HOW TO MAXIMIZE THE VALUE OF NEW ADVANCES IN ONCOLOGY

Faruk Abdullah
Paul Nash, PhD

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How to Maximize the Value of New Advances in Oncology

Cancer remains a global killer. Based on the most recent data recorded by the World Health Organization, globally there are about 14 million cancer cases[1] and about 9 million cancer-related deaths per year.[2] In the United States alone, more than 1.5 million new cancer cases were diagnosed and more than 600,000 cancer deaths were estimated to have occurred in 2017. About 40% of people will develop cancer in their lifetime.[3] Cancer incidence and deaths associated with cancer are expected to increase over the next decade, driven by such factors as the growing aging population and behavioral choices (e.g., smoking and obesity).

While the numbers are daunting, through clinical and commercial efforts, we are making progress to improve cancer patient outcomes. The introduction and commercialization of tyrosine kinase inhibitors (TKIs) is one great example of how the industry is directly improving life expectancy of people with cancer by introducing new science into the market and ensuring patients get access to that science. Earlier detection, improved treatment regimens and guidelines, and increased access to care and patient support services have all played a role in chipping away at the cancer mortality rate and improvements in five-year survival. These trends show no sign of slowing, as new innovative therapies continue to prove themselves and become more widely adopted across the industry.

The future of oncology care will be shaped by advancements that expand what is possible in terms of customer interactions, screening and diagnosis, and the development of targeted medicines. Based on EVERSANA™ MANAGEMENT CONSULTING keynote address at CBI's 11th Annual Oncology Market Access Strategy Summit, this article first looks at the forces driving technological advancements that will reshape oncology treatment in the very near future. We will then examine two new technologies—one biotechnological and one digital—and identify the keys to maximizing the benefits of these technologies in order to ensure greater value for providers, patients, and manufacturers alike.

Forces of Change

Many forces are at play shaping the future, but here we will highlight three technological and economic forces in particular that are unlocking a whole new set of advancements in the world of oncology.

First, technology is making huge leaps forward based on the principle of Moore's Law, the observation that the number of transistors in a dense integrated circuit doubles approximately every two years.[4] The result is faster speed of information flow among patients, physicians, and other stakeholders in the life sciences ecosystem via technologies such as video messaging, telemedicine, and advanced data analytics capable of analyzing reams of data in a matter of minutes or seconds.

Another force enabling considerable technological advancement is the reduction of the cost of sequencing the human genome. The first sequencing of the human genome cost almost $4 billion and took 13 years, while today it costs about $1,000 and can be done in three days or less. By 2020, the cost could be just $100.[5] What this means is that we will see dramatic improvements in the ability to identify genetic targets and design therapies (e.g., monoclonal antibodies or cell therapies) in a much more rapid and targeted fashion. It is difficult to even imagine what new discoveries could be unlocked in the next few years with continued investments and advancements in this space.

Advancement, through new treatments and new technologies, is especially important given the third major force at play: the rising cost of healthcare, particularly in the United States. As healthcare costs continue to rise without producing commensurate improvement in the quality of care, healthcare consumers find themselves paying more without getting the value they expect. With pressure on the system to reduce costs and improve quality, the industry will increasingly look to innovative

solutions, with a focus on outcomes. There is tremendous economic incentive to drive value throughout the healthcare ecosystem, starting with therapeutic manufacturers all the way through to the delivery of care.

With these forces of change at play, two areas of advancement in particular are worth exploring. Later in this article we will examine new innovations on the digital frontier in the form of data analytics, but first we will take a closer look at the progress being made in the field of next-generation cell therapies.

