Epilepsy afflicts approximately 65 million people worldwide. The Lancet recently highlighted the significant unmet medical needs in epilepsy and called on health officials to treat this disease as a global health priority. In those numbers are stories. Not only of the pain and suffering of its patients, but how those patients received treatment: Different kinds of patients took different kinds of treatments at different times. New drug approvals and new research initiatives offer promising new developments, though a cure remains elusive.

THE EVOLVING AED MARKETPLACE

The most recent epilepsy-related development out of the Silver Spring, MD headquarters of the FDA came in June. FDA provided tentative approval of Trokendi XR (Supernus), a novel once-daily extended release formulation of topiramate (formerly known as SPN-538), “for use as recommended in the submitted and agreed-upon labeling.”

Supernus, the company behind the drug, expects to receive Final Approval and then launch the product in the third quarter of 2013. The company had delayed plans to launch Trokendi XR to the third quarter from the end of 2012 in anticipation that final FDA approval would not become effective until a marketing-exclusivity period ended. The previous tentative approval came June 25, 2012 when FDA OK’d the once-daily oral extended-release capsule intended for use as an initial monotherapy in patients 10 years of age and older who suffer from partial-onset or primary generalized tonic-clonic seizures, and for adjunctive therapy for patients six years of age and older with either partial-onset or primary generalized tonic-clonic seizures, or with seizures associated with Lennox-Gastaut syndrome.

Another drug approved recently, Fycompa (perampanel) by Eisai, received FDA clearance in October 2012. Three large studies were published in May 2013 confirming the efficacy of perampanel as an adjunctive treatment for hard-to-treat partial seizures. In Epilepsia, the pooled analysis of these data from nearly 1,500 patients shows that perampanel reduced partial epilepsy seizure frequency and improved responder rates compared to placebo. At randomized doses of 4-12mg, perampanel conferred significant improvements in reducing seizure frequency and 50 percent responder rates.

“We believe that further insight into the epilepsy population could contribute to the personalization of epilepsy care and ultimately the improvement of long-term patient outcomes.”
— Patty Fritz, UCB

New drugs continue to offer new hope to patients, as research seeks for other ways to optimize care.

BY ZAC HAUGHN, SENIOR ASSOCIATE EDITOR
for all partial seizures and complex partial (CP) seizures with secondary generalization (SG seizures), compared with placebo. The analysis also showed that adjunctive perampanel was efficacious irrespective of the co-administered AED.

The drug is a first-in-class treatment, selectively targeting the transmission of seizures by blocking the effects of glutamate, which can trigger and maintain seizures. In addition, perampanel is a once-daily medication taken at bedtime.

An existing drug, Potiga (ezogabine, GSL/Valeant) received an important update recently that caused all neurologists to take notice. The drug was approved by the European Medicines Agency in March 2011 under the name Trobalt and June 2010 by the FDA, working primarily as a potassium channel blocker. FDA issued a warning the drug can cause blue skin discoloration and eye abnormalities characterized by pigment changes in the retina. EU officials followed suit this May.

FDA wouldn’t speculate whether the retinal pigment changes caused by Potiga lead to visual impairment, although several patients have been reported to have impaired visual acuity. Retinal abnormalities have been observed in the absence of skin discoloration, in some cases. The skin discoloration in the reported cases appeared as blue pigmentation, predominantly on or around the lips or in the nail beds of the fingers or toes, but more widespread involvement of the face and legs has also been reported. Scleral and conjunctival discoloration have been observed as well.

According to FDA, all patients taking Potiga should have a baseline eye exam and periodic eye exams that should include visual acuity testing and dilated fundus photography, and may include fluorescein angiograms, ocular coherence tomography, perimetry, and electroretinograms. They also advised that Potiga be discontinued if ophthalmic changes are observed unless no other treatment options are available. If a patient develops skin discoloration, physicians should give serious consideration to changing to an alternate medication.

Potiga is approved as adjunctive treatment of partial-onset seizures in adult patients 18 years and older. It was approved on the heels of three controlled clinical studies involving 1,239 adult patients. The primary endpoint was percent change in seizure frequency from baseline in the double-blind treatment phase. Investigators saw a 35 to 44 percent reduction for those receiving a 1200mg dose, 29 to 40 percent for those taking 900mg/day, and 23 to 28 percent for those taking the 600mg dose, compared against 13 to 18 percent of those receiving a placebo.

### TECHNOLOGY SOLUTIONS?

In efforts to improve therapy selection and potentially improve outcomes, UCB and IBM have completed the initial phase of a project designed to harness the power of analytics to help healthcare providers deliver more highly personalized care to people living with epilepsy. The completion marks the first step in the path toward eventually employing the power of cognitive computing capabilities, such as IBM Watson, for epilepsy care.

