

Efficacy and Safety of Cannabidiol in Adult Patients With Lennox-Gastaut Syndrome: A Post hoc Analysis of Phase 3 and Open-Label Extension Data

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Objective

- To evaluate the effectiveness and safety of cannabidiol (CBD; Epidyolex®, 100 mg/mL oral solution) in adult patients (≥18 years) from the Lennox-Gastaut syndrome (LGS) CBD randomised controlled trials (RCTs), including those who switched to or continued to receive CBD for up to Week 156 as part of the open-label extension (OLE)



Conclusions

- Descriptive results from this *post hoc* analysis support the effectiveness and tolerability of CBD as an ASM for the treatment of adults with refractory seizures associated with LGS
 - CBD is associated with a reduction in drop and total seizures in adults both at the end of the RCTs and 3-year OLE
 - The sustained seizure reduction and patient retention observed in adults were similar to those observed in the overall population
 - The observed safety profile in adults was consistent with the overall safety profile reported in the RCTs and OLE²⁻⁴

References: 1. Specchio N, et al. *Epilepsia*. 2022;63(6):1398–1442. 2. Devinsky O, et al. *N Engl J Med*. 2018;378(20):1888–1897. 3. Thiele EA, et al. *Lancet*. 2018;391(10125):1085–1096. 4. European Medicines Agency. Epidyolex® 100 mg/ml oral solution: summary of product characteristics. 2020. Available from: https://www.ema.europa.eu/en/documents/product-information/epidyolex-epar-product-information_en.pdf (Accessed 19 August 2020). 5. Electronic Medicines Compendium (eMC). Epidyolex® 100 mg/ml oral solution: summary of product characteristics. 2026. Available from: <https://www.medicines.org.uk/emc/product/10781/smpc/print> (Accessed 19 August 2026). 6. US Food and Drug Administration. Epidyolex® Prescribing Information. 2026. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/210365s024s029s030bl.pdf (Accessed 19 August 2026). 7. Patel AD, et al. *Epilepsia*. 2021;62(9):2228–2239. **Support and Acknowledgements:** This study was sponsored by Jazz Pharmaceuticals, Inc. The authors would like to thank all of the study investigators, study staff, patients, and caregivers for their participation in this research. Writing and editorial assistance were provided to the authors by David Griffiths, PhD, on behalf of Synoes Health, UK, and funded by Jazz Pharmaceuticals, Inc., in accordance with Good Publication Practice (GPP) 2022 guidelines. **Disclosures:** All authors met the ICMJE authorship criteria and had full access to relevant data and information. Neither honoraria nor payments were made for authorship. SL has consulted for, conducted studies funded by, or received honoraria for services provided to Jazz Pharmaceuticals, Inc., has received speaker's or consultancy fees from Angelini Pharma, Eisai, GW Pharmaceuticals, Medscape, Hikma Pharmaceuticals, Newbridge Pharmaceuticals, and UCB Pharma, and has served on advisory boards of Angelini Pharma, Arvelle Therapeutics, BIAL, Eisai, GW Pharmaceuticals, Hikma Pharmaceuticals, Rapport Therapeutics, and UCB Pharma outside the submitted work. KV and MH are employees of Jazz Pharmaceuticals, UK Ltd., and hold stock and/or stock options in the company. TG is an employee of Jazz Pharmaceuticals, Inc., Gentium Srl, Villa Guardia, Italy, and holds stock and/or stock options in the company. Epidyolex® is approved in the EU for the adjunctive treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome, in conjunction with clobazam, in patients ≥2 years of age; it is additionally approved in the EU for the adjunctive treatment of seizures associated with tuberous sclerosis complex in patients ≥2 years of age. **Clinical trial IDs:** NCT02224560 (GWPCARE3), NCT02224690 (GWPCARE4), NCT02224573 (GWPCARE5)