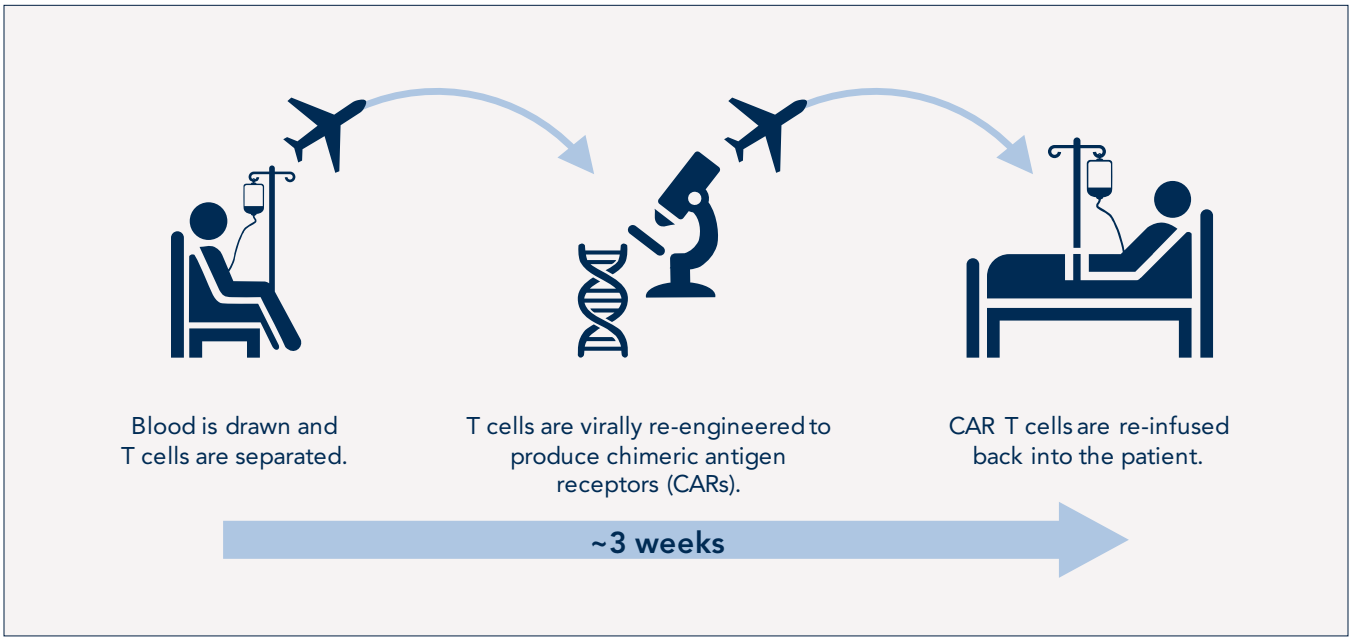
Next-Generation Therapies

Many exciting examples of next-generation therapies are emerging, including cell therapy, gene therapy, immunotherapy, and vaccines. One of the most important advances in oncology is in adoptive cell transfer immunotherapy, including chimeric antigen receptor (CAR) T-cell therapy. Offering a potential cancer cure, the CAR T-cell therapy category saw two products approved by the end of 2017.

The FDA approved Novartis's Kymriah in August 2017 as the first CAR T-cell therapy indicated for the treatment of patients up to 25 years old with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse.[6] Then, in October 2017, the FDA approved Yescarta, developed by Kite, a Gilead Company. Yescarta is the first CAR T-cell therapy for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma (PMBCL), high-grade B-cell lymphoma, and DLBCL arising from follicular lymphoma (transformed follicular lymphoma, or TFL).[7]

CAR T-cell therapy is a complicated, multistep process in which the customized drug is developed from the patient's own immune cells (Figure 1). Put simply, blood is first drawn from the cancer patient, and T cells are separated. The T cells are shipped to the manufacturer, where they are virally re-engineered to produce chimeric antigen receptors. The CAR T cells are then shipped back to the provider so that they can be re-infused back into the patient. The entire process takes approximately three weeks.

FIGURE 1: How CAR T-Cell Therapy Works



It is a complex and expensive process, involving transportation and handling, cell engineering, conditioning chemotherapy, and infusion and monitoring. As such, the issues of reimbursement, patient value, and logistics are all key to maximizing the benefit of CAR T-cell therapy.

Reimbursement

The key issue for CMS when it comes to reimbursing for CAR T-cell therapy is that the organization lacks a reliable model by which to calculate the reimbursement. CMS typically looks at historical or analog examples to understand what the price will look like and calculate the reimbursement they should provide for specific types of therapies. The challenge is that there is no appropriate analog for CAR T-cell therapy.

