

James W. Wheless,¹ Mary Kay Koenig,² Sarah M.L. Wilson,² Debopam Samanta,³ Darcy A. Krueger,⁴ Shelly Meitzler,⁵ Carly Kaye,⁵ Linda D. Leary,⁶ Sherry R. Danese,⁷ Timothy B. Saurer,⁸ Kelly C. Simontacchi,⁸ Karthik Rajasekaran⁸

¹Le Bonheur Comprehensive Epilepsy Program & Neuroscience Institute, Le Bonheur Children's Hospital, University of Tennessee Health Science Center, Memphis, TN, USA; ²Department of Pediatrics, Division of Child and Adolescent Neurology, McGovern Medical School, The University of Texas Health Science Center at Houston, Houston, TX, USA; ³Child Neurology Section, Department of Pediatrics, University of Arkansas for Medical Sciences, Little Rock, AR, USA; ⁴Division of Neurology, Department of Pediatrics, Cincinnati Children's Hospital Medical Center, University of Cincinnati College of Medicine, Cincinnati, OH, USA; ⁵TSC Alliance, Silver Spring, MD, USA; ⁶University of Texas Health Science Center, San Antonio, TX, USA; ⁷Outcomes Insights, Ventura, CA, USA; ⁸Jazz Pharmaceuticals, Inc., Palo Alto, CA, USA

Introduction

- Tuberous sclerosis complex (TSC) is a neurocutaneous disorder characterized by the formation of hamartomas in multiple organs, including the brain, skin, heart, eyes, kidneys, lungs, and liver^{1,2}
- Epilepsy is the most common neurologic manifestation of TSC, with multiple seizure types that often start during infancy and may have lifelong persistence³
- Treatment-resistant seizures are a significant and frequent cause of morbidity in people with TSC^{4,5}
- Epidiolex®, a plant-derived highly purified pharmaceutical formulation of cannabidiol (CBD), is approved in the United States (US) for the treatment of seizures associated with Lennox-Gastaut syndrome, Dravet syndrome, or TSC in patients aged ≥1 year⁶
- BECOME-TSC (BEhavior, COgnition, and More with Epidiolex® in TSC) is an ongoing cross-sectional survey to quantify the real-world impact of CBD on seizure and nonseizure outcomes in people with TSC
 - This poster presents the seizure outcomes (nonseizure outcomes will be presented in Poster 1.433)

Objective

- To present caregiver-reported seizure-related outcomes following initiation of CBD treatment in people with TSC

Methods

- Using electronic health records, healthcare professionals at TSC centers in the US identified people with TSC who were treated with CBD (Epidiolex®, 100 mg/mL oral solution) for ≥6 months
- Caregivers of these individuals completed an online survey, consisting of multiple-choice and rank-order questions, based on the TSC-Associated Neuropsychiatric Disorders questionnaire,⁷ other validated measures, and previous caregiver reports
- Respondents compared the past month to the period before CBD initiation and rated their impressions of change using a symmetrical 3-, 5-, or 7-point Likert scale (from worsening to improvement) depending on the domain
- “Don’t recall” or “Not applicable” responses were excluded
- Continuous variables were summarized as means, medians, and ranges, and categorical variables as frequency distributions and percentages
- CBD-associated adverse events, which can include transaminase elevations, somnolence, decreased appetite, diarrhea, pyrexia, vomiting, fatigue, rash, sleep disorders, and infections, were not assessed
- The survey was conducted with caregivers of people taking Epidiolex®, and the results do not apply to other CBD-containing products

