Anti-programmed cell death-1 (PD-1) monoclonal antibodies- Latest trend in Immunotherapy

Cancer, a primary leading disease for mortality in the world. Immunotherapy is the latest trend for curing cancer and thus biopharmaceutical industry has developed a keen interest and manufactured several drug products such as monoclonal antibodies for immunotherapy. Programmed Cell Death Protein 1 (PD-1) evades immune response and promotes self-tolerance by modulating the activity of T-cells, activating apoptosis of antigen-specific T cells and inhibiting apoptosis of regulatory T-cells. On the other hand, Programmed Cell Death Ligand 1 (PD-L1) is a trans-membrane protein and it's a co-inhibitory factor of the immune response[1]. Cancer Immunotherapy has been designed to increase the specificity and strength of the immune system against cancer. James P. Allison and Tasuku Honjo won the 2018 Nobel Prize of Physiology or Medicine for discovering a cancer treatment by suppressing negative immunomodulation.

The use of anti-programmed cell death-1 (PD-1) monoclonal antibodies are promising for treating solid-organ tumors. Anti-PD-1 antibodies bind with its ligands, PD-L1 and PD-L2. These antibodies maintain self-tolerance during chronic antigen stimulation by normally suppressing T-cell activation[3]. In the tumor microenvironment, tumors inhibit antitumor T-cell-mediated reactions by expressing the PD-L1 ligand, and the blockade of anti-PD-1 antibodies can initiate an antitumor immune response[4].

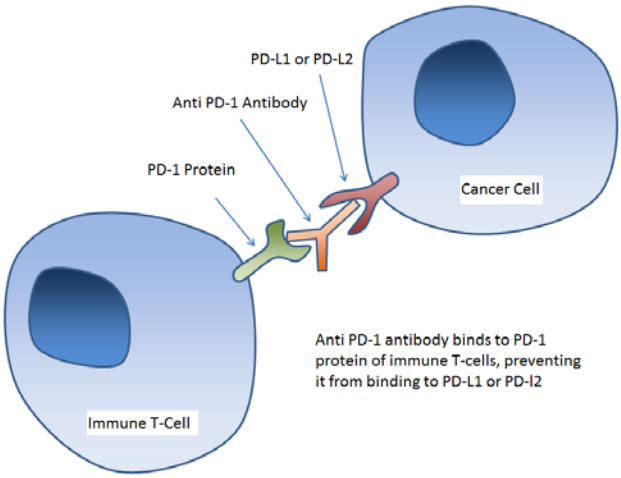

Figure1: Illustration of interaction of PD-1 protein with anti PD-1 antibody

To illustrate with an example, Pembrolizumab, approved by US FDA in 2017 is one such monoclonal antibody that targets PD-1 (Programmed Death 1), an immune checkpoint protein expressed on cytotoxic T cells. Cancerous cells usually overexpress PD-1 ligands (PD-L1 and PD-L2) and ultimately such interactions bring these cancerous cells to the notice of the immune system and elicit the desired immune response thereby blocking the evade mechanism posed by cancer cells to block it's encounter by the immune system.

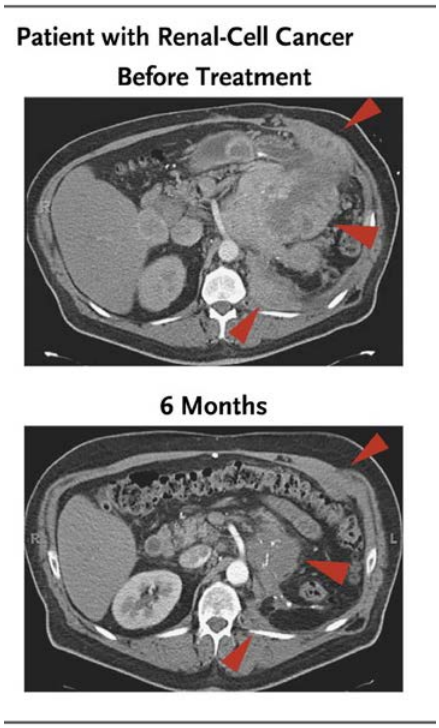

Figure 2: Partial regression of metastatic renal-cell cancer before and after receiving anti-PD-1 antibody

These types of antibodies are anti-programmed cell death-1 (PD-1) monoclonal antibodies and multiple monoclonal antibodies developed and got approval from US FDA (Figure 3). More than 2000 clinical trials are evaluating the safety and efficacy of anti-PD-1 or anti-PD-L1 monoclonal antibodies with other drugs.

