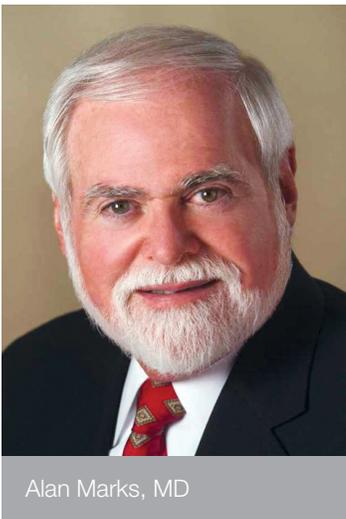


IMPROVING PATIENT ACCESS TO IMMUNO-ONCOLOGY THERAPIES

By Alan Marks, MD, and Mary Ann Chapman, PhD



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Despite major advances in cancer medicine (oncology), cancer remains a deadly disease, accounting for nearly 600,000 deaths in the US annually.¹ For many years, the primary treatments for cancer have been surgery, chemotherapy, and radiation therapy. Over the past decade, medications have been developed that act directly on cancer cells to inactivate molecules that

enable the cells to grow and replicate.² These medications have been joined by immuno-oncology therapies, which do not act directly on cancer cells, but instead harness the body's own immune system to fight cancer.

Prior to immuno-oncology therapies, no cancer treatment had ever significantly extended life for patients with advanced melanoma, a particularly deadly form of skin cancer.³ Based on this and similar reports, immuno-oncology therapy has been deemed a medical breakthrough that many believe will revolutionize cancer treatment.³ However, these therapies are costly and most patients cannot afford them—even with insurance. The lack of patient access to immuno-oncology therapies has stimulated debates about value in healthcare and how best to get these important therapies to patients who need them.

IMMUNO-ONCOLOGY THERAPIES

Immuno-oncology therapies developed out of an understanding that the body's immune system is important in cancer. In fact, the immune system is capable of recognizing and destroying cancer cells just as it does harmful bacteria and viruses. However, the

immune system is not always effective against cancer and, in the late 1980s and early 1990s, researchers began identifying reasons why.³ These findings led to the development of immuno-oncology therapies known as checkpoint inhibitors, which prevent cancer cells from fooling the immune system into treating them like normal cells. Other immuno-oncology therapies take the form of vaccines, which are now available for several cancer types. Yet another strategy is to engineer patients' own immune cells to better recognize and attack cancers; this method is still under study, but has yielded promising results thus far.³

CHECKPOINT INHIBITORS

Cancer cells develop a strategy that prevents immune cells from recognizing them as a threat. They do this by expressing "friendly" proteins on their surface. These proteins bind to immune cells and keep them from attacking, forming a so-called checkpoint. Several new immuno-oncology therapies prevent this "friendly" binding, thereby inhibiting the checkpoint and leaving the immune cells free to attack and destroy the cancer.⁴ Immuno-oncology therapies that work this way are known as checkpoint inhibitors. Notably, former President Jimmy Carter is being treated for advanced melanoma with a checkpoint inhibitor known as pembrolizumab.⁵

Clinical studies showing that immuno-oncology can help some patients with advanced cancer who don't respond to other treatments have excited researchers, patients, and healthcare providers alike.³ Recent research has shown that combining immuno-oncology therapies benefits even more patients than the individual therapies alone.⁶ These findings have generated a huge amount of optimism in the field, but the treatments don't work for everyone and researchers are working to find out why. This may lead to more personalized medicine, in which each patient receives the treatment that is best for him or her, particularly considering molecular features of the cancer.

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Figure 1. Examples of Immuno-Oncology Therapies⁷

NAME OF THERAPY	TYPE OF CANCER
<i>Checkpoint Inhibitors</i>	
Pembrolizumab	Advanced melanoma
Nivolumab	Advanced melanoma, Advanced squamous non-small cell lung cancer
Ipilimumab	Advanced melanoma
<i>Vaccines</i>	
Human papilloma virus	May prevent various cancer types
Sipuleucel-T	Advanced prostate cancer

CHALLENGES WITH PATIENT ACCESS TO IMMUNO-ONCOLOGY THERAPIES

Costs and Coverage Obstacles

High hopes surrounding immuno-oncology therapies are tempered by their high cost, with a course of treatment running about \$120,000 to \$150,000 per patient in the US.⁸ Given that combining therapies seems to yield even better results,⁶ the costs may go even higher. Manufacturers contend that these prices reflect treatment value and permit continued investment in new therapies.⁸ Insurers argue that they simply cannot afford the medications for everyone who could benefit from them. In response, insurers typically include immuno-oncology therapies on so-called specialty tiers.