Results

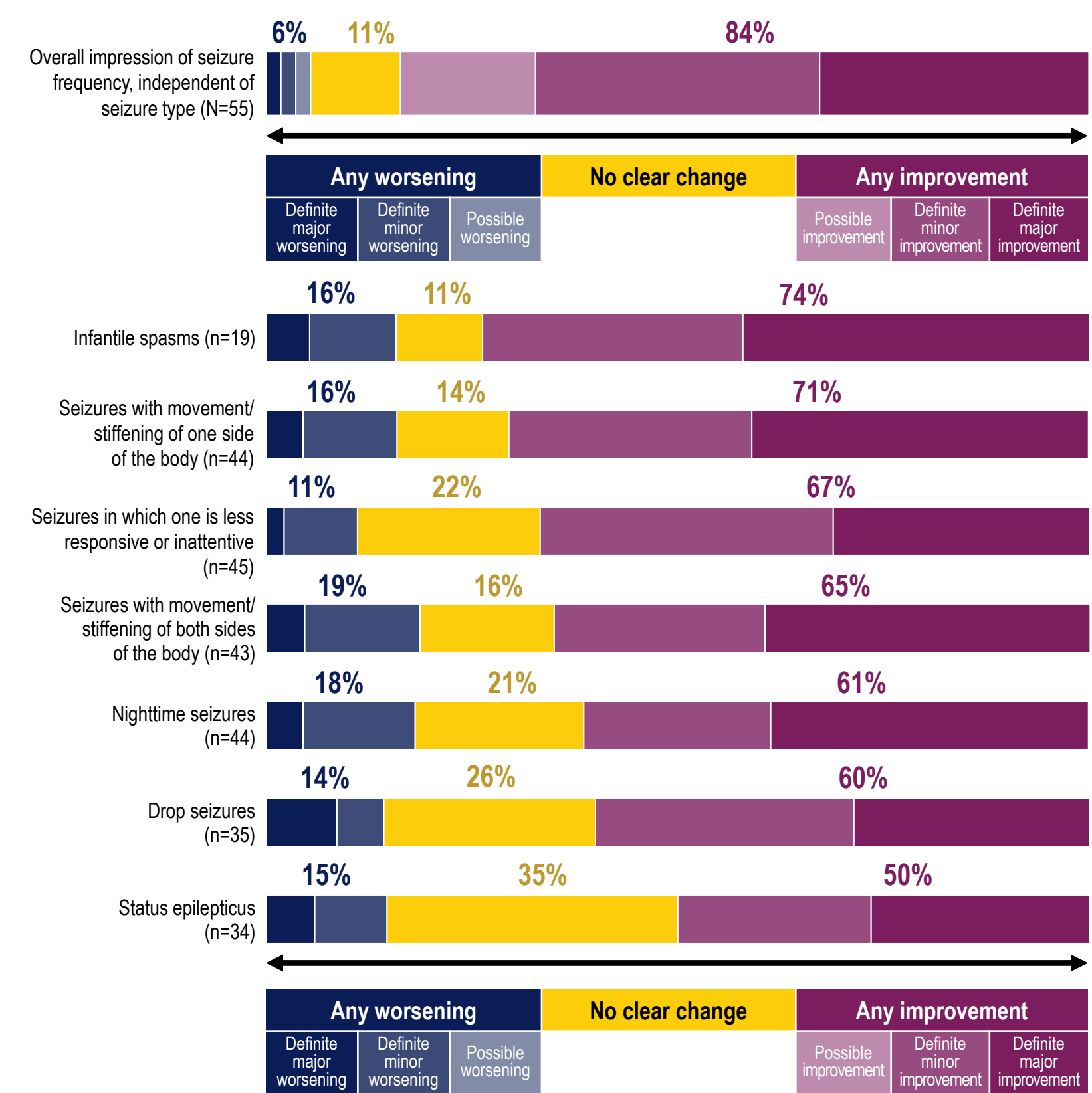
Table. Characteristics of patients

	Patients (N=55)
Age, years, mean (SD)	16.5 (11.3)
17 or younger, n (%)	32 (58)
Age at seizure onset, months, mean (SD)	10 (18.8)
Number of ASMs before CBD initiation, median (Q1, Q3) ^a	2 (1, 4)
Most common (≥25%) concomitant ASMs, n (%)	
Everolimus	22 (40)
Clobazam	17 (31)
Clonazepam	14 (26)
Seizure types (in >10% of patients) at CBD initiation, n (%)	
Focal onset with impaired awareness	36 (66)
Focal to bilateral tonic-clonic	17 (31)
Tonic	12 (22)
Generalized onset tonic-clonic	7 (13)
Atonic	8 (15)
Absence	5 (9)
Clonic	2 (4)
CBD dose at the time of survey, mg/kg/day, median (Q1, Q3)	12 (8, 18)

^an=54. ASM, antiseizure medication, commonly referred to as antiepileptic drugs. CBD, cannabidiol; Q1, first quartile; Q3, third quartile.