Without a historical reference to use, CMS will struggle to figure out the appropriate calculation for payment. As a result, manufacturers must engage far more in depth with CMS and private payers to help them understand the true economics and costs associated with delivering CAR T-cell therapy and the corresponding benefits of that therapy.

In addition to the cost of the drug itself, which can come close to half a million dollars, there is also the cost of delivering the care and managing the side effects. The total cost per patient could be north of $1 million. As there is a curative element to CAR T-cell therapy, this would ostensibly be a one-time cost.

Healthcare budgets are not designed to pay for expensive curative medicine. They are designed to manage chronic therapies, which are relatively lower in cost on an annual basis. For payers, a one-time cost of more than $1 million could be untenable, given the frequency with which patients change health plans. Manufacturers will need to work with payers to educate them that their budget impact models are not going to look the same as they used to and to help them come up with a reimbursement model that works.

Not only will CAR T-cell therapy be expensive, it will also likely be associated with spikes in demand. With most traditional therapies, usage rates follow a familiar pattern: product uptake occurs over a one- or two-year period following launch, usage peaks and holds steady until loss of exclusivity, and then usage slowly declines as generics enter the market. Payers are used to that standard usage curve and orient their budget management toward that curve.

But with CAR T-cell therapy, an initial usage spike might be expected, as interest in the potential cure could be high. With this large influx of patients, insurers will need to pay out considerable money right away, but after the initial spike, usage could decline rapidly until a new indication is approved, setting off another spike.

As potential cures like CAR T-cell therapy become more common, manufacturers will need to work with payers to help them understand the likely spikes in patient flow. Manufacturers can help educate payers and providers on these spikes and work with payers on creative approaches to reimbursement, such as outcomes-based contracting or indication-based pricing. And as payers are worried about patients remaining on their plans for only a few years, it may also be useful to develop ways to amortize payments in such a way that the cost burden follows the patient. Creative approaches to payment models can help payers realize cost savings over a longer period of time.

Novartis tackled the reimbursement issue head on, collaborating with the Centers for Medicare and Medicaid Services (CMS) to make an outcomes-based approach available. Under this model, CMS would only need to pay when pediatric and young adult ALL patients respond to Kymriah by the end of the first month of treatment. The company is pursuing similar contracts with private payers. In the future, Novartis is expected to move toward indication-based pricing, in which the price of the drug will be the same, but the company will offer higher or lower rebates based on the indication.

Patient Value

Cell therapy products must continue to be validated through the gathering of real-world evidence (RWE), collecting data through clinical trials and patient profiles so that the right patients are put on these therapies and adverse events are anticipated.

The industry is still in the early stages of understanding the underlying biology of cell therapies and how they will work. The approved cell therapy products are backed up by clinical trial data, but a wealth of new data and insights will be generated now that cell therapy products are reaching the market and are being used by a diverse set of patients. The ability to track and analyze that information to inform how these therapies can further be improved and how the supporting care around of these therapies can be adjusted will be key.

Because every patient is different—physically, mentally, clinically, and in terms of access to care—some patients are going to respond extremely well to therapy while others may not respond at all. A large, coordinated effort is needed to not only understand patient response to treatment, but also to ensure responses are tracked across provider institutions and across health plans.

Cell therapies also have the potential for severe adverse events. For both providers and cell therapy manufacturers, the ability to understand the risk factors associated with severe adverse events and to preemptively identify potential patients who are at higher risk is critical. The entire healthcare system needs to be prepared to manage patients who experience adverse events as a result of targeted therapies. Providers and manufacturers will need to work hand in hand to build in the appropriate processes and capabilities to address adverse events quickly and to ensure that the overall value of these therapies is being maximized for patients.

Logistics

CAR T-cell therapy brings many logistical complications, including supply chain and order tracking, capacity planning, and the onboarding of provider hospital systems capable of administering the drug.

