

Immuno-Oncology Overview

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Editorial

The essential feature of the immune system is the ability to recognize and differentiate any foreign body or abnormal cells such as tumor cells from normal cells. Tumor cells produce tumor antigens which activate the immune system. These antigens attract immune cells to the tumor site where they invade and attack. Accordingly, the immune system recognizes the tumor cells and targets them for elimination.

In order for the tumor cells to survive and grow, they apply different strategies to avoid recognition and elimination by the immune system through disrupting antigen presentation mechanisms. This might occur either through down regulation of Major Histocompatibility Complex (MHC) molecules or by disabling antigen-processing machinery. In addition, the tumor cells may suppress the immune system through disrupting pathways involved in controlling T cell inhibition (checkpoint) and activation to avoid being attacked by the immune system.

These checkpoints could be activated or inactivated to start an immune response. PD-1 is a checkpoint on the T cells, which acts as a type of "off switch" that helps keep the T cells from attacking other cells in the body including tumor cells. It does this when it attaches to PD-L1, a protein on cancer cells. When PD-1 binds to PD-L1, it basically tells the T cell to leave the other cell alone. Some cancer cells have large amount of PD-L1, which helps them evade immune attack. Monoclonal antibodies that target either PD-1 or PD-L1 can block this binding and boost the immune response against cancer cells.

Immuno-oncology refers to the treatment modalities that are designed to target and harness the patient's immune system directly to kill tumor cells. These modalities include:

1. Cytotoxic T-lymphocyte associated protein 4 (CTLA-4) binding antibody (ipilimumab and tremelimumab);
2. Programmed cell death protein 1 (PD-1) targeted antibodies (Nivolumab and pembrolizumab);
3. Anti-PD-L1 antibodies (Atezolizumab, durvalumab, avelumab).

Safety profile of the immuno-oncology drugs is in some cases unique and different than what may oncologists have experienced with chemotherapy or targeted drugs. These side effects are manageable and can be successfully dealt with. It is mainly immune related adverse events due to excessive immune activity. Early recognition through

patient education, early diagnosis and appropriate management of these toxicities are the key points to minimize life threatening complications.

Immune-mediated adverse events might affect the following organs:

1. Respiratory tract: Dyspnea and cough;
2. Endocrine system: Fatigue, headache, psychological changes/mood swings, significant changes in thyroid function tests and /or serum chemistry;
3. Liver: Increased hepatic values as AST, ALT, total bilirubin;
4. Kidney: Blood in urine, increased serum creatinine, decreased urine output;
5. Gastrointestinal tract: Diarrhea, stomach pain, blood in stool;
6. Skin: Itching, rash.

Rash is the earliest side effect that might be detected. It might appear about 4 weeks after treatment. Diarrhea might appear 5-6 weeks after starting treatment while changes in liver values might start 6-7 weeks after therapy.

Management of the side effects will depend on the severity as follows:

- Grade 1: Generally treated symptomatically;
- Grade 2: Generally treated with oral corticosteroids. Discontinue the treatment until symptoms resolve;
- Grades 3 and 4: Generally treated with intravenous corticosteroids. Delay or stop treatment depending on the affected organ system.

Patient education for early recognition and education of healthcare professionals for early diagnosis and proper management are essential factors to minimize the life threatening side effects of immuno-oncology drugs [1-4].

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