Poster
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Patient Outcomes in KCNQ2 Developmental and Epileptic Encephalopathy (KCNQ2-DEE): Systematic Literature Review

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INTRODUCTION

- KCNQ2 developmental and epileptic encephalopathy (DEE) is an autosomal dominant neurodevelopmental disorder caused by variants in the *KCNQ2* gene[1,2]
- Children with KCNQ2-DEE initially present with frequent seizures in infancy; however, seizures are often well-controlled in early childhood[1,2]
- Despite seizure control or spontaneous resolution, children often experience moderate-to-severe developmental impairments in motor, social, language or cognitive domains[1,3,4]
- Studies evaluating clinical observations and patient-/caregiver-reported outcomes will highlight the impact of KCNQ2-DEE and identify patient-relevant endpoints for clinical studies

OBJECTIVE

- Conduct a systematic literature review (SLR) to identify clinically observed and caregiver-/patient-reported KCNQ2-DEE seizure and non-seizure outcomes

METHODS

- The SLR was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Eligible studies met patient, intervention, comparator, outcome and study (PICOS) criteria (**Table 1**)
- No geographical or publication time restrictions were applied
- Search strategies were designed and databases (MEDLINE, EMBASE and PubMed), select congress proceedings and study bibliographies were searched on 24 August 2023

Table 1. PICOS criteria applied to studies to assess SLR eligibility

Parameter	Inclusion criteria
Patient population	Neonates and children aged ≤18 years
Interventions and comparators	Any
Study designs	Case reports/series, observational, non-randomised and single-arm trials, surveys, database/registry-based studies
Outcomes	**Seizure:** clonic/tonic/tonic-clonic seizures, myoclonic seizures, epileptic spasms, seizures (motor, non-motor, type not specified), status epilepticus, seizure-free, seizure control **Non-seizure[a]:** neurological features, developmental or functional issues, characterisation of overall development/ impairment, other areas

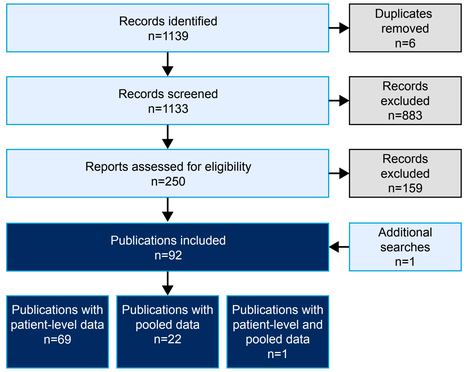
PICOS, patient, intervention, comparator, outcome and study; SLR, systematic literature review.
[a]Non-seizure outcomes were further subdivided into categories. Neurological: muscle tone, cognitive, movement disorders, sensory, autonomic, other. Developmental/functional: gross motor, communication, fine motor, eating. Other areas: behaviour, sleep, orthopaedic, endocrine, other medical, death.

RESULTS

Studies included in the SLR

- Of 250 publications assessed for eligibility, 92 met the SLR inclusion criteria and data were fully extracted (**Figure 1**)
  - Seventy publications reported patient-level data from 354 patients with KCNQ2-DEE

Figure 1. PRISMA flow diagram of the study selection process



Patient characteristics

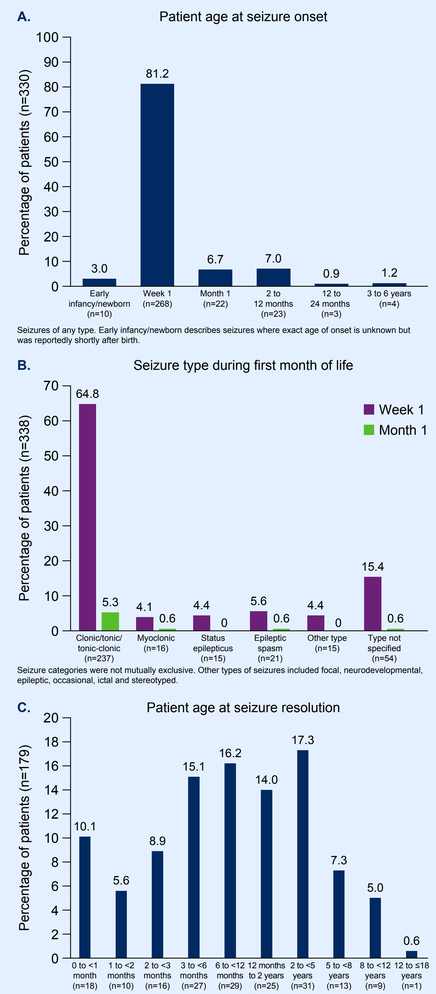
- For publications reporting patient-level data (n=70), age was documented for 146/354 (41.2%) cases
  - Most (66.4%; n=97) patients were <5 years old (**Table 2**)
- The age range of patients in publications reporting pooled data (n=23) was 28 days to 43.6 years