Almost everyone has experienced shipping errors with FedEx or Amazon, but when an expensive, life-saving drug is at stake, even a 1% or 2% error rate is unacceptable. The pharmaceutical industry has not faced logistical issues as complex as this before. The required level of logistical sophistication is exceeding the degree of logistical expertise that has historically been seen in the industry. An asymmetry exists between the strategies, technologies, processes, and skills required versus what the industry currently possesses. The other critical aspect of logistics is capacity planning and forecasting. Manufacturers will need to accurately forecast demand so that they can build up their manufacturing capabilities to meet the demand for product.

To avoid potentially catastrophic errors, the biopharma industry will need to understand the strategies, technologies, processes, and skill sets leveraged by other industries and companies with supply chain expertise. That means looking to companies like Walmart, FedEx, and Amazon, examining their models, and building and improving upon their examples to ensure demand can be met, orders are tracked appropriately, and they are sent in the right time to the right place to the right patient.

When it comes to onboarding provider hospital systems, it is important to be proactive in engaging with a much larger variety of stakeholders than is typical. Currently, key stakeholders include physicians, nurses, and office managers, but manufacturers must go much broader and build relationships with administrators, CEOs, and IT and supply chain personnel. On the clinical side, provider hospital systems must be provided with education, training, resources, and systems they require to care for patients on these therapies. Manufacturers' ability to tailor messages and understand the depth of processes and interactions of these stakeholders will need to be much higher than the typical pharmaceutical model.

Manufacturers will also need to work with the providers to manage the resource demands that arise when patient spikes occur. For example, arrangements could be made such that the manufacturer provides experts and bundled services to assist the Center of Excellence when it experiences a large influx of patients. It should be noted, though, that different provider organizations will require different packages of services and support. Certain providers will have existing capabilities and investments to support CAR T-cell therapy, while others will be less prepared. Not only will manufacturers need to determine which provider organizations to prioritize and onboard, they will also need to develop differentiated bundled packages for each type of provider that is going to be delivering CAR T-cell therapy.

Data Analytics

Next-generation therapies are just one of the major areas where we are seeing a shift happening in life sciences. Another important area is around the utilization of data analytics. Here again, Moore's Law is in effect, with advances in technology providing an ever faster ability to process data. Faster processing of data will unlock an enormous amount of information, helping us discover new areas of value to advance how healthcare is delivered to patients.

Since the 1980s, analytical capabilities have grown rapidly, from simple reporting and visualization, to comparative and predictive analytics, to the cognitive computing of today. With each step, analytical tools have been able to take on increasingly complex data sets and generate more value for addressing commercial and clinical issues within the life sciences industry.

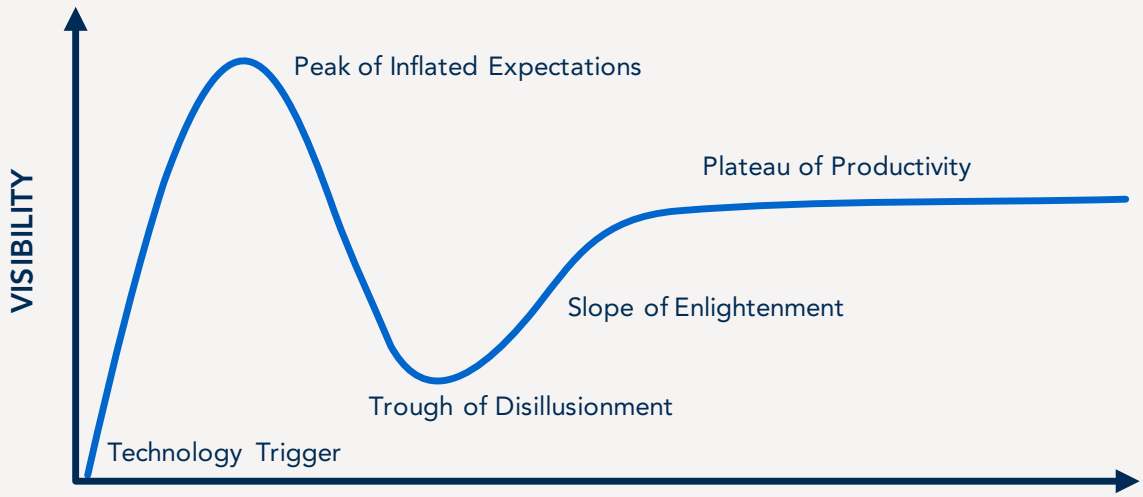
Meanwhile, the volume of data has been growing at an exponential rate, from electronic health record (EHR) system data to sensor diagnostics and so much more, creating an unprecedented opportunity for the life sciences industry to gather insights. With this opportunity come some significant challenges that pharmaceutical executives and professionals will need to address with regard to understanding the specific types of data that are going to be most relevant and useful to inform their decision making. They will also need to identify the organizational and technical capabilities that are required to generate, integrate, and manage all of the available data.

