PRIME THERAPEUTICS®

Specialty Pipeline **MONTHLY UPDATE**

Critical updates in an ever-changing environment

May 2021

NEW DRUG INFORMATION

- **Zynlonta™ (loncastuximab tesirine-lpyl):** The United States Food and Drug Administration (FDA) has granted accelerated approval to ADC Therapeutics SA's Zynlonta for the treatment of adult patients with relapsed or refractory (r/r) large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (NOS), DLBCL arising from low grade lymphoma and high-grade B-cell lymphoma. DLBCL is the most common type of non-Hodgkin's lymphoma in the United States where more than 40% of first line DLBCL treatments fail. Zynlonta is a health care administered, CD19-directed antibody and alkylating agent conjugate. The FDA approval was based on data from the Phase 2, LOTIS-2, single-arm clinical trial. Zynlonta demonstrated an overall response rate (ORR) of 48.3%, which included a complete response (CR) rate of 24.1% and a partial response (PR) rate of 24.1%. Patients had a median time to response of 1.3 months and the median duration of response (mDoR) for the 70 responders was 10.3 months.[1] Zynlonta has launched with a wholesale acquisition cost (WAC) of $23,500 per vial.

- **Jemperli™ (dostarlimab-gxly):** GlaxoSmithKline's Jemperli (dostarlimab-gxly) has been granted accelerated approved by the FDA for the treatment of adult patients with mismatch repair-deficient (dMMR) recurrent or advanced endometrial cancer, as determined by an FDA-approved test, that have progressed on or following prior treatment with a platinum-containing regimen. Jemperli is a programmed death receptor-1 (PD-1) blocking antibody. Patients received 500mg of Jemperli as an intravenous infusion once every three weeks for four doses, followed by 1,000mg once every six weeks until disease progression or unacceptable toxicity. Jemperli was approved based on GARNET clinical trial that demonstrated an ORR of 42.3% with a CR rate of 12.7% and partial response rate (PR) of 29.6%. Of those that responded, 93.3% demonstrated a DOR of six months or more. After a median follow-up of 14.1 months, the median duration of response was not reached (2.6-22.4+).[2] Jemperli has launched with a WAC of $10,369 per vial.

- **Empaveli™ (pegcetacoplan):** The FDA has approved Apellis' Empaveli™ (pegcetacoplan), the first targeted C3 therapy for treatment of adults with paroxysmal nocturnal hemoglobinuria (PNH). Empaveli is approved for use in adults with PNH who are treatment naïve as well as patients switching from C5 inhibitors, Alexion Pharmaceuticals' Soliris® (eculizumab) and Ultomiris® (ravulizumab). PNH is a rare, chronic, life-threatening blood disorder caused by an acquired mutation, which leads to uncontrolled complement activation and the destruction of red blood cells through intravascular and extravascular hemolysis. Empaveli's approval was based on the Phase 3 PEGASUS study, which met its primary endpoint, and demonstrated superiority over Soliris in improving patients' hemoglobin levels at 16 weeks with an adjusted mean increase of 3.84 g/dL of hemoglobin.[3] Additionally, 85% of Empaveli treated patients were transfusion free at 16 weeks compared to 15% of Soliris-treated patients which met non-inferiority standards. Apellis stated they would start their launch of Empaveli by focusing on patients with suboptimal responses to C5 inhibitors, specifically Soliris and Ultomiris, which they estimate is one third of the 1,500 patients in the U.S. They will then move to a broader patient population. Empaveli price and launch date are still pending.

