What’s now and next in Immuno-Oncology?
“Cancer immunotherapy has offered an idea and a hope for a hundred years, but you couldn’t go to your doctor’s office and get a successful immunotherapy. This began to change with interleukin-2 (IL-2) therapy, [Dendreon’s therapeutic cancer vaccine] Provenge, and anti-cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) therapy, but all have their weaknesses.”

Gordon J. Freeman, PhD
Adjunct, Department of Immunology and Virology; Dana-Farber Cancer Institute in Boston, Massachusetts Professor of Medicine, Harvard Medical School

One of the first to discover the PD-L1 protein and elucidate its function in shutting down the T-cell response against cancer.
Foreword

What if immunotherapists could help us build our immune system combat cancer? What if it was possible to cure the 1,688,780 new cancer cases projected to occur in 2017? Will it be possible to find a new niche in our cancer armamentarium for every cancer patient? If yes, when?

Today, we do have the solution, and we call it Immuno-Oncology. Immuno-Oncology is a unique therapy in the precision medicine space that is showing extraordinary promise. These next generation therapeutic drugs differ from conventional methods as they stimulate the immune system to selectively attack cancer cells, while ensuring healthy cells remain unaffected. Conversely, chemotherapy and radiation wipe out the healthy cells along with the affected cells, thus triggering a cascade of unfavorable side effects such as fatigue, alopecia and neutropenia.

Cancer cells adapt to express proteins that let them hide from normal anti-tumor immune response. The objective of Immuno-Oncology is to interrupt this process of spreading cancer cells, and revitalize the immune system to detect and destroy malignancies. Such therapies have shown great promise in several clinical trials, contributing to the widespread adoption across the pharmaceuticals and life sciences industry.

This report describes in more detail how the Immuno-Oncology market evolved and the current market scenario. It also answers the following questions:

- What key drivers are leading to successful development of therapies? (page 6)
- Who are key industry players and what are their initiatives? (page 7ff)
- How can pharmaceutical companies leverage innovative technology to counter major challenges? (page 11f)
Immuno-Oncology Market

Biomarker research has verified that Immuno-Oncology can maximize responsiveness, while decreasing toxicity levels. The increasing capability to effortlessly select appropriate patients from a wider pool has led to an optimistic Immuno-Oncology growth scenario across the globe.
Having demonstrated comparable efficacy in treating cancer, Immuno-Oncology is being rapidly adopted by key industry players, and the market is expected to be worth USD14 bilion by 2019.

The approval of therapeutic solutions in the Immuno-Oncology segment is poised to rapidly increase due to growing recognition of durable tumor responses. Hence, the competition between pharmaceutical players is intensifying as they strive to achieve first mover advantages in specific medical applications.

Over the last 5 years, we have seen exponential revenue growth. Sales are highest in North America, where the revenue share reached 67.1% in 2016. The commercial success is attributed to multiple factors, including speed-to-market, clinical & commercial positioning, marketing approach, and patient group targeting.

Today, forward-thinking pharma companies are turning to Immuno-Oncology to address some of the most pressing challenges in curing cancer. Scientists, pharma companies, and global healthcare organizations are exchanging research results in an increasing number of national and international conferences, such as the Clinical Immuno-Oncology Symposium in Orlando, Florida, organized by ASCO and SITC (Society for Immunotherapy and Cancer). The first edition of the conference (February, 2017) welcomed prominent market players and exhibitors from 33 biotech and pharma companies.
Pharmacogenomics studies help assess and identify appropriate patients, who are likely to respond effectively to Immuno-Oncology therapies. Biomarker research has verified that Immuno-Oncology can maximize responsiveness, while decreasing toxicity levels. The increasing capability to effortlessly select appropriate patients from a wider pool has led to an optimistic growth scenario across the globe.

Regulatory approval is the primary factor driving the growth and rapid adoption of precision medicines like Immuno-Oncology drugs. Accelerated approval processes by regulatory agencies such as fast track and breakthrough designations are significantly contributing to the development of Immuno-Oncology. Equally important, key industry players are innovatively combining Immuno-Oncology with existing antibody therapies for improved results. For instance, Bristol-Meyer Squibb uses a combination of Opdivo and Yervoy regimen for treating melanoma. Moreover, the faster clinical approval continues to support the speedy adoption of Immuno-Oncology therapies. Owing to vast market opportunities, investments are being made to further improve the capabilities of Immuno-Oncology.

### Growth indicators for rising Immuno-Oncology research efforts

#### Disclosed clinical studies as per 15th June 2017

<table>
<thead>
<tr>
<th>Study</th>
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<tr>
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#### Recent breakthrough therapies

- **Alunbrig** (brigatinib) by Ariad Pharmaceuticals
- **Bavencio** (avelumab) by EMD Serono/Pfizer
- **Imfinzi** (durvalumab) by AstraZeneca
- **Kisqali** (ribociclib) by Novartis
- **Rydapt** (midostaurin) by Novartis
- **Zejula** (niraparib) by Tesaro
- **Xermelo** (telotristat ethyl) by Lexicon Pharmaceuticals

2017 marks the first year for the **Clinical Immuno-Oncology Symposium**, sponsored by ASCO and the Society for Immunotherapy of Cancer (SITC).