The goal of the project is to supply an interactive system that translates vast amounts of patient data and scientific literature into insights that healthcare providers can consult at the point of care to inform their treatment decisions.

A database, in this case big data, provides the foundation for the potential to use state of the art analytics to generate truly actionable insights from data, according to Patty Fritz, Vice President, Corporate Affairs and Operational Excellence at UCB. “Big data could allow us to use real world evidence to supplement the data that we have from epilepsy clinical trials and mitigate some of the inherent weaknesses of clinical studies,” she said.

This project’s ultimate goal—“to develop an interactive system that translates massive amounts of patient data and scientific literature into insights that healthcare providers can consult at the point of care”—hopes to address unmet needs for people living with epilepsy by matching individual patients with the most personalized approach to care.

UCB and IBM scientists have been collaborating in hopes of creating “the healthcare industry’s most comprehensive corpus of data on epilepsy.” Upon completion of the project, physicians would be able to combine their own clinical patient assessment with the system’s predictive analytics to
The hope is this project has the potential to make both raising the standard of care in epilepsy, Ms. Fritz observed. and evidence-based medicine will play important roles in based medicine, but we believe that both clinical expertise expertise will not be forgotten or cast aside, according to Ms. Fritz. “We are currently evaluating the results of the first phase and will look to publish them while continuing to build on what we anticipate will be the healthcare industry’s most comprehensive corpus of data on epilepsy. This project is a massive undertaking and specifics of the timeline are still being finalized.”

Such a data mining operation isn’t entirely new to the medical world. Recently, a New York-based cancer hospital began feeding details of 1,500 lung cancer cases into IBM’s Watson, “training” the computer to extract and interpret physician notes, lab results, and clinical research. This was the same Watson that won first prize on “Jeopardy!”. “This epilepsy project is not currently using Watson, but we are following a similar approach to lay the foundation for the potential to leverage cognitive computing, natural language processing, and machine learning capabilities to raise the standard of care in epilepsy,” Ms. Fritz said.

UCB and IBM hope this deeper insight into the epilepsy patient population could potentially provide millions of patients with more personalized care and ultimately improved outcomes. This approach will help seed the foundation for the potential to leverage cognitive computing, natural language processing, and machine learning capabilities to raise the standard of care in epilepsy.

“We believe that further insight into the epilepsy population could contribute to the personalization of epilepsy care and ultimately the improvement of long-term patient outcomes,” Ms. Fritz said. “Epilepsy is one of the least understood and most individualized chronic conditions, despite affecting 65 million people worldwide.”

Of course, it’s difficult for a practicing neurologist to learn of this project and not think of evidence-based medicine. Sackett, et al. once said that “without clinical expertise, practice risks becoming tyrannized by evidence.” Clinical expertise will not be forgotten or cast aside, according to Ms. Fritz.

“This collaboration could represent a boon to evidence-based medicine, but we believe that both clinical expertise and evidence-based medicine will play important roles in raising the standard of care in epilepsy,” Ms. Fritz observed. The hope is this project has the potential to make both sides of the line stronger. “Our vision is to leverage cognitive computing to translate real-world data into evidence-based insights that physicians could combine with their clinical analysis of an individual patient and use to inform their treatment decisions. We do realize that physicians play an important part in generating real-world evidence, and we could not seek actionable insights from big data without the real world evidence that feeds it.”

As part of its open innovation model, UCB says they may look to collaborate with others in the epilepsy and healthcare technology communities to develop and broaden the reach of this project and improve long-term patient outcomes. ■

Rapid-Response Finger Test for AED Levels Developed

Could a point-of-care disposable microfluidic chip that can immediately detect the levels of antiepileptic drugs based on a finger-prick sample of blood improve the care of epilepsy patients? The Epilepsy Foundation seems to think so. The organization awarded first prize in the second annual Epilepsy Therapy Project “Shark Tank” competition to the developers of just such a device in May. The device designers, Utkan Demirci, PhD and Steven C. Schachter, MD, received a $100,000 grant to accelerate this product to the next phase of development and closer to benefitting patients.

“The 2013 Shark Tank award recognizes a pioneering collaboration between Dr. Demirci, an accomplished Harvard and MIT scientist and Dr. Schachter, a leading clinician and researcher in epilepsy with the Center for Integration of Medicine and Innovative Technology (CIMIT) and Harvard. With support from our Epilepsy Therapy Project initiative, we are solving an unmet challenge in epilepsy. This is a true innovation that will allow physicians, individuals with epilepsy and their caregivers to analyze the effects of epilepsy medication on a real time basis,” said Philip M. Gattone, President and CEO of the Epilepsy Foundation.

The AED blood level test can be performed anywhere using a finger prick—similar to blood glucose monitoring for diabetics—and a cellphone to produce a read out in just 15 minutes. The projected cost is less than $1 per test.