICIs. Toxicities can range from mild to severe (Appendix 1).[5] Given the complexity of these presentations and the possibility of poor outcomes, the key management principle for primary care physicians is early recognition followed by timely and appropriate specialist consultation.

4 Treatment of immune-related adverse events typically includes delaying administration of the ICI and starting immunosuppressive therapy[5]

Guidelines for the management of specific toxicities are accessible online from Cancer Care Ontario.[5]

5 Funding for ICI use is approved at the provincial level, which leads to variable access across Canada

Current provincial funding indications can be accessed online via the Canadian Agency for Drugs and Technologies in Health (CADTH) website (www.CADTH.ca). Although funding discrepancies do exist among provinces, gaps are typically filled by private insurers or special access programs. Primary care physicians can help patients navigate funding by consulting with their local oncologists.

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