#### Key takeaways:
- Gut bacteria may determine how well Immunotherapy works
- Predicting prognosis for colorectal cancer may depend on the tumor’s location
Who are dominating the Immuno-Oncology market?

Given the unique characteristics of the therapy, health technology assessment (HTA) agencies might provide positive reimbursement decisions. Therefore, an analysis of influential authorities and key industry players indicates a much positive outlook for the market reach of Immuno-Oncology. The therapy market on the basis of checkpoint inhibitors is likely to reach well over 90% in the coming years. The new breed of Immuno-Oncology therapies represented as checkpoint inhibitors work radically different, inspiring hopes among multiple stakeholders. The four most promising checkpoint inhibitors in the Immuno-Oncology market are:

- Yervoy
- Keytruda
- Opdivo
- Tecentriq

Approved Immuno-Oncology therapies

Bristol-Myers Squibb (BMS)

The Immuno-Oncology portfolio of Bristol-Myers Squibb (BMS) has been the key driver of the company’s growth since 2016. Opdivo, the Immuno-Oncology drug by BMS, has secured regulatory and clinical approval for more than ten cancer indications. Regulatory authorities are confident about Opdivo’s clinical profile, paving the way for a rapid uptake in a short period of time (Exhibit 2).
In 2016, BMS achieved multiple milestones in Opdivo research programs. Altogether, 15 registrational trials were concluded with positive results. Although BMS’s optimistic predictions are reasonably established, the drug is expected to see increased competition from Merck’s Keytruda.

Keytruda, the Immuno-Oncology prescription blockbuster of Merck & Co., recorded sales worth USD1.4 billion in the fiscal year 2016. That’s a 148% year-on-year growth as compared to USD566 million in 2015. To emphasize Keytruda’s growing success, USD483 million global sales were reported alone in the 4th quarter 2016. The US market contributed approximately 65% to Keytruda’s overall sales in 2016. Keytruda is projected to reach sales of USD3.466 billion in 2019. Merck & Co. recently made an audacious bid by getting approval of Keytruda in gastric cancer. This step is expected to outmaneuver Immuno-Oncology market competitors with the first regulatory approval for gastric cancer. The company beefed up biologics operations in Ireland with an investment of USD310 million and plans to add 330 jobs. The initiative will majorly contribute to the future of Keytruda.
Further strengthening their position, Merck & Co. have acquired IOmet, the UK-based drug discovery company focused on cancer metabolism and innovative medicinal drugs for treating cancer. Merck & Co. acquired its comprehensive pre-clinical pipelines. The development of Immuno-Oncology underway is posing certain challenges, and Merck & Co. continues to counter such challenges efficiently.

However, study designs with time-to-event endpoints assume exponential distribution growth of the therapy. Such a process of distribution might lead to wrong estimates of study duration, piloting challenges in effective distribution of the therapy, as well as delayed clinical effects and statistical analysis.

Pfizer is actively involved in multiple research programs in the Immuno-Oncology space. While the company is exploring different compounds in a clinical setting, it expects to develop doublet and triplet Immuno-Oncology therapies. The list of therapies under development will include drugs like 4-IBB, Avelumab, and OX-40, among other chemotherapy agents and antibody drug conjugates. Pfizer’s target cancer segments include blood, ovarian, lung, and gastric cancer.

Immuno-Oncology therapies currently make up about 2.3% of Pfizer’s total portfolio holdings. Collaborative development of Immuno-Oncology drugs is creating immense opportunities for Pfizer. Together, Pfizer and Merck have lined up plans for an investigational drug Avelumab, which would help patients counter carcinoma. Avelumab is being explored in the oncology regimen with 3,000 people enrolled in clinical trials.

The positive onset of Immuno-Oncology therapies indicates a likely increase in Pfizer’s share price. With all the success, Pfizer continues to face challenges in inadequate measures for reliably identifying patients who will respond to immunotherapies.

NeoGenomics, a leader in cancer-focused genetic testing services, recently announced an expansion of its Immuno-Oncology profiling menu. The company has already established cancer profiles, including Tumor Mutation Burden (TMB) and microsatellite instability (MSI). Such initiatives are drawing positive response from investors as TMB is a genomic biomarker designed to predict the checkpoint inhibitor response in PD-1 and PD-L1.

