

# EFFICACY AND SAFETY OF BEXICASERIN (LP352) IN ADOLESCENT AND ADULT PARTICIPANTS WITH DEVELOPMENTAL AND EPILEPTIC ENCEPHALOPATHIES: RESULTS OF THE PHASE 1B/2A PACIFIC STUDY

Randall Kaye,<sup>1</sup> Chad Orevillo,<sup>1</sup>  
Dennis J. Dlugos,<sup>2</sup> Ingrid E. Scheffer<sup>3</sup>

<sup>1</sup>Longboard Pharmaceuticals, La Jolla, CA, USA;

<sup>2</sup>Children's Hospital of Philadelphia (CHOP), Philadelphia, PA, USA;

<sup>3</sup>The University of Melbourne, Austin Health, Melbourne, VIC, Australia

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## BACKGROUND

- DEEs are the most severe group of epilepsies and are characterized by drug-resistant seizures, epileptiform abnormalities, and developmental slowing or regression<sup>1-3</sup>
- DEE trials have focused on patients with specific epilepsy syndromes, including Dravet Syndrome, tuberous sclerosis complex, and LGS; the latter has etiologic heterogeneity
- Bexicaserin is a potent and selective 5-HT<sub>2C</sub> receptor superagonist specifically designed for use in patients with DEE
  - Preclinical and clinical data support the use of 5-HT<sub>2C</sub> receptor superagonists in modulating the frequency and threshold of seizure onset<sup>4-6</sup>
  - Bexicaserin was generally well tolerated in double-blind, placebo-controlled studies<sup>7,8</sup>
- Here, we present the key findings from the phase 1b/2a study of participants with DEEs treated with bexicaserin

## OBJECTIVE

- To assess the safety, tolerability, pharmacokinetics, and efficacy of bexicaserin for treatment of seizures in participants with DEEs