POSTER

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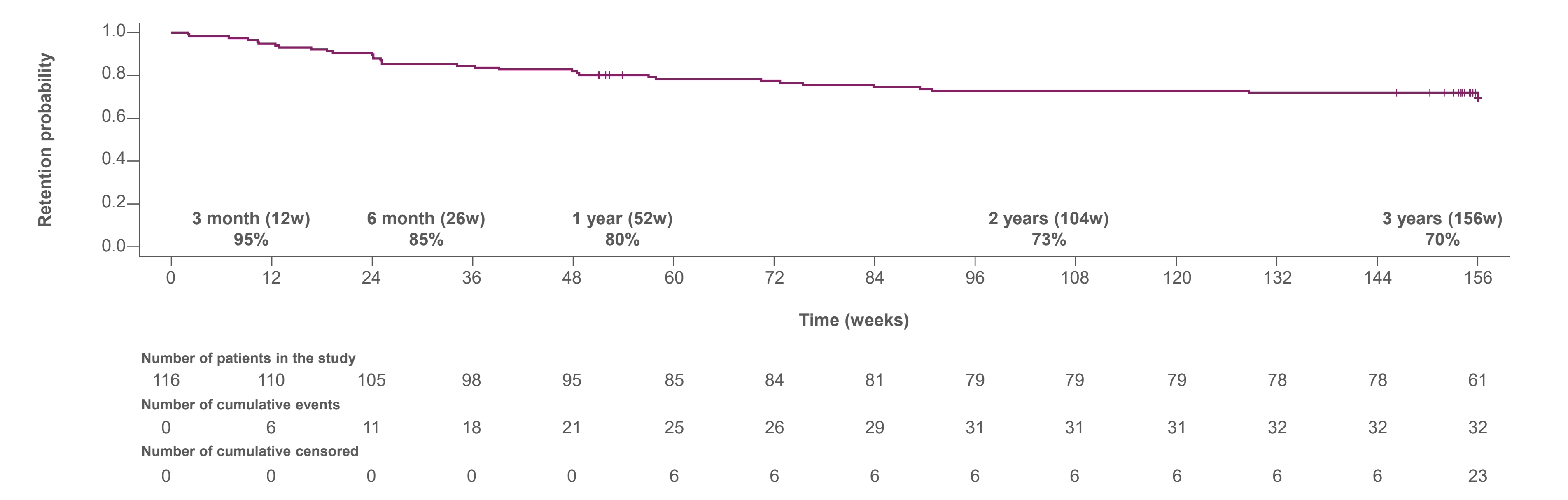
INTERVIEW

Presented at the 16th European Epilepsy Congress; 5–9 September 2026; Athens, Greece