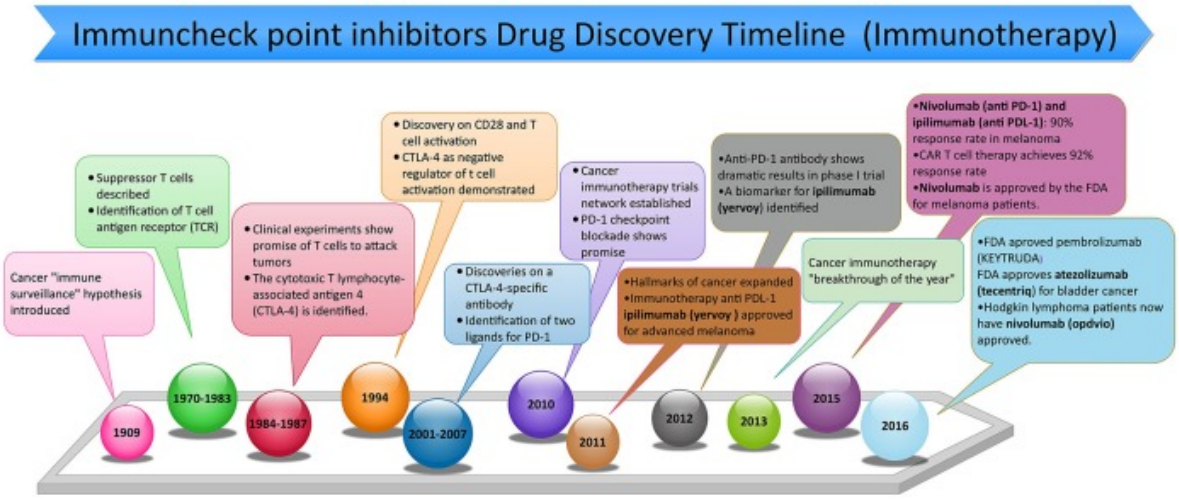

Figure 3: Timeline of discovery of anti-programmed death 1 (PD-1) and anti-programmed death ligand 1 (PD-L1) inhibitors used in cancer immunotherapy from ~1900s to February of 2017[2]

Some of the US FDA approved Anti-PD-1 monoclonal antibodies are given below:

Generic Name	Brand Name	Year of FDA Approval
Pembrolizumab	Keytruda	2017
Nivolumab	Opdivo	2022
Atezolizumab	Tecentriq	2022

PD-1 and PD-L1 Inhibitors Market size was valued at USD 28,091.93 Million in 2021 and is projected to reach **USD 1, 12,430.64 Million by 2030**, growing at a **CAGR of 19.29% from 2023 to 2030.**

However, there are also certain risks associated with this kind of therapy since there is a possibility that such monoclonal antibodies attack non-cancerous cells in addition to cancerous cells. But it is important to mention that these risks related to immunotherapy can surely be overcome by understanding the underlying mutation of these cancer cells.

References:

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2. Alsaab H O, Sau S, Alzhrani R, Tatiparti, K, Bhise K, Kashaw SK, Iyer AK. PD-1 and PD-L1 Checkpoint Signaling Inhibition for Cancer Immunotherapy: Mechanism, Combinations, and Clinical Outcome, Front Pharmacol 2017; 8: 561.
3. Sharpe AH, Pauken KE. The diverse functions of the PD1 inhibitory pathway. Nat Rev Immunol 2018;18:153–67.
4. Pardoll DM. The blockade of immune checkpoints in cancer immunotherapy. Nat Rev Cancer 2012;12:252–64.