## METHODS

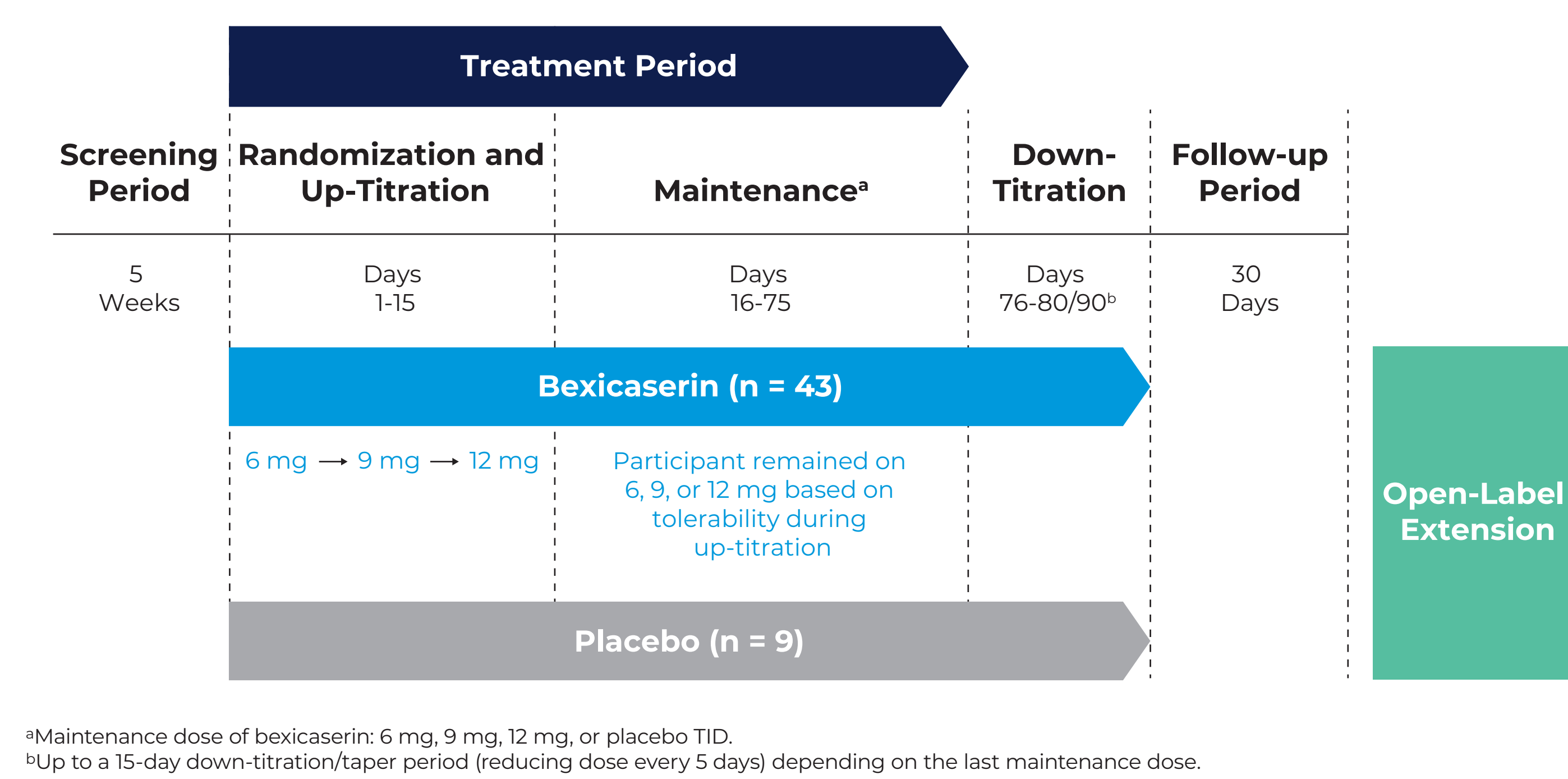
### Study Design

- This was a randomized, double-blind, placebo-controlled, parallel-group, dose-escalation study in participants  $\geq 12$  to  $\leq 65$  years of age with DEEs (PACIFIC, NCT05364021)
- Participants were randomly assigned (4:1) to receive bexicaserin or placebo
- Following a 15-day flexible titration period (maximum dose of 12 mg TID, based on tolerability), participants went through a 60-day maintenance period and a 5- to 15-day tapering period (**Figure 1**)
- Key inclusion criteria included the following:
  - DEEs with average of  $\geq 4$  motor seizures per 4-week period during the 12 weeks before screening and  $\geq 4$  motor seizures in the 4-week period of screening
  - Additional criteria for participants with Dravet Syndrome, LGS, and DEE Other are found in **Table 1**
- Key exclusion criteria included the use of fenfluramine and lorcaserin

### Outcome Measures

- The primary safety endpoint was safety measured through the incidence and severity of TEAEs and other safety parameters
  - No echocardiogram monitoring was required
- The primary efficacy endpoint was the percentage change from baseline in observed countable motor seizure frequency during the treatment period

**Figure 1. PACIFIC Study Design**



**Table 1. Diagnostic Eligibility Criteria by Participant Subgroup**

	Dravet Syndrome	LGS	DEE Other
Onset	Between 3–19 months of age	Before 8 years of age	Unprovoked seizures before 5 years of age
Seizure Type	Generalized tonic-clonic, unilateral clonic, or bilateral clonic seizures	Tonic or tonic/atonic seizures and more than 1 type of generalized seizure (tonic-clonic, tonic-atonic, atonic, tonic, myoclonic, or drop)	Combined focal and generalized seizure types, or multiple generalized seizure types
Developmental History	Initially normal, then delayed	Delayed	Delayed
Electroencephalography	—	Consistent with LGS diagnosis <sup>a</sup>	Slow or disorganized
Additional Criteria	One of the following: <ul style="list-style-type: none"><li>Emergence of another seizure type after the first</li><li>Induced by warm temperatures, fevers, or visual stimuli</li><li>Genetic test consistent with Dravet Syndrome</li></ul>	More than 1 type of generalized seizure for $\geq 6$ months before screening	No history of idiopathic generalized seizures

<sup>a</sup>Abnormal inter-ictal electroencephalography background activity with inter-ictal slow spike-and-wave pattern  $\geq 2.5$  Hz or inter-ictal generalized paroxysmal fast activity.