Like all new technologies, data analytics followed a recognizable pattern of adoption, demonstrated by the Gartner Hype Cycle[8], shown in Figure 2. The innovative technology first rises to a high peak of outsized expectations before reality sets in and expectations normalize. The technological innovation then begins the slow climb up what Gartner calls "the slope of enlightenment." During this period, people gain a better understanding of the potential and appropriate uses for the innovation and how exactly it can be integrated into their businesses. It is the point in time where innovative technologies become useful tools capable of being operationalized.

While the use of data analytics in healthcare has trailed other industries, some aspects of this technology are finally reaching Gartner's slope of enlightenment. Healthcare industry professionals have gone through the experience of testing, using, and experimenting with analytics, working through the failures and challenges to develop a better appreciation for what it takes to draw value from data analytics from a strategic, organizational, and technical standpoint.

As companies figure out how to leverage different types of data analytic capabilities, they are also developing the expertise and capabilities to do so and gaining a better perspective of the type of analytic capabilities that are suitable for different types of clinical and commercial problems.

FIGURE 2: Gartner Hype Circle



Advanced methods of data analytics can be applied throughout a product's life cycle, as illustrated in Figure 3. As an example, if a manufacturer is concerned that its product is not receiving sufficient uptake, the company could partner with providers to analyze electronic medical record (EMR) data and quantify the true clinical and economic value of the product.

This information can be shared with treatment decision makers to drive improved product uptake. In addition, the analysis can be used to identify specific patient segments that show disproportionate response to the treatment. Providers can then be shown the patient populations where a stronger case exists for using the product.

To maximize the value of data analytics, it must be approached with three guiding principles: strategic orientation, an appreciation for the business case, and an operations mindset.

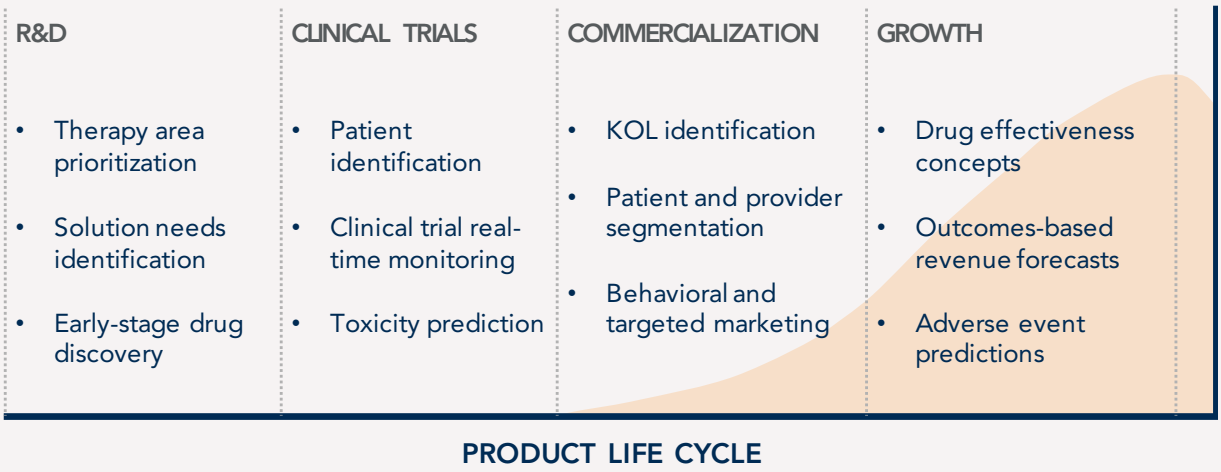
Strategic Orientation

Senior leadership needs to treat data as a true strategic lever in the business, with an equal footing to the clinical, commercial, and business development strategy. The analytics team must have a seat at the table, and the data itself should be treated as an asset, as if it were an item on the balance sheet. When data stands as an equal and is viewed as an asset, it can be invested in, grown, shaped, refined, and tailored. And it will have a direct linkage to addressing unmet needs and increasing revenue. When such a mindset is adopted and data is given the proper weight, the data is more likely to be used correctly to inform strategy.

