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Global Cancer Immunotherapy to hit $115 Bn by 2023

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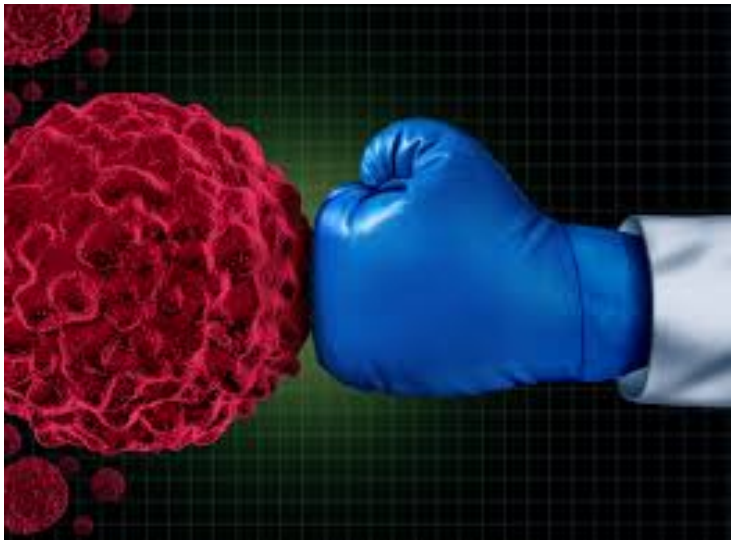
The main challenges associated with CAR T therapy include manufacturing, regulations, pricing and toxicity in patients



Immunotherapy is forecast to become the oncology treatment of choice by 2026 with an estimated 60% of previously treated cancer patients likely to adopt immunotherapy in this timeframe. Multiple treatment lines, combination therapy and the opportunity for repeat treatment are likely to accelerate fast growth. Cancer immunotherapy also expands into multiple indications and our analysis indicates that key immunotherapies including anti-PD-1 drugs, dendritic cell vaccines, T-cell therapies and cancer vaccines are all driving the market. The rising incidence and prevalence of numerous cancers globally is a significant accelerator of growth. This is due to more sensitive early detection techniques, higher patient awareness and a growing aging population. Furthermore, the FDA's pro-science attitude will accelerate development and regulatory approval for these drugs. To that end, the cancer immunotherapy market is forecast to hit $115 billion by 2023. Overall strong growth rates are expected due to a significant unmet need and increasing trends of hematological cancers.

Prior to the launching of Yervoy, the five-year survival rate for patients with early stage melanoma was 98%; but the five-year survival rate for late-stage melanoma was just 16%. Yervoy has been reported to have a survival rate of 25% when tested alone. When tested as part of a combination therapy treatment with Bristol's nivolumab, the two-year survival rates rose to 88% for patients with late-stage cancer. Increase in patient survival rates brought about by cancer immunotherapy treatment is similar to that seen when bone marrow transplantation changed our conception on how blood cancer was treated. Other key therapeutic players in this market include Opdivo (nivolumab), Keytruda (pembrolizumab), Tecentriq (atezolizumab), Ibrance (palbociclib) the newly approved Bavencio (avelumab) and Imfinzi (durvalumab) and of course the first CAR-T therapies Kymriah (tisagenlecleucel) and Yescarta (axicabtagene ciloleucel).

Opdivo (nivolumab) from BMS is one of the most exciting agents in the immunotherapy space, and is indicated for melanoma, lung cancer, kidney cancer, blood cancer, head and neck cancer, and bladder cancer. It was given a fast-track approval on December 22, 2014. The majority of immune-oncology agents are anti-programmed death-1 (PD-1) monoclonal

antibodies, which will certainly guide the market over the coming years. Projects that currently are valuable include combined immunotherapies on our knowledge of CD137 and PD-1/PDL1 mechanisms. A study on a novel effector activating monoclonal antibody known as IMAB362 for the treatment of solid cancers is also exciting. Other projects comparing CAR-T cell effectiveness against T-cells that target CD19 or mesothelin are interesting in a preclinical setting. Of course, Novartis gained the first CAR-T FDA approval for Kymriah (tisagenlecleucel, CTL019), in August 2017, for children and young adults with B-cell ALL. In October 2017, Yescarta (axicabtagene ciloleucel) from Kite Pharma for adult patients large B-cell lymphoma was also given FDA approval. This is a major boost for the global and US immunotherapy, and gene therapy markets.

What Are CAR-T Therapies? How Will They Impact the Market?

CAR T (chimeric antigen receptor T) cells are engineered specificity using antibody fragments directed to the tumor cell, and also T-cell CD8/CD3 plasma membrane proteins that elicit specific activity towards the tumor cell, via intracellular signaling pathways. To date publications have revealed a number of effective intracellular molecules in the engineered T cell including CD28, 4-1BB (CD137) and CD3 zeta.

These engineered T cells have numerous advantages including:

- Intracellular domain can be modified to increase efficacy and durability of CAR-T
- CAR-T are still subject to the same regulatory and tolerogenic constraints of natural T cells, including checkpoints, Treg, MDSC
- CAR-T can be engineered to express cytokines and chemokines that further enhance function and migration
- Can be modified to express suicide genes that limit CAR-T population if toxicity occurs

To date, the main challenges associated with CAR T therapy include manufacturing, regulations, pricing and toxicity in patients. Currently there are over 100 recruiting CAR-T clinical trials globally, mainly in the US, China and Europe. To date a number of CAR T Cells (autologous/allogeneic) trials are demonstrating clinical benefit to patients, but others have demonstrated toxicity such as cytokine release syndrome. In July 2017, an FDA advisory panel determined that the benefits of CAR T outperform the risks. Kymriah (tisagenlecleucel) by Novartis is indicated to treat children and young adults with acute leukemia and performed well in the ELIANA trial. The FDA's Oncologic Drugs Advisory Committee (ODAC) recommended this agent for approval and became the first CAR-T cell therapy on the US market. In October 2017, Yescarta (axicabtagene ciloleucel) from Kite Pharma for adult patients large B-cell lymphoma was also given FDA approval.

The CAR-T industry is addressing unmet needs in specific relapsed cancers, and trials have indicated that some patients show long term activity and high remission rates, but there is a large proportion of patients with toxicities such as cytokine release syndrome and neurotoxicity. The main players within the CAR-T market are Novartis, Juno Therapeutics, Kite Pharma and Cellectis. The market is moving ahead, backed by years of R&D, from both academia and industry, investors capitol and small clinical studies. From now on, Kelly Scientific forecasts that CAR T therapy will become more streamlined, with faster manufacturing times as advances in technologies take hold and clinical trials provide more robust evidence that this immunotherapy is robust. These factors, plus strategies to reduce adverse reactions and toxicities and larger players like Novartis taking stage will push CAR-T therapy ahead. However, recent deaths in the Juno ROCKET trial are creating questions amongst investors. How will the CAR T space influence the total immunotherapy industry going forward? This comprehensive report scrutinizes the total market and provides cutting-edge insights and analysis.

Within the cancer therapeutics space, which today is worth over $100 billion globally, immunotherapeutic drugs have gained worldwide acceptance. This is because they are targeted therapeutics that have high specificity for cancer cells. Today, cancer immunotherapy drugs have captured nearly 50% of the overall oncology drugs market, generating about $75 billion in 2019 alone and are forecast to surpass $115 billion in 2023.