PRIME THERAPEUTICS®

Specialty Pipeline MONTHLY UPDATE

Critical updates in an ever-changing environment

January 2020

NEW DRUG INFORMATION

- **Padcev™ (enfortumab vedotin-ejfv):** The U.S. Food and Drug Administration (FDA) granted accelerated approval to Astellas and Seattle Genetics for treatment of adults with locally advanced or metastatic urothelial cancer who have previously received a PD-1/L1 inhibitor and a platinum-containing chemotherapy before or after surgery or in a locally advanced or metastatic setting. Padcev is the first FDA-approved treatment for these patients. Padcev is a first-in-class antibody drug conjugate that is directed against Nectin-4, a protein located on the surface of cells and highly expressed in bladder cancer. The FDA granted Padcev Breakthrough Therapy and Priority Review. The FDA approved Padcev based on a Phase 2, single-arm study, (EV-201) that measured objective response rate (ORR). The confirmed ORR was 44% (95% CI; 35.1, 53.2). Among patients treated with Padcev, 12% experienced a completed response (no cancer detected at time of evaluation), and 32% experienced a partial response (decrease in tumor size).[1] Seattle Genetics is currently conducting a global, randomized Phase 3 confirmatory clinical trial (EV-301). Padcev is expected to launch by the end of January with a wholesale annual cost (WAC) estimated between $110,000 and $120,000.[2]

- **Enhertu™ (fam-trastuzumab deruxtecan-nxki):** Daiichi Sankyo and AstraZeneca's Enhertu has been granted accelerated approval by the FDA for the treatment of adults with unresectable or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 based regimens in the metastatic setting. Enhertu is the first FDA-approved treatment with this indication. The FDA based its approval on a single-arm, Phase 2 trial (Destiny-Breast01) which achieved a confirmed objective response rate of 60.3% (95% CI: 52.9, 67.4), including a 4.3% complete response rate and a 56% partial response rate.[3] Daiichi Sankyo and AstraZeneca currently are conducting three ongoing Phase 3 trials to explore further potential of Enhertu. Enhertu has a Boxed warning for interstitial lung disease/pneumonitis and embryo-fetal toxicity. Enhertu has launched with an annual estimated WAC of $159,600.[4]

- **Ayvakit™ (avapritinib):** The FDA has approved Blueprint Medicine's Ayvakit for the treatment of adults with unresectable or metastatic gastrointestinal stromal tumor (GIST) harboring a platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation. The FDA's approval is based on results from the Phase 1 Navigator clinical trial; as well as combined safety results from multiple clinical trials. Ayvakit had an ORR of 84% (95% CI: 68%, 93%) and a median duration of response not reached.[5] Blueprint Medicines plans to submit a supplemental New Drug Application (sNDA) to the FDA for Ayvakit for third-line GIST in the second half of 2020.[6] Blueprint Medicines plans to launch Ayvakit by the end of January 2020 with an annual estimated WAC of $384,000.

NEW INDICATIONS

- **Vascepa® (icosapent ethyl):** The FDA broadened its approval of Amarin's Vascepa to include it as an adjunctive (secondary) therapy to reduce the risk of cardiovascular events among adults with elevated triglyceride levels (a type of fat in the blood) of 150 milligrams per deciliter or higher.
- **Lynparza® (olaparib):** The FDA expanded AstraZeneca's Lynparza label to be used as a first-line maintenance therapy for patients with BRCA gene mutations whose cancer had spread beyond the pancreas and whose tumors did not worsen after chemotherapy of at least 16 weeks.
- **Keytruda® (pembrolizumab):** The FDA expanded Merck's label of Keytruda to include the treatment of patients with Bacillus Calmette-Guerin (BCG)-unresponsive, high-risk, non-muscle invasive bladder cancer (NMIBC) with carcinoma in-situ (CIS) with or without papillary tumors who are ineligible for or have elected not to undergo cystectomy.

JANUARY NEWS

- "Intercept emerged early on as the lone winner from the Year of NASH. In February, they announced the first positive results from a Phase III NASH trial, showing their drug, obeticholic acid, could reduce liver scarring. The news was fitting; many investors were first clued in on NASH when the biotech announced a positive Phase II results six years ago, sending their stock up over 500%. Intercept hit on only one of two primary end points, but it was enough to file for the first FDA-approved NASH drug. The advisory committee hearing will be in April and those who still believe in a NASH market—and that's many—will be watching closely for how the FDA handles endpoints and diagnosis for a disease that is still less-than-perfectly understood."[7]
- "With their third-to-market spinal muscular atrophy drug risdiplam now cruising on the FDA's VIP lane toward a May decision, Roche is thinking through its pricing strategy. Novartis' gene therapy, Zolgensma, is the world's most expensive medicine by one-time cost at $2.1 million. And while Biogen's Spinraza has a list price of $750,000 in the first year and $375,000 in subsequent years, the annual prices could quickly add up to the millions for an antisense oligonucleotide patients are supposed to take for life. Unlike the two rival therapies, which are administered intravenously and intrathecally respectively, risdiplam is an oral medication to be taken daily. By modifying how the SMN2 gene is spliced, the drug supposedly increases functional SMN protein levels in both the central nervous system and peripheral tissues."[8]
- "Merck's star checkpoint drug Keytruda missed a key endpoint in their Phase III trial as a frontline therapy for extensive-stage small cell lung cancer, failing to provide a significant improvement in overall survival. The drug combined with chemo did hit the endpoint for significance in progression-free survival, leaving it in a weak but competitive position in this hard-to-treat form of cancer."[9]
- "The FDA granted rare pediatric disease designation to ARU-1801, Aruvant's experimental gene therapy for the treatment of sickle cell disease (SCD) and beta-thalassemia. This designation means the company will be eligible to receive a priority review voucher once the FDA approves a biologics license application for ARU-1801. ARU-1801 uses a proprietary technology that is intended to increase the number of functional red blood cells by inserting a modified version of the gene that provides instructions to make a protein called fetal hemoglobin directly into the patients' own stem cells."[10]

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