## RESULTS

### Participants

- 52 participants (43 bexicaserin, 9 placebo) were randomly assigned to treatment (29 LGS, 4 Dravet Syndrome, and 19 DEE Other) across 34 sites (**Tables 2 and 3**)

**Table 2. Participant Disposition**

Parameter n (%)	Bexicaserin (n = 43)	Placebo (n = 9)
Safety set	43 (100)	9 (100)
Full analysis set	35 (81.4)	9 (100)
Participants completed	32 (74.4)	9 (100)

**Table 3. Demographics and Baseline Characteristics**

	Bexicaserin (n = 43)	Placebo (n = 9)	Overall (N = 52)
Age, mean (SD), years	23.8 (9.62)	26.7 (7.73)	24.3 (9.31)
Min, max	12, 55	19, 41	12, 55
Sex, n (%)			
Male	21 (48.8)	7 (77.8)	28 (53.8)
Female	22 (51.2)	2 (22.2)	24 (46.2)
BMI, median (min, max), kg/m <sup>2</sup>	22.4 (17, 35)	28.1 (19, 34)	23.0 (17, 35)
Baseline countable motor seizures	40.0	24.1	38.2
Concomitant medications, n (%)			
Clobazam	21 (48.8)	2 (22.2)	23 (44.2)
Valproate	17 (39.5)	6 (66.7)	23 (44.2)
Cannabidiol	14 (32.6)	3 (33.3)	17 (32.7)
Lamotrigine	13 (30.2)	4 (44.4)	17 (32.7)
Levetiracetam	16 (37.2)	1 (11.1)	17 (32.7)

- 35 participants received bexicaserin in the full analysis set; 30 (85.7%) reached the highest dose (12 mg TID) and 27 (77.1%) reached and tolerated the maximum dosing through the maintenance period (**Table 4**)

**Table 4. Highest Tolerated Dose Achieved and Maintained for the Maintenance Period**

n (%)	Bexicaserin	Placebo	Overall
All participants	35	9	44
6 mg	4 (11.4)	0	4 (9.1)
9 mg	4 (11.4)	1 (11.1)	5 (11.4)
12 mg	27 (77.1)	8 (88.9)	35 (79.5)

### Safety

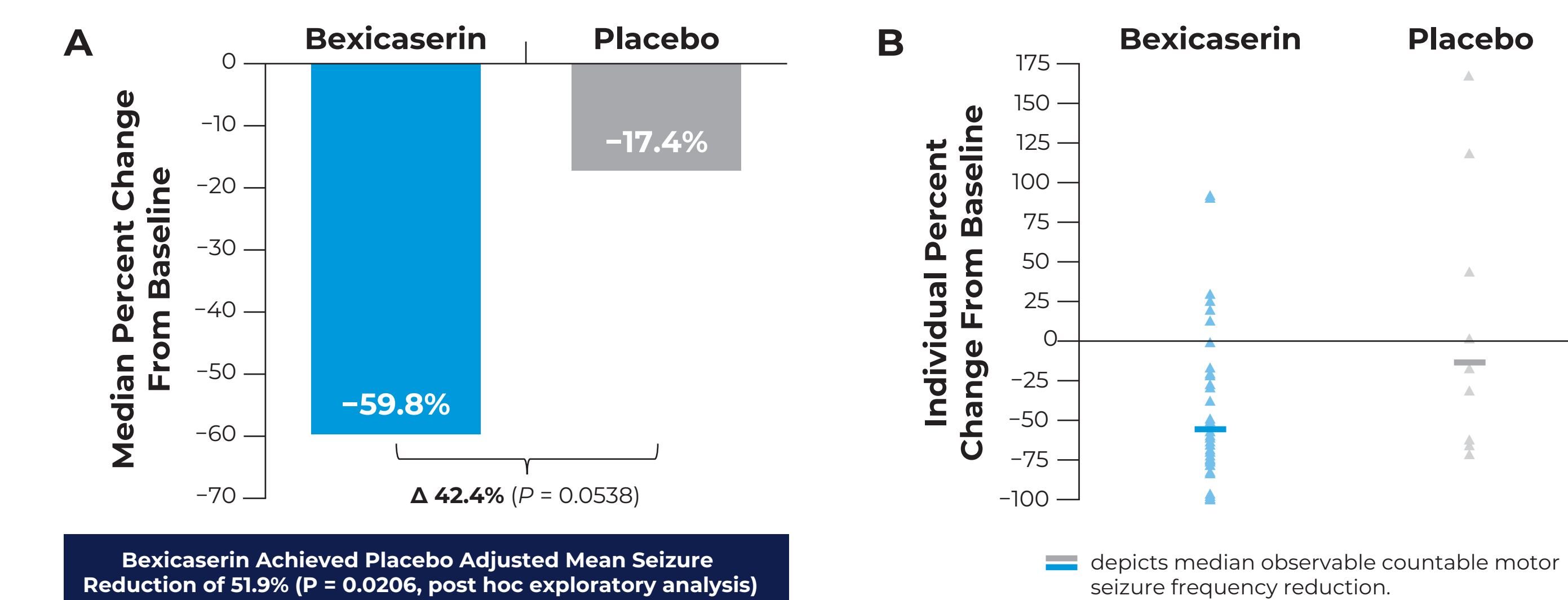
- The most common TEAEs were somnolence, decreased appetite, constipation, diarrhea, lethargy, tremor, urinary tract infection, fatigue, pyrexia, agitation, and hypotension (**Table 5**)
- Three participants (7.0%) in the bexicaserin group reported an SAE (ankle fracture  $\times$  2, constipation, and increased seizures)
- During the titration period, 16.3% of bexicaserin-treated participants discontinued due to an AE, while during the maintenance period, 4.7% of bexicaserin-treated participants discontinued due to an AE