A large number of patients do not respond to therapies, and NeoGenomics’ solutions are expected to precisely identify the subset of patients that might respond. The company’s unique combination of genomic profiling and Immuno-Oncology profiling demonstrates its commitment to lead the precision medicine space.
Opdivo vs Keytruda

Trending toward precision medicine

Keytruda, developed by Merck, requires a diagnostic test for identifying proteins in the tumor. On the contrary, Opdivo by BMS is carried out without any additional tests. Although no trials have ever been conducted to demonstrate the comparison between the two drugs, a deep analysis has revealed that both drugs are equally effective.

Opdivo remains way ahead as it had clocked sales worth USD2.1 billion in 2015, while Keytruda’s sales stood at USD566 million. Bristol-Myers Squibb’s mass-marketing approach has been a competitive advantage in successfully positioning its Immuno-Oncology portfolio. Even though both drugs compete with each other by a large margin, they are approved and tested to work appropriately among other drugs that have failed.
Future of Immuno-Oncology

New distribution methodologies and innovative patient interface technologies will help pharma companies successfully establish Immuno-Oncology therapies in emerging markets.
Changing times: Which path will we take?

The pharmaceutical & life sciences industry is experiencing major intensification in the Immuno-Oncology space. However, as per our analysis of industry leaders, checkpoint inhibitors come with challenges including unreliable identification of patients and ineffective distribution of therapies.

So, what’s the bottom line?

Certainly, new distribution methodologies and innovative patient interface technologies will help pharma companies successfully establish Immuno-Oncology therapies in emerging markets.

Firstly, companies can leverage cloud technology to share data securely and economically with suppliers, while collaborating with therapists for end-consumer reviews. Such an initiative will help pharma companies analyze data and respond to drastic changes in supply and demand. As the insights of patients’ ailments flow in, companies will be able to better identify the right therapy for categorized patients. Industry manufacturers can similarly power up factory-to-patient features by monitoring product effectiveness and delivery requirements. Finally, innovative patient interface technologies will help pharma companies come closer to patients than ever before.

As patient identification is the biggest challenge for the distribution of Immuno-Oncology, companies can adopt such technologies to counter challenges effectively. For instance, a set of prototype chip and receiver developed by Proteus Biomedical will help companies record data based on the metabolism insights of therapies and drugs. We expect to see many such technological transformations in the patient interface segment that will help companies monitor their compliance standards in real-time.

As the future comes closer, pharmaceutical & life sciences companies will have a distinguished distribution of Immuno-Oncology therapies based on precise categories of patients. Industry players in the precision medicine landscape will need to get closer to patients, as reliable patient data remains the prerequisite of distributing Immuno-Oncology therapies.
Road ahead for Immuno-Oncology

Even though other immune therapies are in the pipeline, drugs for manipulating microbiome and breaking down stroma hold out promise for the future of Immuno-Oncology. However, this next generation drug is facing challenges including complexities in rapidly changing healthcare standards and faster clinical trial enrollments. A few market leaders have also expressed concerns over adopting Immuno-Oncology due to specialized laboratory criteria.

Undoubtedly, this futuristic drug has a widespread scope, and will need a synergic approach which will involve entities of drug development and immunotherapists at the consumers’ end.

Firstly, drug development companies must strive to achieve the promises made during the clinical development setting. To enumerate, they can do so by initiating leadership in lung cancer, developing combination regimens of Immuno-Oncology, and early-stage development of therapies in macro clinical settings. Additionally, pharmaceutical players must also strategize effective patient identification for drug compatibility to meet the unmet needs. Correspondingly, immunotherapists must promote marketing agendas of pharma units in order to ensure consumers are wary of the hype resulting from the media ecosystem. Accessibility to adequate information is another significant factor for businesses and immunotherapists to focus on.

For all the current excitement, Immuno-Oncology is a highly marketable and dynamic space. However, as niches become saturated, drug developers must look out for and employ novel approaches. Indeed, much lies in the cross-class combinational regimen, and companies must realize the opportunities.

As per the current pace of expansion, we predict vibrant efficacy of systematic therapies in the Immuno-Oncology space. And who knows, advanced computers might start assisting oncologists in explaining the best intervention for patients. Eventually, we might also get to see a more personalized approach toward distributing Immuno-Oncology drugs, creating immense scope in precision medicine. Perhaps, a mechanistic understanding of the immune response is the need of the hour for pharma companies.

To sum up, the human immune system is a defense structure full of healthy cells to combat some cancer cells. They just need the right orders.

- The Immuno-Oncology industry might very well be preparing for the unseen to secure human health!
References


Bristol-Myers Squibb's Strategies to Dominate Immuno-Oncology Market (http://marketrealist.com/2016/10/bristol-myers-squibbs-strategies-to-dominate-immuno-oncology-market/)


Data sources


https://clinicaltrials.gov (access date: 19th June 2017)

http://immunosym.org/


https://www.fda.gov/

QuintilesIMS DDD + Xponent
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