Appreciation for the Business Case

The business case has to drive how data is used. It is always necessary to first ask, what is the business question to be addressed? Then one must ask, how does data analytics fit within the strategies and tactics needed to answer that business question? Once the true business question is determined, companies can shape a business case to address the question that is inclusive of data analytics. The business case will inform the specific type of data analytics to use and the specific type of information or data to be analyzed. It will also inform how the organization will feed the generated insights to specific decision makers both internally and externally in order to change behaviors in a way that addresses the business question at hand.

FIGURE 3: Data Analytics Applications Across the Product Life Cycle



As an example, a pharmaceutical manufacturer may want to address clinical trial costs. It is first necessary to understand that more than 30% of clinical trial costs are due to patient recruitment. Therefore, the organization will want to prioritize recruiting of patients as an area of focus for the business case and address that particular business question. From there, leaders can think about strategy, tactics, and services as well as analytics that will help identify patients and improve the recruitment of those patients.

Operations Mindset

It can be difficult enough to collect the data, conduct the right analysis, and develop the appropriate insights. It is far more difficult to apply those insights and translate them into change. To do that, it is necessary to understand the cascading impact that these insights will have on internal and external stakeholders. Organizations must think about effort required to use insights to educate stakeholders and articulate how their processes or efforts need to change. It is also necessary to get organizational alignment so that people understand what these changes will mean and how it will benefit them.

One of the ways to do this is to introduce analytics and its impact through small tests. Through a series of small experiments where the demand on teams and stakeholders is modest and the duration of the project is short, the ability to make a difference and make an impact, although compartmentalized, will be much more feasible and faster to see. The compounding results from each of these small experiments can be used to further scale, grow, and expand analytics and its scope over time.

Conclusion

In our look at next-generation therapies and data analytics, we have taken just a cursory glance at what these new advances can mean for how the future of healthcare could change. Many different scenarios exist for what the future can look like, such as these potential future states:

INCREASED APPLICATION OF RWE AND ANALYTICS

- Use of EMR data to identify attributes driving disproportionate patient response in order to prioritize patient populations for a manufacturer's therapies
- Leveraging of predictive analytics to control for serious adverse events

INNOVATIVE THERAPIES COMBINING WITH INNOVATIVE REIMBURSEMENT MODELS

- Analysis of genetic data and other cellular profiles to select patients with certain receptors on the tumor cells and certain tumor cell microenvironments
- Genetic engineering of cells for that specific patient population
- Alignment with payers and providers on outcomes-based contracts

TECHNOLOGY LEADING THE WAY TO PATIENT-CENTRIC PRECISION MEDICINE

- Extending the reach of specialists to those in need through technology-assisted patient/provider communication
- Increasing the probability of successful clinical outcomes through tailored therapies

The potential for the future is vast, but we do not have to simply sit back and watch the future come. The pharmaceutical industry and other stakeholders have a say in shaping the future state. We are all involved. We can influence change and actually turn potential advancements into reality.

About the Authors

Faruk Abdullah is a Managing Director at EVERSANA MANAGMENT CONSULTING. A life sciences consulting veteran, for years he has been helping clients consider novel approaches to developing and commercializing their products as well as to rethink how to develop and integrate analytic capabilities to inform critical strategic decisions.

Faruk can be reached at faruk.abdullah@eversanaconsulting.com.

Paul Nash, PhD, is a Principal at EVERSANA MANAGEMENT CONSULTING. He has assisted biopharma companies with questions across all stages of the product life cycle, including trial design, pre-launch activities, pricing and access strategies, launch, and life cycle management.

Paul can be reached at paul.nash@eversanaconsulting.com.

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