**Table 5. Summary of Safety Results**

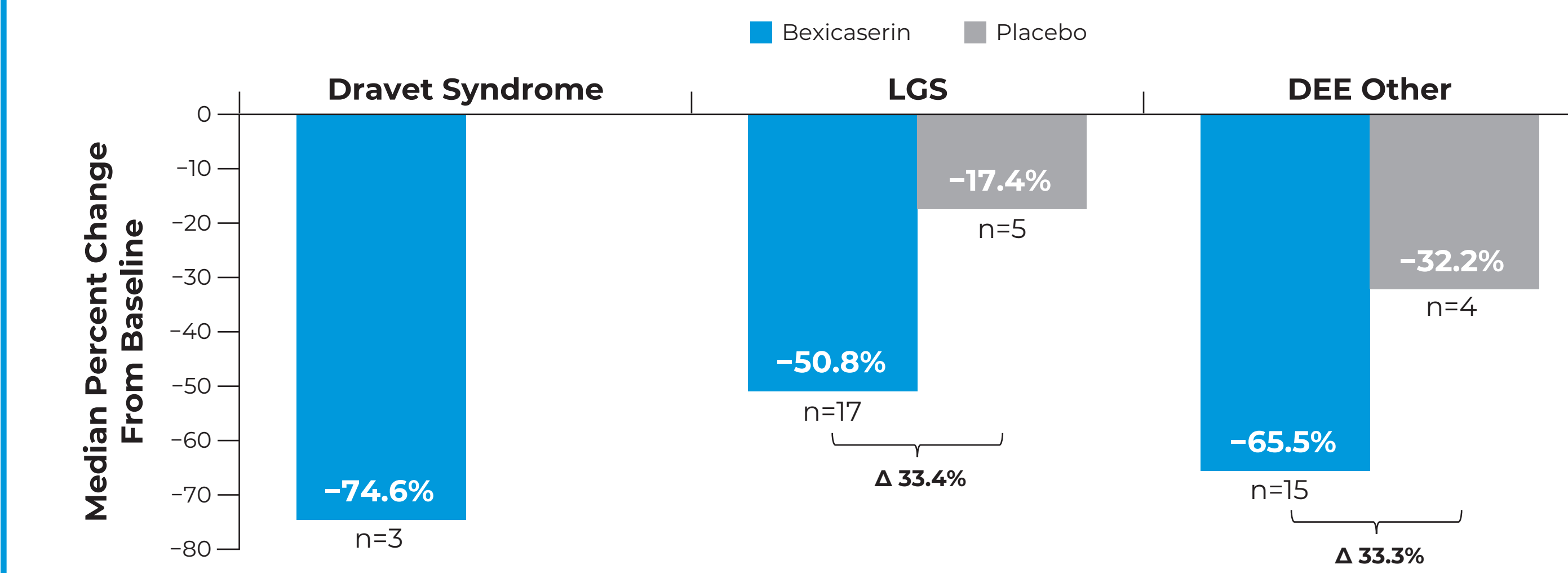
n (%)	Bexicaserin (n = 43)	Placebo (n = 9)	Overall (N = 52)
Participants with $\geq 1$ TEAE	35 (81.4)	8 (88.9)	43 (82.7)
TEAEs by SOC <sup>a</sup>			
Nervous system disorders			
Somnolence	12 (27.9)	1 (11.1)	13 (25.0)
Lethargy	4 (9.3)	0	4 (7.7)
Tremor	3 (7.0)	0	3 (5.8)
Gastrointestinal disorders			
Constipation	6 (14.0)	0	6 (11.5)
Diarrhea	5 (11.6)	0	5 (9.6)
Infections and infestations			
Urinary tract infection	3 (7.0)	0	3 (5.8)
General disorders and administration site conditions			
Fatigue	3 (7.0)	0	3 (5.8)
Pyrexia	3 (7.0)	0	3 (5.8)
Metabolism and nutrition disorders			
Decreased appetite	9 (20.9)	0	9 (17.3)
Psychiatric disorders			
Agitation	3 (7.0)	0	3 (5.8)
Vascular disorders			
Hypotension	3 (7.0)	0	3 (5.8)

