Capturing Seizures in Clinical Trials of Anti-Seizure Medications (ASMs) for KCNQ2 Developmental and Epileptic Encephalopathy (KCNQ2-DEE)

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OBJECTIVE

- We sought evidence as to whether seizures in infants and young children with *KCNQ2* developmental and epileptic encephalopathy (KCNQ2-DEE) could be reliably counted by clinical observation.
- This evidence would support using seizure diaries instead of video electroencephalography (VEEG) to assess the outcome of an anti-seizure medication (ASM) trial.

BACKGROUND

- The FDA typically recommends VEEG for assessing seizure counts in infants; however, the seizure characteristics of KCNQ2-DEE may enable seizure counting by clinical observation.
- Further, for patients who have seizures less than daily, VEEG presents feasibility challenges.

METHODS

- All published reports of KCNQ2-DEE were reviewed for seizure and EEG descriptions.
- Caregivers from a patient advocacy group were surveyed[4] for information regarding recognition of seizure occurrence.

[4] Please also refer to "An Online Survey of Caregivers of Patients with KCNQ2 Developmental and Epileptic Encephalopathy (KCNQ2-DEE) "/ Poster #263

RESULTS

- Out of 137 KCNQ2-DEE patients described within 16 case series, 94% (129 patients) had clear motor seizures which correlated with EEG findings.
- Focal tonic was the most common seizure type, present in 81% (n=111) of the patients (see Table 1).
- Other seizures were generalized tonic clonic, generalized tonic, focal motor, myoclonic and epileptic spasms, all clinically apparent motor seizure phenomena.
- Apnea was frequently associated with tonic seizures. There were no reports of subclinical seizures.
- The caregiver survey (n=51) revealed that 80% were very confident in their ability to recognize and count seizure occurrence.

(First Author/Year)	Patients (n)	Motor Seizures* (Patients, n)	Total Focal Tonic (Patients, n)
Duan et al., 2018	1	1	1
Hortiguela et al., 2017	13	13	9
Kato et al., 2013	12	11	11
Ko et al., 2018	7	7	7
Lee et al., 2019	7	7	7
Milh et al., 2013	16	14	12
Millichap et al., 2016	23	19	15
Numis et al., 2014	3	3	3
Olson et al., 2017	10	10	6
Pisano et al., 2015	15	15	12
Schubert-Bast et al., 2017	1	1	1
Serino et al., 2013	1	1	1
Spagnoli et al., 2018	3	2	2
Vilan et al., 2017	9	9	9
Weckhuysen et al., 2012	8	8	8
Weckhuysen et al., 2013	9 with severe DEE	9	8
	Total N=137†	**129†/137 (94.2%)**	**111†/137 (81.0%)**

* Including focal tonic, generalized tonic, clonic, tonic-clonic, generalized tonic-clonic seizures.

†One patient (who had focal tonic seizures) was reported in both Millichap 2016 and Olsen 2017. That patient is only counted once; therefore, the totals in each column appear to be one patient less than when patients from all the reports are added together.

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- Literature Review: Seizure Types Observed in Patients with KCNQ2-DEE

CONCLUSIONS

- We conclude that the seizures of KCNQ2-DEE are characteristic, clinically evident and families are recognizing seizures confidently.
- This evidence provides support for the accuracy of families using seizures diaries to count seizures in an ASM clinical trial of KCNQ2-DEE patients.

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