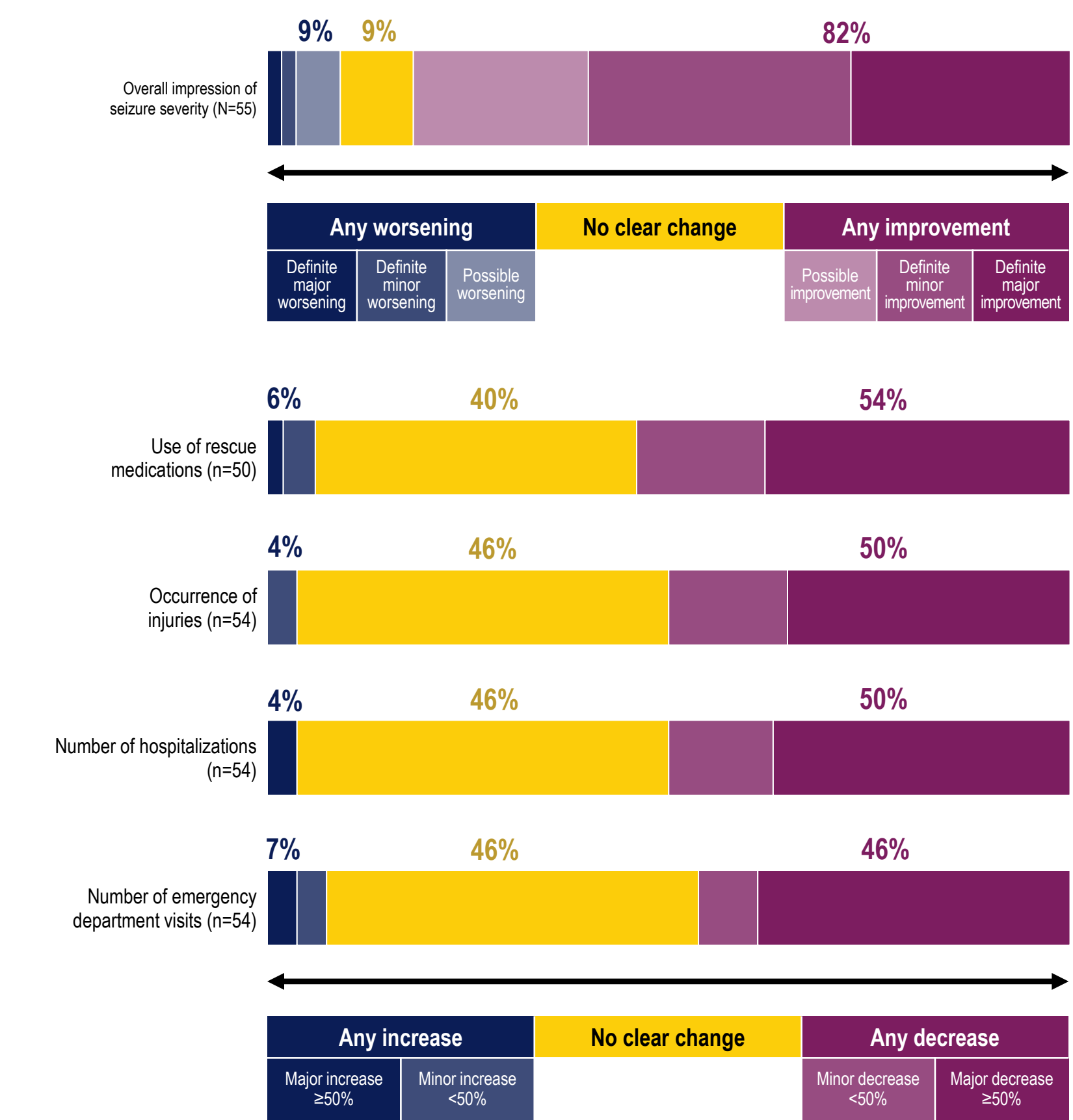
- At the time of analysis, 55 caregivers had completed the survey (Table)
- Among respondents, 62% reported that the patient had a history of infantile spasms
- At the time of CBD initiation, focal onset with impaired awareness and focal to bilateral tonic-clonic were reported as the most frequent (44% and 20%) and most severe seizure types (36% and 26%)