<sup>a</sup>Over 5% of bexicaserin participants and greater than placebo.

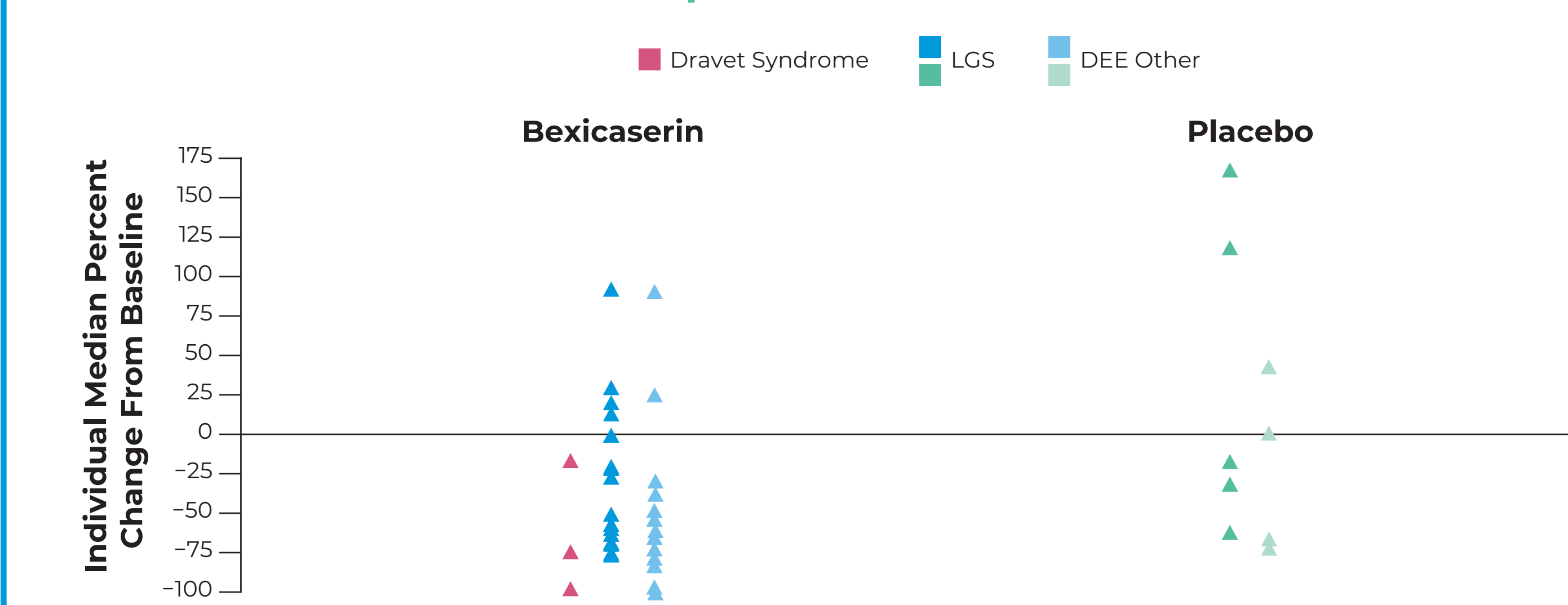
**Figure 2. Participants Receiving Bexicaserin Had a Greater Reduction in Observable Countable Motor Seizure Frequency During the Treatment Period Versus Placebo**