Table 2. Patient age range in publications reporting patient-level data

Patient age range (N=146)[a]	Patients, n (%)
0 to <12 months	35 (24.0)
12 months to <2 years	22 (15.1)
2 to <5 years	40 (27.4)
5 to <8 years	30 (20.5)
8 to <12 years	11 (7.5)
12 to ≤18 years	8 (5.5)

[a]Patient-level data only.

Figure 2. Seizure outcomes reported in patient-level publications

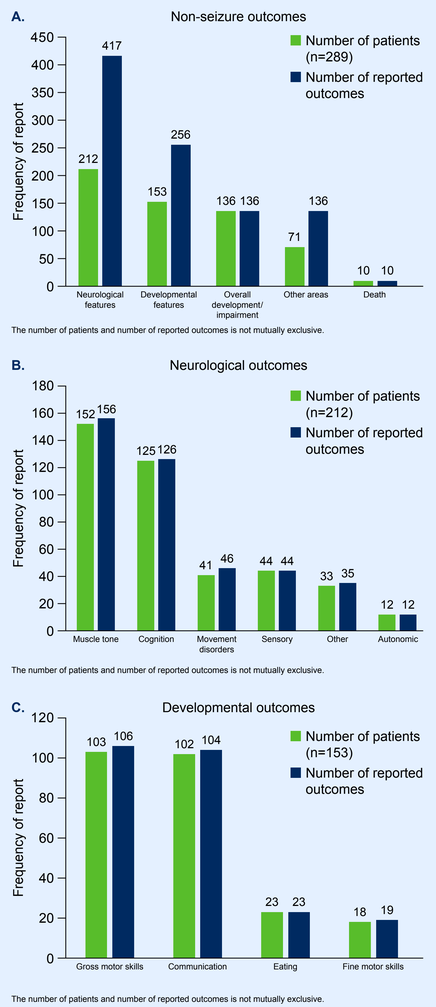


Seizures of any type. Early infancy/newborn describes seizures where exact age of onset is unknown but was reportedly shortly after birth.

Seizure categories were not mutually exclusive. Other types of seizures included focal, neurodevelopmental, epileptic, occasional, ictal and stereotyped.

Includes patients who developed seizures at any age during childhood.

Figure 3. Non-seizure outcomes reported in patient-level publications



The number of patients and number of reported outcomes is not mutually exclusive.

Seizure outcomes

- Seizures were reported for 338/354 (95.5%) patients with KCNQ2-DEE across 69 publications reporting patient-level data
  - Age of seizure onset was reported for 330/338 (97.6%) patients; seizure onset within the first week after birth was most common (**Figure 2A**)
  - Clonic/tonic/tonic-clonic seizures were the most common seizure type reported during the first month of life (**Figure 2B**)
  - Seizure resolution was reported for 190/338 (56.2%) patients; age of resolution was recorded for 179/190 (94.2%) patients. Most (87.0%) patients achieved seizure resolution by the age of 5 years (**Figure 2C**)
- Nineteen of 23 pooled data publications reported seizure outcomes; clonic/tonic/tonic-clonic seizures were the most common (11/19 studies; 57.8%). The proportion of affected patients ranged from 4.5–100.0%

Non-seizure outcomes

- Overall, 932 non-seizure outcomes were reported for 289 patients with KCNQ2-DEE in 70 publications reporting patient-level data
  - Neurological and developmental/functional issues were most common (**Figure 3A**) and were typically reported in patients aged 2 to 5 years
  - The most common neurological impairments were related to muscle tone and cognition (**Figure 3B**)
  - Gross motor skills and communication difficulties were the most common developmental impairments (**Figure 3C**)
- Non-seizure outcomes were reported in 23 pooled data publications; neurological (n=11/23; 47.8%) and developmental impairments (n=10/23; 43.5%) were the most common

CONCLUSIONS

- In patients with KCNQ2-DEE, both seizure and non-seizure outcomes are clinically relevant and impact child development
- While seizures typically present in infancy and resolve in early life, non-seizure outcomes manifest at birth and gain more prominence as children age, resulting in the majority of patients experiencing neurological and/or developmental impairments
- This study highlights the frequency of reported seizure and non-seizure outcomes that may inform the development of patient-relevant endpoints for clinical studies investigating KCNQ2-DEE therapies

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