NEW INDICATIONS

- **Sarclisa® (isatuximab-irfc):** The FDA expanded the indication for Sanofi's Sarclisa to include use in combination with carfilzomib and dexamethasone (Kd) for treatment of patients with multiple myeloma who have received at least one prior therapy.
- **Xolair® (omalizumab):** The FDA has approved a new prefilled syringe for self-administration of the immunoglobulin E (IgE)-blocking monoclonal antibody for treatment of persistent asthma and chronic idiopathic urticaria.
- **Opdivo® (nivolumab):** The FDA has expanded Bristol-Myers Squibb's Opdivo indication to include initial treatment of patients with advanced or metastatic gastric cancer, gastroesophageal junction cancer and esophageal adenocarcinoma. Additionally, the FDA approved Opdivo in combination with fluoropyrimidine- and platinum-containing chemotherapy for first-line treatment of patients with advanced or metastatic gastric cancer, gastroesophageal junction cancer (GEJC) or esophageal adenocarcinoma (EAC).
- **Trodelvy® (sacituzumab govitecan-hziy):** The FDA has expanded the indication of Gilead Sciences' Trodelvy to include treatment of adult patients with triple-negative breast cancer that has spread to other parts of the body. Patients must have received at least 2 prior therapies before taking Trodelvy.
- **Keytruda® (pembrolizumab):** The FDA granted approval of Merck's Keytruda for use in combination with trastuzumab and fluoropyrimidine- and platinum-containing chemotherapy for first-line treatment of patients with locally advanced unresectable or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma.

MAY NEWS

- "SVB Leerink biotech analyst Geoffrey Porges said in an investor note in May that although Sandoz has a strong reputation for quality biosimilars since the inception of biosimilars in the U.S. (the first-ever FDA approval for a biosimilar went to Sandoz's Zarxio), an approval for the Eylea biosimilar may not come until 2024 or 2025. And by then, the market may have changed. "We believe 2024 will be a disadvantageous time for an Eylea biosimilar to enter the market since Eylea may potentially have the high-dose formulation on the market along with competitors that should extend treatment intervals much longer than every 12 weeks," Porges wrote. He also said to expect market share loss from Eylea to be driven by the entrance of competitors that enable improved visual acuity."[4]
- "A draft report from the Institute for Clinical and Economic Review, known as ICER, found that there is insufficient evidence to determine whether the investigational therapy aducanumab will provide health benefits to people with Alzheimer's disease. ICER is an independent non-profit research institute that works to assess the effectiveness and value of medicines and other medical services. Notably, the institute's Draft Evidence Report represents the midpoint of ICER's assessment of the evidence on aducanumab — not a final decision. In its report, ICER conducted several analyses to examine the cost-effectiveness of aducanumab. The goal was to determine if the medication is likely to provide enough health-related benefits to patients to be worth the cost of treatment. Results using data from both EMERGE and ENGAGE indicated that the medication might be cost-effective at prices of about $2,500 to $8,300 per year. Although the report stresses that these estimates are necessarily uncertain, since the data on the therapy's effectiveness is unclear. In other analyses that only included data from the positive EMERGE trial, a price between $11,100-$23,100 per year was calculated as likely cost-effective."[5]
- "The FDA's Arthritis Advisory Committee voted 10 for and 8 against the approval of ChemoCentryx's investigational drug avacopan as a treatment for adults with a rare and serious disease known as anti-neutrophil cytoplasmic autoantibody (ANCA)-vasculitis. The vote on whether the FDA should approve the drug was preceded by a split vote of 9 to 9 on whether the efficacy data support approval, and 10 to 8 that the safety profile of avacopan is adequate enough to support approval. There was a contentious debate over whether the one, relatively small Phase III trial comparing avacopan with prednisone was robust enough for a full approval. FDA raised concerns about the statistical analyses of the data in the trial and what effect the use of glucocorticoids on top of cyclophosphamide or rituximab in both treatment arms had on the avacopan efficacy. ChemoCentryx defended its trial design and explained how it met its primary endpoint and showed a reduction in the use of steroids with avacopan. Those voting against approval raised concerns about relying on the single trial as evidence, the insufficient amount of safety data, and questions on whether the trial was statistically robust enough. Some panelists called for ChemoCentryx to run another trial."[6]

- "Liminal BioSciences has been engaged in a process to find a commercialization partner for Ryplazim® (plasminogen) ("Ryplazim"), which has to date not resulted in an executable transaction. As a consequence, and considering the ongoing cash burn associated with the plasma-derived therapeutics business, the Company announced that it has commenced a process to evaluate potential strategic alternatives for that portion of its business aimed at minimizing cash burn. These alternatives may result in a divestment, in whole or in part, of the plasma-derived therapeutics business and/or other non-core assets, or in other courses of action including but not limited to other strategic transactions or the closure of its Ryplazim-related operations."[7]

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