Specialty tiers typically require beneficiaries to pay 20% to 25% of the medication cost,⁸ thereby shifting a substantial portion of the financial burden onto patients. With medication costs of more than \$100,000, a 20% or 25% co-pay makes immuno-oncology therapies unaffordable for most patients. Moreover, these high co-pays hit patients just as they are fighting for their lives, creating an inordinate amount of stress. Many patients are unable to work while undergoing cancer treatment, which causes them to lose their insurance, compounding the problem and often leading to bankruptcy.⁹ This is clearly an unacceptable situation that we, as a nation, must seek to remedy, particularly for breakthrough treatments such as immuno-oncology therapies that hold so much promise for patients.

MEDICATION TIERS IN HEALTHCARE BENEFIT PLANS

Healthcare plans often specify tiers that determine the amount of medication cost to be paid by beneficiaries, also called co-pays. Tier 1 is the lowest level of cost sharing, which usually includes generic drugs—exact copies of name-brand medications produced in laboratories using established chemical reactions. Tier 2 typically includes preferred name-brand drugs, and Tier 3 usually includes non-preferred, name-brand drugs. The “specialty tier” includes more unique and expensive medications such as immuno-oncology therapies. Specialty tier medications are often biologics—treatments produced by cells or living organisms—which includes the immuno-oncology therapies.

Figure 2. Typical Medication Tiers in Healthcare Benefit Plans¹⁰

TIER	TYPE OF MEDICATIONS	BENEFICIARY CO-PAY
Tier 1	Generic drugs	Lowest; typically flat rate
Tier 2	Preferred name brand drugs	Medium; typically flat rate
Tier 3	Non-preferred name brand drugs	Higher; typically flat rate
Specialty tier	Unique, higher-cost medications, including immuno-oncology therapies	Highest; typically % of medication cost

For the lower tiers, the amount of cost sharing to be paid by beneficiaries tends to be a flat fee. However, for specialty tiers, cost sharing is typically a percentage of the medication cost—often 20% to 25%.⁸

Novel Approaches to Cancer Care

The costs of cancer in the US currently exceed \$125 billion annually¹¹ and are expected to reach \$157 billion by 2020.¹² The enormous annual expenditures have stimulated attempts at restructuring cancer care to reduce costs, which have led to a focus on value. According to the National Comprehensive Cancer Network (NCCN), value refers to the benefits of treatment weighed against the economic cost.¹³ Although this definition seems straightforward, in practice it is difficult to calculate. For instance, is it possible to determine the benefit

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of extending life by several months? What about several years? How should adverse side effects be considered in the equation? Who defines the benefits of cancer care?

Several professional organizations have developed methods for calculating the value of cancer therapies. One example is the American Society for Clinical Oncology, whose Value in Cancer Care Task Force focuses on three main elements in its estimation of value: clinical benefit (efficacy), toxicity (safety), and cost (efficiency).¹⁴ Similar methods have been developed by the

NCCN and Memorial Sloan Kettering Cancer Center. These methods begin to address the issue of value that is critically important in cancer care, particularly given the development of high cost, high value therapies. However, these methods are not perfect, as they omit total cost of care and patient preferences.¹⁵ Moreover, they tend to rely on averages, net benefits, and statistics as opposed to the patient-physician relationship, where decisions are made on an individual basis taking into account each patient's unique characteristics and preferences.

CONCLUSIONS

Immuno-oncology therapies are breakthrough treatments for a number of cancers, with the potential to benefit many more patients as their development proceeds. However, patient access to these high value treatments is limited because of their cost

and the high co-pays required by insurers. It is imperative that manufacturers, insurers, physicians, and patients seek a mutually acceptable solution that allows patients to access treatments that meaningfully benefit them.

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