Programme de
GESTION THÉRAPEUTIQUE
des médicaments

PGTM Clinical Intervention Model (CIM)

Descriptive analysis of the use of anti-PD-1 antibodies in cancer patients in Quebec's university teaching hospitals (UTHs) - 2020

Background:

The development of the field of cancer immunotherapy has revolutionized cancer treatment in recent years, and the use of antibodies that target the immune system has only increased since then. The use of anti-PD-1 antibodies for different cancer treatment indications has contributed significantly to this development. When this study was carried out, the use of anti-PD-1 antibodies was approved for three indications: the treatment of melanoma, non-small cell lung cancer (NSCLC) and kidney cancer.

In its April 2017 letter aimed at cautioning about the safety of immunotherapy, the Direction générale de cancérologie (DGC) (now called the Quebec Cancer Program [Programme québécois de cancérologie [PQC]) asked health-care facilities to keep a list of patients who receive any drug in the class of immune checkpoint inhibitory immunotherapies. The list could enable physicians and pharmacists to track the use of these drugs and to study the therapeutic outcomes. The PGTM has chosen to develop a profile of the use, since 2011, of nivolumab and pembrolizumab, two antibodies that target the PD-1 receptor, with a view to improving the understanding of their use and for the purpose of comparing their efficacy and safety with the Phase III pivotal studies and a few observational studies in a real-world setting.

The PGTM's scientific recommendations

In the spring of 2017, the Quebec Cancer Program published a caution. The letter urged clinicians to monitor the use of drugs in the class of immune checkpoint inhibitory immunotherapies in order to track their use and study the therapeutic outcomes.

In light of the results obtained for the population treated with an anti-PD-1 at the UTHs, the PGTM recommends:

- No longer keeping a list and not conducting a monitoring study to analyze therapeutic outcomes, since the treatment algorithms have since changed. Indeed, (1) new drugs have been added to the therapeutic arsenal for several types of cancer, (2) immune checkpoint inhibitors are used in the earlier stages of disease (adjuvant and first-line treatment) and (3) combinations of these drugs with each other or with chemotherapy are currently being studied and are approved or are in the process of being approved.
- Ensuring, after treating an immune-related adverse event (IRAE), a prednisone dose of no more than 10 mg before resuming the immunotherapy, if applicable. The clinician should clarify the risks with the patient and document the prednisone dose at resumption;
- Finding the parameters mentioned in the literature that can influence the effectiveness of the treatment and encouraging a discussion between clinicians before the start of treatment;
- Making entries in the medical records in order to:
    - Keep track of the duration of treatment with immunotherapy by encouraging clinicians to clearly record the start date in the treatment and retreatment history (where applicable);
    - Find the details for better assessing the severity of any adverse effects, which would make for better management;
- Providing a closer clinical follow-up for the first 3 or 4 months after the start of treatment (e.g., every other week for nivolumab). This would permit earlier detection of IRAEs that occur relatively soon after treatment is initiated;
- Recording in the medical record any prior autoimmune condition in the patient and clearly reporting the occurrence of any immunological adverse events;
- Introducing into medical records a coding system specific to IRAEs to make them easier to trace, for example, by archivists. Although they are expected, grade 3 and 4 IRAEs that have led to hospitalization could be described more thoroughly from the outset, as required by Vanessa's Law.

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Objective: To promote the optimal use of anti-PD-1 antibodies and the optimal management of their adverse effects (including IRAEs) at the UTHs.

Intervention measures: Each UTH is to determine which interventions apply to its situation and to make one or more of them priorities.

Timetable: Institute applicable measures at each UTH within 12 months of June 2020.

Proposed intervention plan:

1. Present the results to the Pharmacy and Therapeutics Committee and/or the Cancer/Oncology Subcommittee, if applicable, and to other committees concerned, if relevant.

2. Present the results to the health professionals concerned: pharmacists and oncologists who prescribe immunotherapy for cancer treatment.

3. For the purpose of meeting the selection criteria for patients eligible for anti-PD-1 therapy, discuss with the oncologists the best methods/tools to be developed or modified for recording in the medical record the various parameters to be considered that can influence the treatment's effectiveness, in order to guide the decision to initiate, continue or discontinue the treatment at the appropriate time, such as the ECOG performance status and the presence of brain metastases.

   Each UTH could choose to record certain parameters in various places, e.g., on a pre-written prescription, a pre-printed oncology medical visit form or a specific eligibility form similar to those developed by the CCO.

4. To optimize IRAE management, discuss with the oncologists the best methods/tools to be developed for recording in the medical record the parameters to be considered in order to guide the decision to initiate, resume, continue or discontinue the treatment at the appropriate time, in particular:

   - When initiating a drug from the class of immune checkpoint inhibitory immunotherapies, use a specific place in the medication profile to indicate if the patient has an autoimmune disease before the start of treatment. At each dose, track and document any adverse events, if a corticosteroid was taken and the dose, if the patient was hospitalized since the last dose, etc.
   - If the patient experiences an IRAE, record in the medication profile the details for better assessing its severity, using notes in the medical record, nurse's notes or the discharge summary, or after consultation with the patient.
   - If the immunotherapy treatment is continued despite the presence of an IRAE or on resumption following an IRAE, ensure that a prednisone dose of no more than 10 mg is used and record the dose in the medication profile. If the prednisone dose is greater than 10 mg, contact the oncologist to clarify the situation and record this in the profile.

5. Conduct a study to assess progression-free survival and OS with more-mature data for NSCLC patients who have received first-line treatment with pembrolizumab (excluding the 25 patients who received pembrolizumab in this analysis). This study would also aim at obtaining more information on treatments for this indication stopped prematurely (before 12 weeks).