Families of patients with Dravet syndrome join forces to carry out one of the largest scientific studies ever published for this rare disease

New data might help companies to design better clinical trials for orphan drugs

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The Dravet Syndrome Foundation Spain (DSF) estimates that restrictive inclusion criteria in clinical trials for this rare disease might reduce the already small patient population and thereby delay the approval of new medicines, according to a new study that looked at data from 15 European countries. Dravet syndrome is a life-threatening genetic disease affecting mostly children who suffer from recurrent uncontrolled seizures, cognitive delays and behavioral problems.

The study, published on-line by the journal *Epilepsy and Behavior,* comes at an important time, with two experimental new drugs about to start clinical trials for Dravet syndrome in Europe. “Before these trials start we wanted to know what drugs the patients were already taking and how many patients would qualify for the clinical trials”, says Luis Miguel Aras, M.D., Executive Director of the DSF Spain and leading author of the study. “But Dravet syndrome is a rare disease so physicians rarely see more than a few patients with this syndrome during their entire careers. We realized that if we were to collect data on hundreds of patients we would need to ask the patients directly”.

In an unprecedented study, Aras and his colleagues surveyed 274 families from across Europe in one of the largest studies ever published for this rare disease. “One of the most important findings in our study is that 42% of the European patients are taking stiripentol, the only drug ever approved for this syndrome”, says Ana Mingorance, Ph.D., Scientific Director of the DSF Spain and senior author of the study. “We had some idea that stiripentol was widely prescribed in some countries, but the actual magnitude was really not known until now. This finding has important implications for clinical trials because it means any new drug developed for Dravet syndrome will need to be compared to stiripentol”.

Mingorance says she was most struck by the frequent reported use of antiepileptic drugs that can make Dravet syndrome worse. “About a third of the European patients with Dravet syndrome had taken carbamazepine and other sodium channel blockers in

the past to control their seizures. These are common antiepileptic drugs but should be avoided in patients with Dravet syndrome. Neurologists should screen to see if their patients have this particular syndrome, which can be diagnosed with a genetic test, before prescribing these drugs".

The researchers also found that, while the new clinical trials require eligible patients to have a minimum of four convulsive seizures per month, only 45% of the European patients with Dravet syndrome meet that requirement. "If you combine the seizure frequency with specific age requirements, we estimate that less than one third of the patients with Dravet syndrome will actually qualify for the studies" says Aras. " This is both a problem for the patients that cannot get enrolled in the studies, and for the pharmaceutical companies wanting to recruit enough patients to start their clinical trials".

The study also comes at an important time when patient organizations are participating more actively in research, in particular in rare diseases. "We are a research organization founded by parents of children with Dravet syndrome, and we reached out to other patient groups in Europe through the Dravet Syndrome European Federation to help us with the study", says Julian Isla, Chairman of DSF Spain and the Dravet Syndrome European Federation, who is also a co-author in the study. "The European Medicine Agency had already flagged the need for this type of data in Dravet syndrome. So we brought together hundreds of families from 15 countries to make this publication possible. It represents an important milestone for our organizations and for the rare disease patient community. It shows that patients and their families have a voice and want to be active partners in the development of new and better therapies for rare diseases".

The study "The European patient with Dravet syndrome: Results from a parent-reported survey on antiepileptic drug use in the European population with Dravet syndrome" published as part of the March issue by *Epilepsy and Behavior,* can be already accessed on-line for free at http://authors.elsevier.com/a/1QVH85Qt1GTeJ6

About Dravet Syndrome

Dravet syndrome is a rare genetic form of epilepsy that starts during the first year of life in an otherwise typically developing infant and for which there is no effective treatment. Patients with Dravet syndrome also suffer from cognitive delays, behavioral problems, motor problems and other co-morbidities. It is estimated that 1 in 30,000 people has Dravet Syndrome, but because of a high rate of under-diagnosis only a few thousand are known in Europe.

About the Dravet Syndrome Foundation Spain

Founded in 2011, the Dravet Syndrome Foundation Spain is a research organization focused on finding better treatments and a cure for Dravet syndrome. DSF Spain manages a portfolio of projects ranging from genetics to preclinical and clinical research and eHealth applications. It also provides genetic diagnostic for free to suspected Dravet syndrome patients world-wide and maintains a national patient registry.
www.dravetfoundation.eu

About the Dravet Syndrome European Federation

Dravet Syndrome European Federation is a federation of European Dravet syndrome patient organizations aiming to improve the quality of life of patients and caregivers, promote research and knowledge exchange around Dravet syndrome, raise funds for medical and social research and raise disease awareness.
www.dravet.eu