ABC of Immunotherpay

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Introduction

Systemic therapy of cancer involves various types of therapies like chemotherapy, hormonal therapy, targeted therapy and Immunotherapy. Immunotherapy is the most recent addition to the basket of various anticancer treatments.

Basic of Immunotherapy

In our body, we have adaptive immunity like Immunisation, immunity due to infections, antibody transfers etc. Our body also has innate immunity involving Dendritic cell, NK cell and Macrophages. Inpatients with cancer, immune response is directed to a particular tumour-associated antigen. Antigen presenting cells including dendritic cells, activate T cells by presenting these antigens to them. T cells initiate an activation programme against these antigens. T cell activation is regulated by Immune Checkpoints. These are co-stimulatory and inhibitory interactions that protect against autoimmunity and excessive immune response. The drugs called as Immune Checkpoint inhibitors (ICPi), suppress these inhibitory actions and lead to excessive immune reaction against cancer cells.

Role of PD-L1 pathway

This pathway down regulates the anticancer Immune response by two mechanisms -

1. PD-L1 expression prevents T-cell priming and activation in the lymphnode
2. It also inhibits T-cell activity in tumour microenvironment

This is one of the commonest pathways used in clinical use.

Types of Immunotherapy

1. Cancer vaccines
2. Immune checkpoint inhibitors (ICPi)
3. CAR-T-cell therapy

Sicne ICPi are used widely in clinical practice, they are described in details below.

Immune checkpoint inhibitors

Immune checkpoint inhibitors (ICPi) are now approved for treatment of many types of cancers. There re three types of ICPi depending on targets.

1. PD-L1 Target : Atezolizumab, Durvalumab, Avelumab
2. PD-1 Target : Nivolumab, Pembrolizumab
3. CTLA4 Target: Ipilimumab, Tremelimumab

Nivolumab and Pembrolizumab are now used frequently even in Indian patients with various advanced stage malignancies hence they are being described in more details below.

NIVOLUMAB

This ICPi is approved in following indications

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1. Second line treatment of Non-Small cell lung cancer
2. Second line treatment of Renal cell carcinoma
3. Second line treatment of Head and Neck malignancies
4. Second line treatment of Hepatocellular carcinoma
5. Melanoma
6. Relapsed Hodgkin's lymphoma

Pembrolizumab

This ICPi is approved in following indications

1. Second line treatment of Non-small cell lung cancer with PDL-1 expression >1%
2. First line treatment of Adenocarcinoma of lung with PDL-1 expression > 50%
3. Recurrent advanced solid tumours expressing MSI-High status
4. Recurrent CA Cervix expressing PDL-1
5. Advanced Gastric and Gastro-oesophageal tumours expressing PDL-1
6. Melanoma
7. Second line treatment of Head and Neck cancers
8. Second line treatment of Hepatocellular carcinoma
9. Relapsed Hodgkin's Lymphoma

Immune-Related Adverse Events seen with ICPi

Any organ of the body can have inflammatory reaction to these agents. The common toxicities seen are Dermatitis, Pneumonitis, Colitis, Hepatitis, Diabetes, thyroiditis, Hypophysitis, Arthralgia, Myocarditis, Nephritis etc. The symptoms of all these toxicities need to be identified quickly hence close monitoring of all these patients is necessary. Early diagnosis and initiation of steroids at the onset of any of the toxicities can revert most of the toxicities. It is clear that toxicity profile of ICPi is entirely different than that of chemotherapy. Multidisciplinary medical expertise and ICU set up is necessary for giving immunotherapy.

Take Home Message

1. Immunotherapy has evolved as an effective anticancer therapy in recent times
2. Most of the approved indications are for advanced recurrent stage disease except use of Pembrolizumab in Lung cancer with high PDL-1 Expression.
3. Immunotherapy is being combined with chemotherapy in certain clinical setting. It may also be used in early stages in due course of time.
4. Toxicity profile of Immunotherapy is entirely different than that of chemotherapy, requiring close monitoring
5. Right selection of patient is the key to effective Immunotherapy as it may not be applicable to all patients with cancer.