DRUGS & TARGETS

FDA approves first treatment for rare adrenal tumors

FDA approved Azedra (iobenguane I 131) injection for intravenous use for the treatment of adults and adolescents age 12 and older with pheochromocytoma or paraganglioma that cannot be surgically removed, have spread beyond the original tumor site and require systemic anticancer therapy.

FDA granted the approval of Azedra to Progenics Pharmaceuticals Inc. This is the first FDA-approved drug for this use.

The efficacy of Azedra was shown in a single-arm, open-label, clinical trial in 68 patients that measured the number of patients who experienced a 50 percent or greater reduction of all antihypertensive medications lasting for at least six months.

This endpoint was supported by the secondary endpoint, overall tumor response measured by traditional imaging criteria. The study met the primary endpoint, with 17 (25 percent) of the 68 evaluable patients experiencing a 50 percent or greater reduction of all antihypertensive medication for at least six months. Overall tumor response was achieved in 15 (22 percent) of the patients studied.

As it is a radioactive therapeutic agent, Azedra includes a warning about radiation exposure to patients and family members, which should be minimized while the patient is receiving Azedra. The risk of radiation exposure is greater in pediatric patients.

FDA granted this application Fast Track, Breakthrough Therapy and Priority Review designations. Azedra also received Orphan Drug Designation.

TheraBionic P1 device receives European regulatory approval

TheraBionic GmbH, a German company co-founded by Boris Pasche, director of the Wake Forest Baptist Comprehensive Cancer Center, and Alexandre Barbault, co-inventor of the TheraBionic technology, has received European regulatory approval for its TheraBionic P1 medical device for use in the treatment of advanced hepatocellular carcinoma.

The TheraBionic P1 device received the CE mark as a Class IIa medical device according to Annex II of the Medical Devices Directive 93/42/EEC guidelines and in compliance with the EN ISO 13485:2016 quality management systems regulatory requirements for medical devices. Class IIa medical devices are considered low risk and this class includes hearing aids and dental implants.

The TheraBionic P1 device was approved as a breakthrough medical product for unmet medical needs fulfilling the requirements of the European MEDDEV 2.7/1 revision 4 guidelines on medical devices.

Approval was based on a feasibility study by Barbault et al. [Barbault, A., F. P. Costa, B. Bottger, R. F. Munden, F. Bomholt, N. Kuster and B. Pasche ["Amplitude-modulated electromagnetic fields for the treatment of cancer: discovery of tumor-specific frequencies and assessment of a novel therapeutic approach." *J Exp Clin Cancer Res* 28(1): 51], a phase I/II study by Costa et al. [Costa, F. P., A. C. de Oliveira, R. Meirelles, M. C. C. Machado, T. Zanesco, R. Surjan, M. C. Chammas, M. de Souza Rocha, D. Morgan, A. Cantor, J. Zimmerman, I. Brezovich, N. Kuster, A. Barbault and B. Pasche (2011). "Treatment of advanced hepatocellular carcinoma with very low levels of amplitude-modulated electromagnetic fields." *Br J Cancer* 105(5): 640-648.], and data from compassionate use.

The data demonstrate efficacy for the treatment of patients with hepatocellular carcinoma who have no other therapeutic options, and the risks associated with the use of the device are remarkably low, the company said. The approved intended use of the TheraBionic P1 device is the systemic treatment of patients with advanced hepatocellular carcinoma who have either failed or are intolerant to first line and second line therapies.

The TheraBionic P1 medical device emits low levels of specific radiofrequency electromagnetic fields that block the growth of tumor cells, while not affecting the growth of normal cells. Systemic treatment is administered with a portable, battery-operated device connected to a coaxial cable ending with a spoon-shaped antenna placed on the anterior part of the patient's tongue, which results in whole-body delivery of low levels electromagnetic fields. There is preliminary evidence that the TheraBionic P1 may increase progression-free survival and overall survival when used for three 60-minute treatments daily.

Pasche and Barbault started their research work about 20 years ago, and demonstrated that human cancer growth may be affected by low levels of electromagnetic fields.

