OPTUMRx®

OptumRx Drug Pipeline Insights Report

Q3 2020

Looking ahead: 2020 pipeline

From Sumit Dutta, Chief Medical Officer at OptumRx

At OptumRx, we are committed to providing our clients, members and the broader health care community with up-to-date information regarding drug access, cost management and notable FDA approvals. As part of that commitment, we provide routine updates designed to increase your understanding of the pharmaceutical pipeline for 2020.

As might be expected, we've seen delays in drug development and postponement of FDA submissions due to COVID-19. For example, several of the gene therapies expected in the first half of 2021 are likely now pushed back to late 2021 or even into 2022.

For some approved drugs, there may be slow uptake as manufacturers delay commercializing activities because of the pandemic. For example, challenges in detailing physician offices have led certain manufacturers to postpone launch. Also, reduced patient office visits may result in less opportunity to diagnose conditions and prescribe therapy.

Still, new drugs will continue to launch. Through July, the FDA has approved more than 30 new drugs this year — somewhat ahead of the average annualized number — and five have been delayed because of COVID-19.[1]

In this report, we discuss several significant new drugs. Two were expected to be approved by the FDA during this time period but were not. Three others have been approved. In addition, we review a few critical trends to watch this year.

We hope this report helps increase your understanding of the pharmaceutical pipeline for 2020.

Sumit Dutta
Chief Medical Officer, OptumRx

Drug overview

Two of the drugs on our list of important launches recently received unexpected setbacks from the FDA:

valoctocogene roxaparvovec (Roctavian)

An FDA decision was expected by August 21, 2020. Instead, on August 18, 2020, the FDA requested additional information.

Valoctocogene roxaparvovec is intended to treat hemophilia A in adults. Existing treatments for this condition are extremely expensive, costing up to $500,000 per year. Valoctocogene roxaparvovec would offer a one-time gene therapy that could replace the need for these treatments in some patients.

While the FDA had initially announced that they would issue a decision in August, instead the FDA informed the manufacturer that a decision would be delayed in order to review an additional two years of trial data.[2]

The FDA's concern centers on the durability of Roctavian's effect, in other words, how long the therapy can be expected to last in real life. Recent data appear to indicate that the effects begin to fade within a few years. In this case, the duration of effect is important because the projected wholesale acquisition cost (WAC) for valoctocogene roxaparvovec is expected to be in the range of $2 million to $3 million per one-time dose. It will be important to understand whether the durability or Roctavian justifies the high projected price for treatment.

filgotinib (Jyseleca®)

An FDA decision was expected by August 19, 2020. Instead, on August 18, 2020 the FDA requested additional information.

Filgotinib is a treatment for adults who are living with moderate-to-severe rheumatoid arthritis (RA).

Just one day prior the scheduled decision date, the FDA announced that it will require additional data from two ongoing safety studies of the drug. Relatedly, the FDA has expressed concerns regarding the overall benefit/risk profile of filgotinib at the 200 mg dose used in trials.[3]

Industry analysts speculate that if these concerns cannot be satisfied, the entire development program may be dropped by the manufacturer.[3]

Drug overview

The following drugs have either already been recently approved, ahead of expected FDA approval date, or are still considered to be on track for approval this summer:

Tecartus™ (brexucabtagene autoleucel, formerly KTE-X19) — Approved July 24, 2020.

Tecartus is a cancer therapy intended to treat adult patients with relapsed or refractory mantle cell lymphoma (MCL), a rare and aggressive form of non-Hodgkin's lymphoma (NHL). In the U.S., 1 in 100,000 individuals are diagnosed with MCL each year. The five-year overall survival rate ranges from 20% to 60% depending on the extent of the cancer.[4]

Tecartus is a chimeric antigen receptor T-cell (CAR T) therapy. CAR T is a form of immunotherapy — therapy that leverages and strengthens the power of a patient's immune system to attack cancer cells.[5]

Tecartus becomes the first CAR T-cell therapy for MCL, offering an additional treatment option for patients with relapsed or refractory MCL that only requires a one-time dose administered by IV infusion.[5]

In trials with a median follow-up period of 12.3 months, 93% of patients responded to a single infusion of Tecartus, including 67% of patients who achieved a complete response.[5]

Common adverse events include systemic inflammatory reactions, neurologic events, anemia, decreased platelet count, and decreased white blood cell count.

For a more detailed discussion of the FDA approval and relevant trial results, please look here.

Competitive environment

Tecartus will be competing against five other FDA-approved drugs for the same indication, four of which are taken orally.[4] However, Tecartus offers a unique mechanism relative to other approved treatments for MCL and was effective in patients who had already failed other treatments.

While the early trial data for Tecartus are promising, we still lack long-term remission data for CAR T-cell therapies, which is important considering their high cost.