Figure 1. Seizure frequency



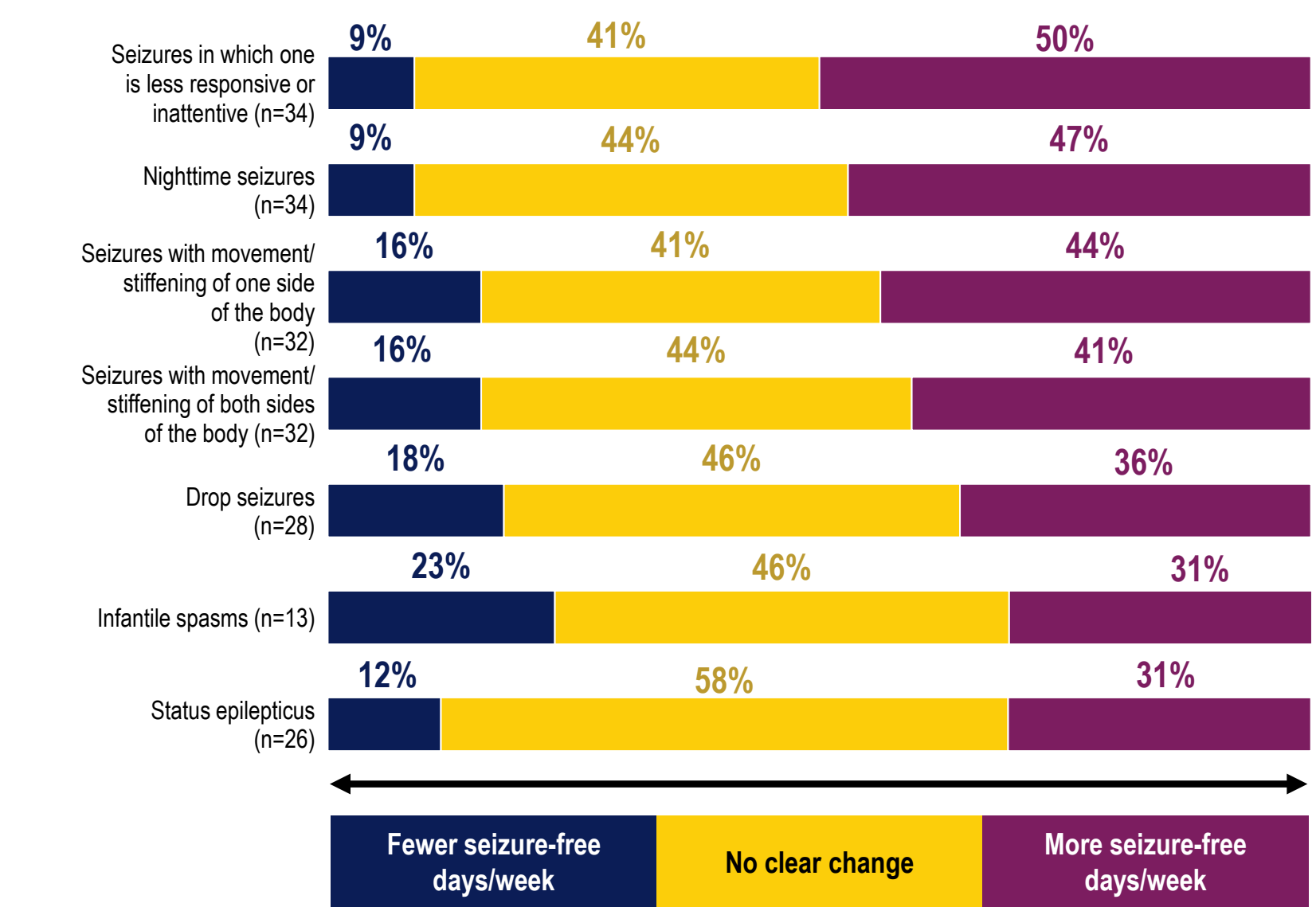
- Improvements in overall seizure frequency were reported by 84% of respondents; 6% reported worsening in seizure frequency (Figure 1)
- ≥50% of respondents reported improvements in the frequency of seizures that involve infantile spasms, movement or stiffening of one or both sides of the body, seizures where one is less responsive/inattentive, nighttime seizures, drop seizures, and status epilepticus

