Pharmacy Focus:
The Evolution of Cancer Treatment

Overview

Cancer is a genetic disease that can start almost anywhere in the body, causing affected cells to grow uncontrollably and potentially spread to other areas. It can be inherited or caused by the environment. Cancer is an umbrella term that covers more than 100 different disease types, so each treatment approach is specific to both the disease and the patient.[1]

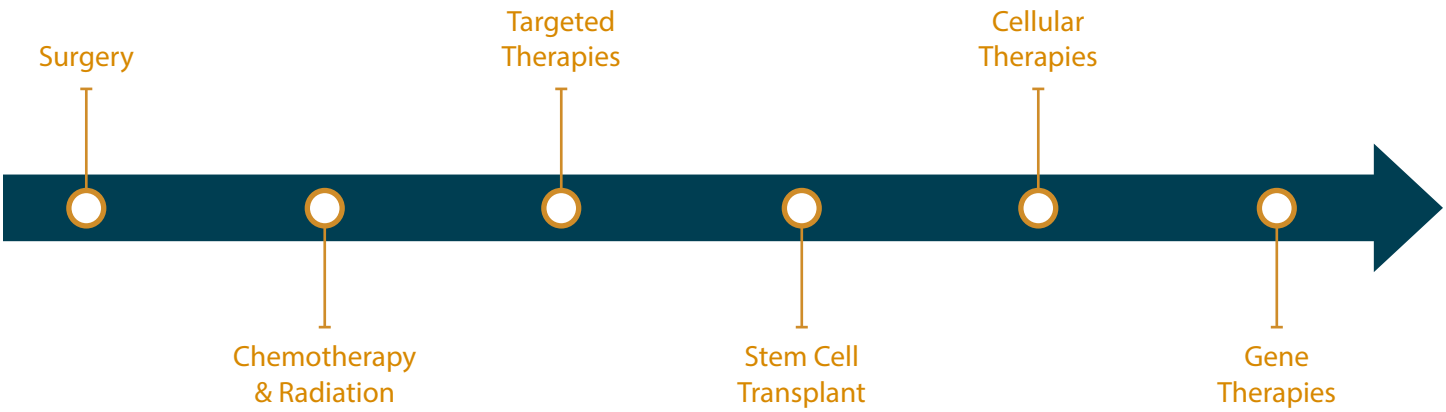
Although there are many treatment options out there – from chemotherapy to the newer biologic agents – there is still a need for even better alternatives. In 2021, it is estimated that there will be close to 1.9 million new cancer cases diagnosed and more than 600,000 cancer deaths in the United States alone.[2] To help improve outcomes, the medical community is making continual progress on advancements, and more options for cancer-specific gene and cell therapies are beginning to come through the pharmaceutical pipeline. These innovative treatments are expensive, but they offer new hope for longevity and better quality of life for those with the types of cancer they address.

During a lifetime, approximately 39.5 percent of men and women will be diagnosed with cancer.[3] With such a large percentage of people affected by this disease, the medical costs involved can become collectively tremendous. According to the Agency for Healthcare Research and Quality (AHRQ), in 2001 $57 billion was spent on cancer, compared with $88.3 billion in 2011.[4] By 2018, the estimated expenditure for cancer care in the United States grew to $150.8 billion, and costs are projected to increase to $246 billion by 2030.[2]

One of the driving factors for the high cost of cancer treatment is that each patient tends to be given numerous therapies since it is such a complex disease. While treatments vary based on the specific patient and type of cancer diagnosed, a general principle is that combination therapy is used most often.

Therapies are billed through both pharmacy and medical benefits depending on the treatment and the way it is administered. When treatments are billed through the medical coverage, costs are challenging to evaluate because items can be grouped together. This makes it difficult to predict the costs of treatment and can lead to seemingly inflated costs, non-competitive pricing and possible overpayment for these therapies.[5]

Cancer Therapy Evolution



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Cancer Therapy Evolution, *continued*

Treatment	Description	Billing
Surgery	The oldest treatment for cancer is surgery. This practice has been used since ancient times, as noted by Hippocrates, Celsus and Galen. Surgery is best for solid tumors and often is used in combination with other cancer treatments.[6]	Medical Billing
Radiation	Radiation was first used for cancer treatment in the late 1800s. It causes breaks in DNA by generating free radicals, and it is best used for superficial tumors. Radiation is non-specific, which means that it harms healthy cells along with cancer cells, causing a lot of collateral damage to nearby tissues. Although radiation can cure cancer, it also can cause cancer from the damage it does to the body's healthy cells. Fatigue and skin irritation are the most common early side effects of radiation. Late side effects can take months or years to develop.[6,7]	Medical Billing
Chemotherapy	Conventional chemotherapies target DNA structure or DNA replication. They have a lot of side effects because they have non-specific targets. Traditional chemotherapy agents blindly destroy all rapidly dividing cells – such as tumor cells (which is the purpose), but also blood cells, hair cells, GI cells and reproductive tissues. Common side effects of chemotherapy are hair loss, nausea and vomiting, fatigue, low blood cell counts, neuropathy and more. Chemotherapy can be very difficult on patients, and these side effects may lead to poor quality of life.[6,7]	Medical Billing
Targeted Therapies	Targeted therapies act on a specific molecular target like proteins or enzymes found on the patient's cancer cells. By having a specific biologic target, these therapies attack the cancer cells and have less of an effect on normal, healthy cells. These therapies do not typically cause hair loss, nausea and vomiting or the other traditional chemotherapy side effects. They do, however, have their own side effects, which are product-specific and based on how the agent works. The most common targeted therapies are various monoclonal antibodies, proteasome inhibitors, signal transduction inhibitors and angiogenesis inhibitors.[2] Side effects seen with some of these classes of medications are slower wound healing, increased blood pressure, skin rash and irritation. Overall, these therapies have a better side effect profile than chemotherapy and are generally better tolerated. Immune checkpoint inhibitors are another type of targeted therapy. They are considered an immunotherapy treatment and work to keep T-cells "on" and continually fighting the cancer cells. Most patients treated with these targeted therapies also are on combination therapy, such as chemotherapy, radiation and/or surgery.[6,7]	Medical Billing and Pharmacy Billing
Stem Cell Transplant	A stem cell transplant is still considered the only curative therapy for eligible cancers. It can be used before and/or after cell therapies. Stem cell transplants are the only option for "curative" therapy for some patients, but unfortunately, they are not always curative.[7]	Medical Billing