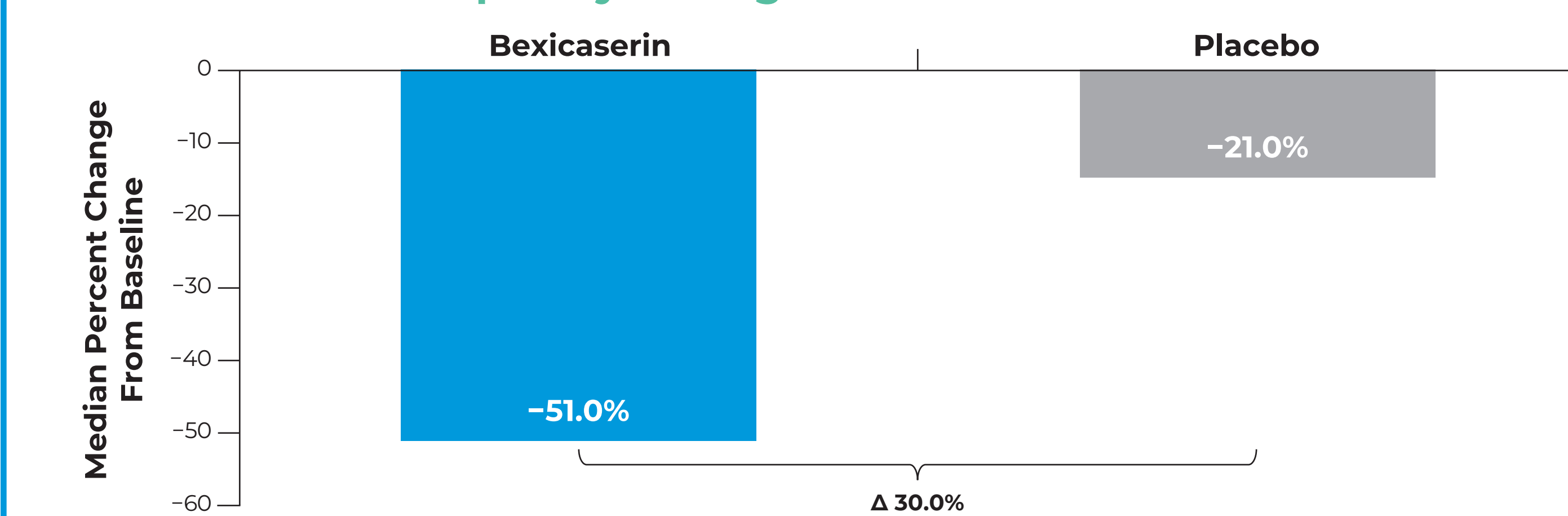
**Figure 3. Countable Motor Seizures Were Reduced in All 3 Groups**