In 2013, Pasche and Barbault created TheraBionic GmbH with the goal of seeking European regulatory approval for the marketing of the medical device they had developed. TheraBionic Inc. based in Winston-Salem, NC, is preparing US regulatory filing for the treatment of advanced hepatocellular carcinoma.

Keytruda + pemetrexed and platinum gets EMA's positive opinion for first-line NSCLC

Merck said the Committee for Medicinal Products for Human Use of the European Medicines Agency has adopted a positive opinion recommending approval of Keytruda, Merck's anti-PD-1 therapy, in combination with pemetrexed (Alimta) and platinum chemotherapy (cisplatin or carboplatin) for the first-line treatment of metastatic nonsquamous non-small cell lung cancer in adults whose tumors have no EGFR or ALK genomic tumor aberrations, regardless of PD-L1 expression.

If approved, this would mark the first approval in Europe for an anti-PD-1 therapy in combination with chemotherapy, and is based on overall survival and progression-free survival data from the phase III KEYNOTE-189 trial.

CHMP also adopted a positive opinion recommending approval of Keytruda as monotherapy for the treatment of recurrent or metastatic head and neck squamous cell carcinoma in adults whose tumors express PD-L1 with a tumor proportion score of ≥50 percent, and who progressed on or after exposure to platinum-based chemotherapy, based on data from the phase II KEYNOTE-040 trial. These two recommendations will now be reviewed by the European Commission for marketing authorization in the European Union. A final decision on both recommendations is expected in the third quarter of 2018.

Tafinlar + Mekinist gets positive CHMP opinion for adjuvant BRAF V600 mutation-positive melanoma

Novartis said the Committee for Medicinal Products for Human Use of the European Medicines Agency has adopted a positive opinion recommending approval of Tafinlar (dabrafenib) in combination with Mekinist (trametinib) for the adjuvant treatment of adult patients with stage III melanoma with a BRAF V600 mutation, following complete resection.

The CHMP recommendation is based on findings from the COMBI-AD study, which was published in The New England Journal of Medicine.

Patients who have been diagnosed with stage III melanoma are at a higher risk of recurrence after surgical resection. The COMBI-AD study found a statistically significant 53% reduction in the risk of recurrence or death in patients treated with the BRAF and MEK inhibitor combination therapy after surgical resection versus placebo.

The COMBI-AD study evaluated Tafinlar and Mekinist among patients with stage III, BRAF V600E/K-mutant melanoma without prior anticancer therapy, randomized within 12 weeks of complete surgical resection.

Patients received the Tafinlar (150 mg BID) and Mekinist (2 mg QD) combination (n = 438) or matching placebos (n = 432). After a median follow-up of 2.8 years, the primary endpoint was met in that combination therapy significantly reduced the risk of disease recurrence or death by 53% vs. placebo (HR: 0.47 [95% CI: 0.39-0.58]; median not yet reached vs. 16.6 months, respectively; p<0.001).

The relapse-free survival benefit among the combination arm was observed across all patient subgroups, including stage III A, B and C. The estimated one-year, two-year, and three-year RFS were consistently higher than placebo (one year: 88% vs. 56%; two year: 67% vs. 44%; three year: 58% vs. 39%).

The combination treatment group also saw an improvement in a key secondary endpoint of OS (HR: 0.57 [95% CI: 0.42-0.79] p=0.0006, which did not cross the predefined interim analysis boundary of p=0.000019 to claim statistical significance).

Other secondary endpoints where the combination demonstrated a clinically meaningful benefit include distant metastasis-free survival (HR: 0.51 [95% CI: 0.40-0.65]), and freedom from relapse (HR: 0.47 [95% CI: 0.39-0.57]).

Adverse events were consistent with other Tafinlar and Mekinist studies, and no new safety signals were reported. Of patients treated with the combination, the most frequently reported AE's were pyrexia, fatigue, nausea, headache, chills, diarrhea, vomiting, arthralgia and rash.

Lenvima + Keytruda get Breakthrough designation for endometrial carcinoma

Eisai Co. Ltd. and Merck said FDA granted Breakthrough Therapy des-