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Cancer Therapy Evolution, *continued*

Treatment	Description	Billing
Cellular Therapies	Current cell therapies on the market are CAR T-cell therapies. CAR T is the abbreviation for chimeric antigen receptor T-cell therapy, and it is when T-cells are taken from the blood by a process called leukapheresis and altered in the lab to have a chimeric antigen receptor (CAR) that allows them to identify patient-specific surface antigens. The surface antigens that are identified also are targeted on normal cells, contributing to the side effects. They are training the body's immune system on how to fight the cancer and also can be considered an immunotherapy treatment. Once the CAR T-cells have been modified and grown in the lab, chemotherapy is necessary to lower the number of immune cells, something that is done to improve the ability to fight off the cancer when the CAR T-cell therapy is reintroduced. There are five currently approved CAR T-cell therapies for lymphomas, leukemias and multiple myeloma (blood cancers) with more in the pipeline. Those approved include: • Kymriah® (tisagenlecleucel) • Yescarta® (axicabtagene ciloleucel) • Tecartus™ (brexucabtagene autoleucel) • Breyanzi® (lisocabtagene maraleucel) • Abecma® (idecabtagene vicleucel) Associated side effects include: Cytokine Release Syndrome (CRS) – high fever, chills, dizziness, increased heart rate, fatigue; nervous system problems – confusion, seizures, tremors, headaches; and hypogammaglobulinemia – an issue with the immune system that prevents it from making enough antibodies and immunoglobulins and may require long-term management.[6,8]	Medical Billing
Gene Therapies	Gene therapy works by using a viral vector, plasmid DNA or other means to correct an error in a patient's genes that is causing disease. Currently, there are two gene therapies on the market for cancer: **Provenge® (sipuleucel-T)** • An IV infusion for metastatic hormone refractory prostate cancer that is an immunotherapy specific to each individual being treated and created by using the patient's own immune cells; Provenge® was shown in phase 3 trials to have a hazards ratio of 0.77, indicating a 23% lower risk of death when compared to the placebo; no conclusions could be made regarding the clinical significance of the observed immune responses due to Provenge® • This treatment is administered every two weeks for a total of three IV infusions • The cost is approximately $500,000 for a full course of treatment **Imlygic® (talimogene laherparepvec)** An intralesional injection for unresectable melanoma that is a genetically modified oncolytic viral therapy on a weakened HSV-1 virus; Imlygic® has not yet been proven to improve overall survival or have any effect on visceral metastases • Initial dose ~$300,000 • First maintenance dose is given three weeks after the initial treatment and then requires consecutive treatments every two weeks for at least six months or until there are no lesions left. There are maintenance treatment baseline costs of ~$30,000.[9,10,11,12,13,14,15]	Medical Billing

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What's Coming through the Pipeline

Adstiladrin™ (nadofaragene firadenovec): A intravesicular injection for non-muscle invasive bladder cancer (NMIBC) that is unresponsive to standard treatment; FDA approval is currently pending, and it could be approved as early as the end of 2021[16,17]

Tavo™ (tavokinogene telsaplasmid): Gene therapy for advanced or metastatic malignant melanoma in adults whose cancer has progressed while on a checkpoint inhibitor in combination with Keytruda®; it will be an intralesional injection therapy similar to Imlygic®.[18]

Cilta-cel (ciltacabtagene autoleucel): IV infusion CAR T-cell therapy for the treatment of relapsed/refractory multiple myeloma in adults; FDA approval is pending.[17]

AUTO1 (obecabtagene autoleucel): An IV CAR T-cell therapy for the treatment of Acute Lymphoblastic Leukemia that is currently in phase 1 studies.[19]

HMConnects™ Cost Containment Considerations

As part of its HMConnects™ cost containment program, HM Insurance Group (HM) works to support cost management opportunities around the use of gene and cell therapies and other high-cost pharmaceutical treatment options that can impact our clients' bottom line. The Pharmacy Operations (RxOps) team watches the market – and our book of business – and anticipates how current and future advancements will impact financial risk levels for HM's client base. Standard practices include reviewing, auditing and collaborating on the content of current policies, monitoring trends and implementing appropriate cost savings techniques, all of which are provided to HM's clients at no additional cost to them.

Pharmacy Focus provides valuable information about pharmaceutical industry developments and their associated costs that can impact the growing claims trend in the self-funded insurance market. Be aware of influences and gain insight into approaches that may help to contain costs. Please share topic suggestions or feedback with **HMPharmacyServices@hmig.com**.

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