FDA advisory panel votes against approval of DMD drug

A drug company's difficulty gaining approval for a drug for Duchenne muscular dystrophy is highlighting an issue at the heart of ethics in medicine: whether to fast-track drugs that could possibly benefit those with life-threatening, devastating diseases, or wait longer for more evidence of efficacy.

On Monday, April 25, 2016, an advisory panel to the FDA voted against approval of eteplirsen, a DMD drug made by Sarepta Therapeutics, because of what they called a lack of "substantial evidence" proving the drug's efficacy.

Duchenne muscular dystrophy is a genetic disease that affects about 15,000 boys in the United States. Patients often lose their ability to walk in their teens, and die in their twenties or thirties from progressive respiratory and cardiac deterioration. The cause of these progressive, life-threatening health problems is the lack of a protein called dystrophin, which leads to degeneration of muscle fibers. Currently, there are no FDA approved treatments; the prognosis for those diagnosed with DMD is bleak.

The Wall Street Journal reports, "The FDA's hearing and decision highlighted the tension between the agency's requirement that a drug be proven to work and the need to find anything that might help the people with a lethal disease that has no cure."

The FDA's concerns

Eteplirsen is the first medication to address the underlying cause of DMD.

Sarepta Therapeutics, Inc. conducted one eteplirsen study on 12 patients. The chairman of the advisory committee, G. Caleb Alexander, an associate professor of epidemiology at Johns Hopkins University, expressed strong concerns that the study was not well controlled. The committee voted 7-3, with 3 abstentions.

Despite the small sample size, executives at Sarepta hoped that results of muscle dystrophin levels tests and 6-minute walk tests would provide compelling "surrogate endpoints" to warrant a hastened approval of the drug. And parent testimonial given at the hearing provided a powerful and sobering reminder of just how much is at stake for DMD patients.

But FDA doctors were not convinced that the 12-person study proved unequivocally that dystrophin levels in muscle fibers increased from taking eteplirsen. Further, it was unclear whether higher muscle levels of dystrophin correlated with improved performance in a walk test.

The FDA has encouraged Sarepta to design a larger, randomized, double-blind placebo-controlled trial. "Accelerated approval cannot be used to compensate for weak or insufficient data," said Eric Bastings, FDA Deputy Director of the Office of Drug Evaluation's Division of Neurology Projects

Upon hearing the panel's verdict, patients and their families were devastated.

An ethical dilemma

For those with life-threatening progressive diseases, time is the enemy, and bringing drugs down the pipeline fast is the highest priority. Yet research and development, clinical trials, and the FDA approval process can take years, or even decades. Patients with illnesses like Duchenne muscular dystrophy, and their families, don't have the

luxury of time, and are thus often willing to take big risks on medications not backed by years of data on hundreds of patients. With another drug for DMD, drisapersen (developed by BioMarin), recently rejected in January, the future remains bleak.

The FDA does have the ability to reject the advisory panel's recommendation, though that is not common; they until May 26 to give their final decision. Given the panel's outcome, hopefully Sarepta can pull together the resources to design a better study with a larger sample size to yield more conclusive data, and fast. Unless the FDA rejects the recommendation, DMD patients will have to bide their time until then.

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