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Epilepsy Device Gets High Marks from FDA Staff

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WASHINGTON -- A neurological device under review by the FDA helped reduce the incidence of seizures while not greatly increasing side effects, the agency said Thursday.

The NeuroPace RNS System lowered the rate of seizures by 37.9% during a 3-month blinded evaluation period when turned on, compared with 17.3% when not turned on (*P*=0.012), briefing documents released ahead of an FDA advisory committee meeting showed.

"Following implant of the device and prior to initiation of stimulation, there is a reduction in seizure frequency in terms of mean or median," FDA reviewers said in the document.

The FDA's Neurological Devices Panel of the Medical Devices Advisory Committee will meet Friday to review the application of Mountain View, Calif.-based NeuroPace for approval of its RNS System for use as adjunct therapy to reduce the frequency of seizures in adults.

The RNS System is surgically implanted under the skin on the skull and records electrocorticographic (ECoG) patterns via electrodes. The device delivers short electrical pulses intended to interrupt the triggers in the brain that cause epileptic seizures.

Physicians can review ECoG recordings and assess the relationship between the device's detections and reported clinical seizures, and then adjust the RNS System's electrical pulses accordingly.

The device was studied in a randomized, double-blinded, sham-controlled trial of 191 people. Patients were required to remain on a stable anti-epileptic drug regimen; patients included in the trial had had three or more disabling seizures per month for 3 consecutive months. Roughly half the patients were randomized to have the RNS System turned on, while it remained off in the other half during a 3-month study period.

While most patients appeared to benefit from the device, there were some even in the treatment arm who worsened. "There were four subjects in the treatment group and 10 subjects in the sham group who experienced a greater than 50% increase in seizures during the blinded-evaluation period," the FDA said.

NeuroPace said 53% of patients implanted with its device experienced a 50% drop in the number of seizures 2 years after implantation.

The company also conducted a post-hoc, month-by-month analysis and found that by the end of the third month, patients with the device turned on experienced a 41.5% decrease in seizure frequency, compared with 9.4% of those who had the device off.

The FDA noted that the analysis excludes two outlying patients from the sham arm. When included in that post-hoc analysis, the efficacy difference was 40.1% versus 22.9% for the treatment and sham groups, respectively, the agency found.

The agency found that the number of adverse events -- mild and serious -- didn't differ significantly between the two trial arms. Serious adverse events (SAEs), including brain hemorrhaging and implantation-site infections, occurred in 4.2% of treatment patients and 5.4% of sham patients during the blinded evaluation period.
"Although comparable to the incidence of SAEs with other invasive intracranial procedures ... the majority of these SAEs would not be expected to occur in a comparable medically treated population with intractable epilepsy," the FDA said.
The FDA noted nine deaths in all the trials, including six from epilepsy. There were also 14 intracranial hemorrhages.

NeuroPace initially filed a marketing application with the FDA for the RNS System in July 2010, but the agency requested 12-month follow-up data on all patients in the trial. The FDA also sent a Major Deficiency Letter in June 2011 seeking clarification on statistical and clinical issues.

Although there are many approved medications for epileptic seizures, they cause significant adverse events when used in combination, the FDA said this week.

"These adverse effects can be especially problematic in vulnerable populations such as young patients still in school, those with jobs requiring cognitive skills, those operating dangerous equipment, or the elderly already on multiple drugs," the agency said.

The FDA is not required to follow the opinion of its advisory committees but usually does.