Figure 2. Seizure severity



- Improvements in overall seizure severity were reported by 82% of respondents (Figure 2)
- ≥50% of respondents reported a decrease in rescue medication use (54%), reduced occurrence of seizure-related injuries (50%), and reduced number of hospitalizations (50%)

Figure 3. Seizure-free days



- Seizure freedom in the past month was reported by 39% (16 of 41 caregivers)

Plans for continuing CBD treatment

- Compared with the time before initiation of CBD treatment, 76% of all caregivers reported any improvement in the overall condition of patients
- A total of 89% (49 of 55) of caregivers reported planning to continue CBD treatment
- Of caregivers who planned to continue CBD treatment, reduced seizure frequency and severity/duration were given as the most important reasons for continuing by 86% and 71% of respondents; improved cognition (53%) and language/communication (51%) were other reasons cited by ≥50% of respondents for continuing CBD treatment

Conclusions

- In this analysis of BECOME-TSC, an ongoing cross-sectional survey of caregivers of people with TSC who are taking CBD treatment:
 - Most caregivers reported improvements in seizure frequency (84%) and severity (82%)
 - Complete seizure freedom in the past month was reported by 39% (16 of 41 caregivers) of respondents
 - Improvements were most commonly reported in the frequency of seizures that involve infantile spasms, movement or stiffening of one or both sides of the body, seizures where one is less responsive/inattentive, nighttime seizures, drop seizures, and status epilepticus
 - The majority of respondents planned to continue CBD treatment primarily because of reduced seizure severity/duration but also because of improvements in nonseizure outcomes, including cognition and language/communication
 - Limitations of the study include use of retrospective caregiver accounts and selection bias because of the study design. Adverse effects were not assessed and the effect of concomitant antiseizure medications was not considered in this analysis

References: 1. Northrup H, et al. *Pediatr Neurol*. 2021;123:50–66. 2. Rout P, et al. Tuberous Sclerosis. In: StatPearls [Internet]. 2024. Accessed October 28, 2024. <https://www.ncbi.nlm.nih.gov/books/NBK538492/>. 3. Curatolo P, et al. *Eur J Paediatr Neurol*. 2018;22(5):738–748. 4. Amin S, et al. *Dev Med Child Neurol*. 2017;59(6):612–617. 5. Jeong A, et al. *J Child Neurol*. 2017;32(14):1092–1098.

6. Epidiolex® (cannabidiol) oral solution. Prescribing Information. Jazz Pharmaceuticals, Inc.; 2024. Accessed July 10, 2024. [https://www.epidiolex.com/sites/default/files/pdfs/1120/EPX-03645-1120_EPIDIOLEX_\(cannabidiol\)_USPI.pdf](https://www.epidiolex.com/sites/default/files/pdfs/1120/EPX-03645-1120_EPIDIOLEX_(cannabidiol)_USPI.pdf). 7. de Vries P.J, et al. *Pediatr Neurol*. 2015;52(1):25–35.

Acknowledgments: Writing and editorial assistance were provided by Ritupathak, PhD, and Dena McWain of Ashfield MedComms, an Inizio company, and Bhargavi Ramesh of Syneos Health and was funded by Jazz Pharmaceuticals, Inc., in accordance with Good Publication Practice (GPP) 2022 guidelines.

Support: The study was sponsored by Jazz Pharmaceuticals, Inc.

Disclosures: This poster presents an update of the data previously presented at the Child Neurology Society 2024 Annual Meeting; November 11–14, 2024; San Diego, CA, USA. All authors met the ICMJE authorship criteria and had full access to relevant data. Neither honoraria nor payments were made for authorship. JWW, MKK, SMLW, DS, DAK, SM, CK, LDL, and SRD have consulted for, conducted studies funded by, or received honoraria from Jazz Pharmaceuticals, Inc., and hold stock and/or stock options in Jazz Pharmaceuticals, Inc.