All CAR T treatments have certain limitations. For example, Tecartus has a boxed warning in its product label regarding the risks of systemic inflammatory reactions and neurologic toxicities. And, delays can be experienced with CAR T treatments due to the long preparation process needed to withdraw, process and re-introduce the cells for each patient.[6] (For more about the CAR T production process, and potential steps to reduce its time and cost, see "Trends to Watch," below.)

Tecartus has launched with a list price of $373,000.[6] Wholesale Acquisition Cost prices for the other CAR T-cell therapies, Kymriah®(tisagenlecleucel) and Yescarta® (axicabtagene ciloleucel), are $373,000 and $475,000 respectively.[6] For reference, OptumRx estimates the average cost of several existing non-CAR T treatments for MCL at approximately $150,000 per year.

Drug overview

Ofatumumab (Kesimpta®) — Approved August 20, 2020.

The subcutaneous form of ofatumumab is meant to treat relapsing forms of multiple sclerosis (MS). Ofatumumab is currently available in intravenous (IV) form as Arzerra® which is FDA approved for the treatment of chronic lymphocytic leukemia.[4]

MS is an autoimmune disease that results in damage to the central nervous system. Patients with relapsing forms of MS have episodes of worsening function (relapses) followed by remissions. Some patients accrue a degree of residual disability over time.[4]

According to the National Multiple Sclerosis Society, approximately 914,000 adults are affected by MS in the U.S. and approximately 85% of patients initially present with the relapsing form of the disease.[4]

Ofatumumab is an antibody against a protein called CD20, which is found on the surface of certain types of immune cells called B-cells. The treatment binds to the CD20 protein, which may decrease the number of immune cells that attack the nerve cells.[7]

Studies compared Kesimpta against Aubagio® (teriflunomide), an approved oral MS treatment. Researchers concluded that ofatumumab treatment was superior to Aubagio in treating RRMS based on the number of confirmed relapses recorded for up to 2.5 years.[7]

The most common adverse event was mild to moderate injection-related reactions. Vaccination is not recommended during or shortly after treatment, as it poses a high risk of infection.

For a more detailed discussion of the most recent published trial results, please look here.

Competitive environment

Kesimpta will be entering a crowded MS marketplace, competing not only with its trial comparator Aubagio, but also with other well established oral and injectable products with different mechanisms of action.[4]

Analysts say that being self-administered by subcutaneous injection may give Kesimpta an advantage.[7] The only other CD20-targeting therapy for MS is Ocrevus® (ocrelizumab), which is administered via IV infusion once every 6 months after initial dosing.[4] Kesimpta is dosed once every month after initial dosing.

The WAC price for Kesimpta is $83,000 per year for maintenance treatment (after the initial dosing phase). For reference, the maintenance WAC price for Ocrevus is approximately $65,000 per year and Aubagio costs approximately $93,000 per year.[4]

Drug overview

Tafasitamab-cxix (Monjuvi™) Approved July 31, 2020.

Monjuvi is now the first FDA-approved second-line regimen approved for the treatment of patients with a type of cancer called relapsed or refractory diffuse large B-cell lymphoma (DLBCL). Monjuvi is to be used in combination with Revlimid® (lenalidomide).[8]

DLBCL is the most common type of non-Hodgkin's lymphoma in adults worldwide and causes rapidly growing masses of malignant B-cells in the lymph nodes, spleen, liver, bone marrow or other organs.[9]

- In the U.S., approximately 10,000 patients are diagnosed with relapsed or refractory DLBCL who are not eligible for autologous stem cell transplant.[9]
- About one in three patients either do not respond to initial therapy or experience relapse.[9]
- Autologous stem cell transplant is the preferred treatment for patients experiencing a relapse if eligible. Patients who are not eligible for stem cell transplant are difficult to treat, and the prognosis for long-term disease control is poor. Treatment options now include the new Monjuvi/ Revlimid combination, plus CAR T therapy, chemotherapy, or enrollment in a clinical trial.[10]

Monjuvi is a genetically engineered antibody that targets CD19, the same protein targeted by Kymriah and Yescarta, which are both CAR T therapies that are used as third-line treatments for certain types of large B-cell lymphoma. However, Monjuvi is not a CAR T therapy, which may make it more suitable for certain patients, for example those not eligible for stem cell transplantation.[8]

The most common adverse events with Monjuvi were abnormally low count of a type of white blood cell, a deficiency of platelets that can cause bleeding into tissues, and anemia.

For a more detailed discussion of the most recent published trial results, please look here.

Competitive environment

The manufacturer plans to move forward with launching Monjuvi during the COVID-19 pandemic, despite the challenges outlined above (i.e., limited or no in-person access to physicians and clinics). They plan to substitute virtual versions of visits, conferences, advisory boards, etc.[11]

Monjuvi will be competing with Polivy™ (polatuzumab vedotin), which was approved in June 2019 for a similar indication. Both Monjuvi and Polivy are IV administered, however, Monjuvi is dosed once weekly, while Polivy is dosed once every 21 days.[4]

Monjuvi will have an average wholesale price (before rebates or discounts) of $16,500 per month in the first year of therapy, followed by an average of $13,000 per month in subsequent years.[11] For reference, the WAC price for Polivy is approximately $15,000 per 21-day cycle.[4]

As noted, Monjuvi may also be an alternative to CAR T therapies, which are costly and have delays in therapy due to the long production process. (See "Industry trend to watch," below.)