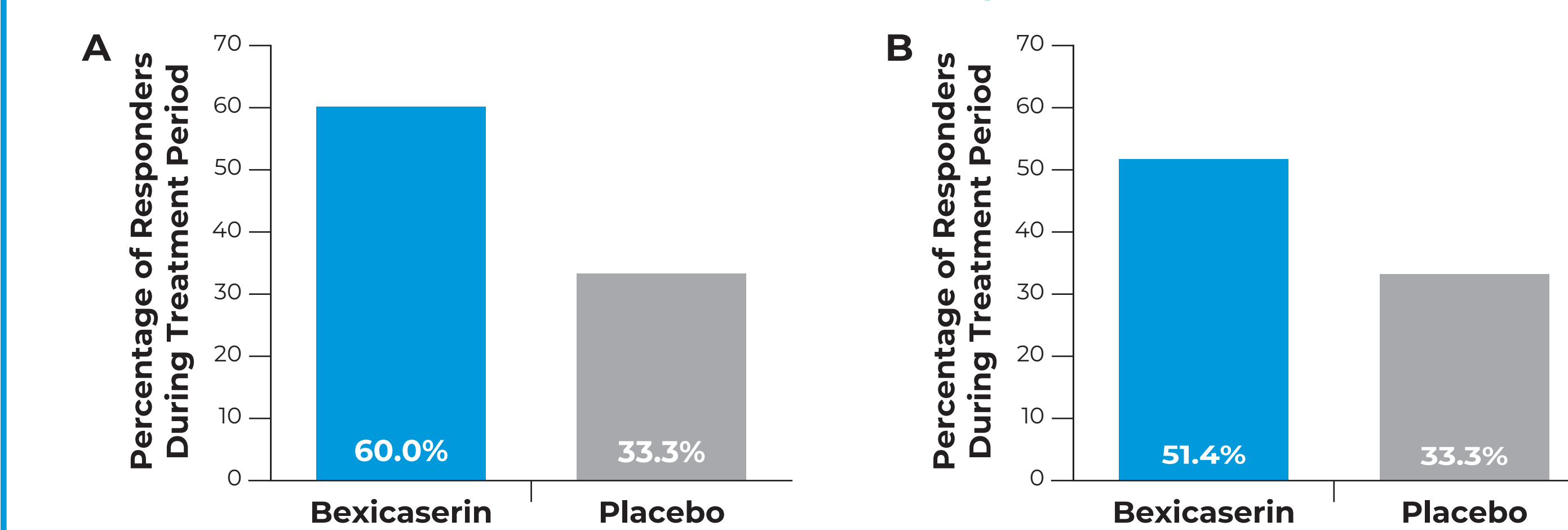
**Figure 4. The Overall Pattern of Response in the LGS Group Was Highly Similar to the DEE Other Group**



**Figure 5. Participants in the Bexicaserin Group Had a Greater Reduction in Total Seizure Frequency During Treatment Period Versus Placebo**



**Figure 6. Higher Proportion of Participants in the Bexicaserin Group Had a  $\geq 50\%$  Reduction in Frequency of (A) Observed Countable Motor Seizures and (B) Total Seizures Versus Placebo During Treatment Period**



## CONCLUSIONS

- In this study, bexicaserin exhibited a favorable safety and tolerability profile in a broad DEE population
- Treatment with bexicaserin reduced seizures in all participant subgroups, including LGS and DEE Other
  - Efficacy was demonstrated in participants with a polytherapy background, including multiple antiseizure medications, including cannabidiol

**Abbreviations** 5-HT, 5-hydroxytryptamine; AE, adverse event; BMI, body mass index; DEE, Developmental and Epileptic Encephalopathy; LGS, Lennox-Gastaut Syndrome; SAE, serious adverse event; SD, standard deviation; SOC, system organ class; TEAE, treatment-emergent adverse event; TID, 3 times daily.

### References

- Scheffer IE et al. *Epilepsia*. 2017;58:512-521.
- Scheffer IE, Liao J, Eur J Paediatr Neurol. 2020;24:11-14.
- Gallop K et al. *Epilepsy Behav*. 2021;124:108324.
- Gharehdaghi MH et al. *Exp Brain Res*. 2014;232:347-367.
- Bagdy G et al. *J Neurochem*. 2007;100:857-873.
- Sourbron J, Lagae L. *Epilepsia Open*. 2022;7:231-246.
- Parasuramurthy DA et al. Single ascending dose pharmacokinetics (PK), pharmacodynamics (PD), and tolerability of LP352 in healthy participants. Presented at the American Academy of Neurology 2022 Annual Meeting, April 2-7, 2022; Seattle, WA.
- Parasuramurthy DA et al. A randomized, double-blind, placebo-controlled, multiple ascending dose pharmacokinetics (PK), pharmacodynamics (PD), and tolerability study of LP352 in healthy participants. Presented at the American Academy of Neurology 2022 Annual Meeting, April 2-7, 2022; Seattle, WA.