A first-year cost of approximately $198,000 for Monjuvi compared to one-time CAR T treatments that cost between $373,000 and $475,000.[12]

Industry trend to watch

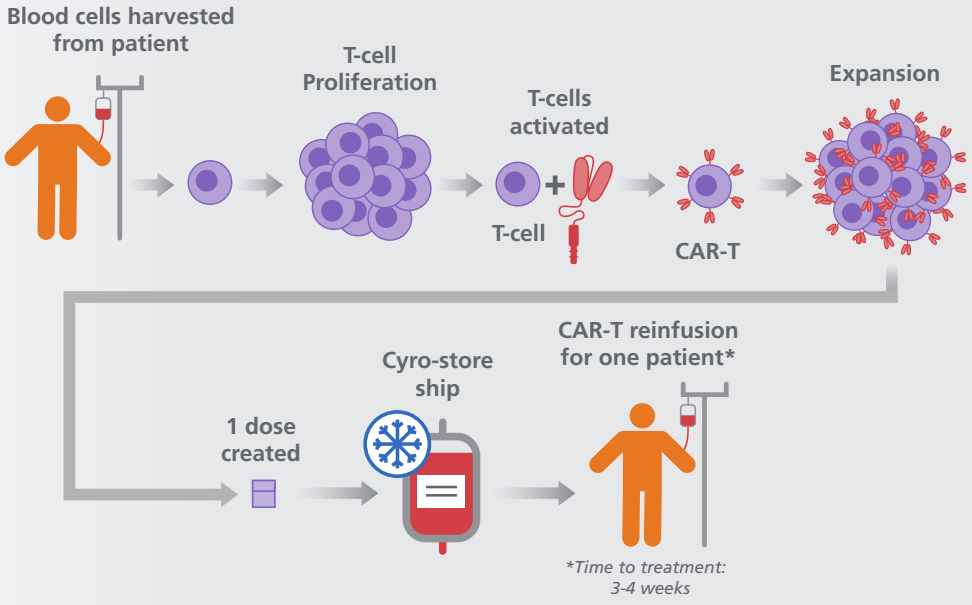
Like its fellow CAR T treatments, Tecartus will come at a high cost — between $373,000 and $475,000, continuing the trend of new expensive CAR T treatments. This is the beginning of what we expect to be a wave of new gene therapies and CAR T-cell therapies. One analyst is tracking nearly 150 CAR T therapies in development around the world. At least some of these are aimed at much larger patient populations than are currently targeted.[13, 14]

Why is CAR T so costly? Manufacturers cite the high cost of drug development as a major reason for high drug prices.[15] But in addition, the current CAR T manufacturing process is labor-intensive and time-consuming.[12] One study estimates the cost to manufacture CAR T using current methods at $95,780 per dose.[16]

Existing CAR T treatments are expensive in part because they are completely personalized using what is called autologous therapy. This means that T cells are taken from the patient they intend to treat.[13] As the graphic below shows, the cells are treated in the lab, multiplied, and then re-introduced into that same patient:

Current process: autogolous therapy

Completely personalized — T-cells taken from the patient they intend to treat



As a result, the industry is still searching for a scalable, robust and cost-effective manufacturing model for CAR T.[16]

A new approach, called **allogeneic** CAR T is currently under study as one possible solution. This process uses previously extracted and banked donor cells, making them more like an off-the-shelf product compared to the customized process we now use.[16]

The allogeneic process uses a healthy donor and the T cells can be multiplied many times over for use in many patients.[13] If successful, allogeneic CAR T could help by spreading the high initial manufacturing costs across a larger number of doses and reducing the per-dose cost.[16, 17]

For a more detailed look at the work currently under way in allogeneic CAR T, click here.

Of course, these processing costs are only a fraction of the overall cost of a drug like CAR T, so the new allogeneic process may not dramatically lower CAR T prices.[15] This simply emphasizes the point that there will be no one 'silver bullet' solution to high drug prices. It's going to take a long list of other incremental improvements to help bring these prices under control. Learn more about what OptumRx is doing to control drug prices here.

About OptumRx

OptumRx is a pharmacy care services company helping clients and more than 59 million members achieve better health outcomes and lower overall costs through innovative prescription drug benefits services, including network claims processing, clinical programs, formulary management, specialty pharmacy care and infusion services. OptumRx is part of Optum®, a leading information and technology-enabled health services business dedicated to making the health system work better for everyone. For more information, visit **optum.com/optumrx.**

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