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Results

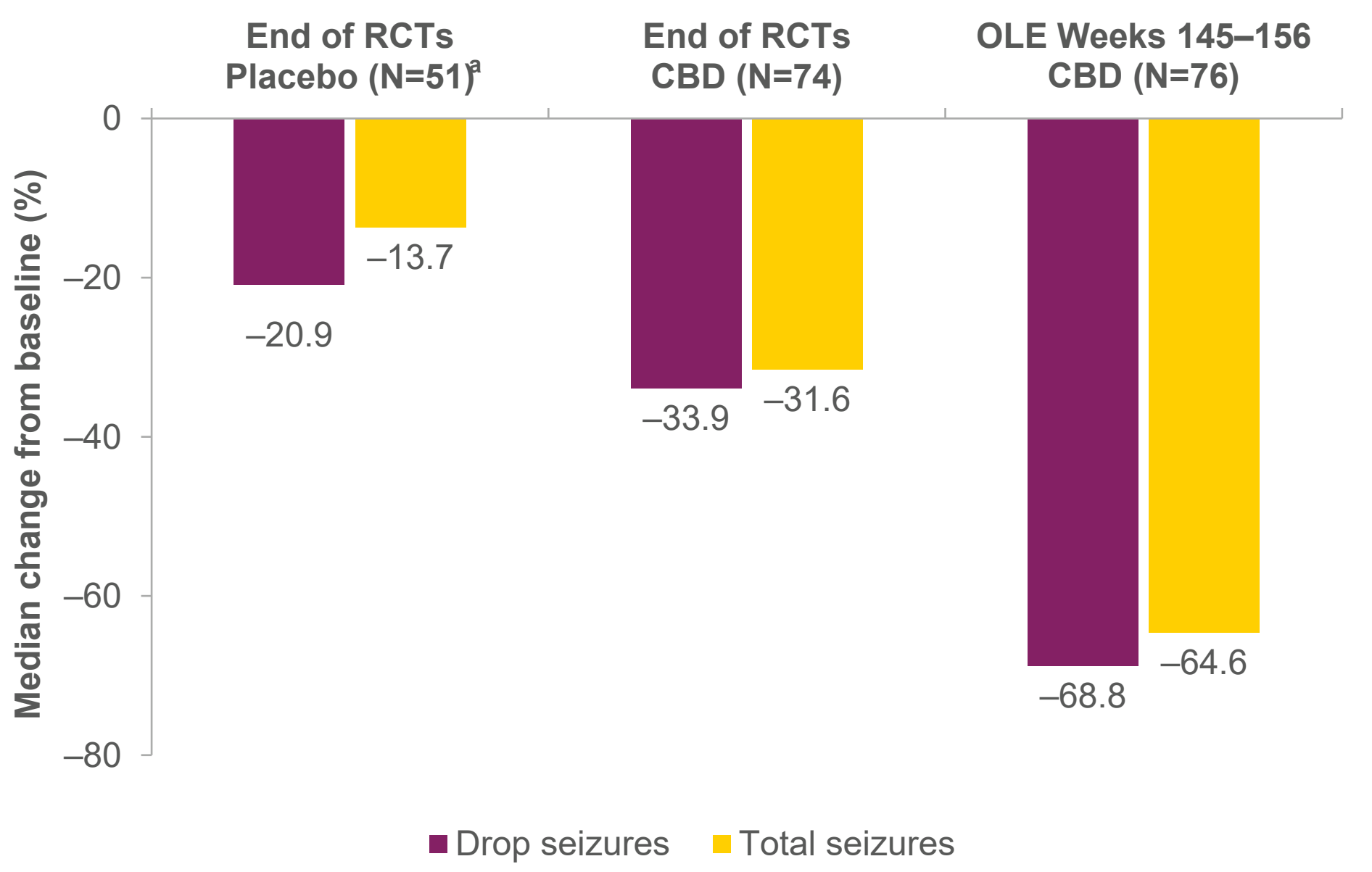
Figure 2. Kaplan-Meier plot of CBD retention probability in adult patients during the OLE



CBD, cannabidiol; OLE, open-label extension; w, weeks.

- One- and 3-year OLE retention rates were 80% (95% confidence interval [CI]: 72, 86) and 70% (60, 77), respectively (Figure 2)

Figure 3. Median changes from baseline in average 28-day seizure frequency in adults at the end of the RCTs (Week 14) and OLE



^aPlacebo data are presented for transparency only; this exploratory *post hoc* analysis was not designed or powered for formal statistical comparisons between CBD and placebo. OLE includes adults who entered the OLE after receiving CBD or placebo during the RCTs; all received CBD during the OLE. N values indicate patients with evaluable seizure data at each time point. CBD, cannabidiol; OLE, open-label extension; RCT, randomised controlled trial.

- Median percentage change (Q1, Q3) from baseline in 28-day seizure frequency with CBD increased from 33.9% (–59.6, 8.6) to 68.8% (–84.8, –40.7) for drop seizures, and from 31.6% (–54.5, –1.4) to 64.6% (–80.6, –37.0) for total seizures between the end of the RCTs and OLE Week 156 (Figure 3)
 - Corresponding reductions with placebo at the end of the RCTs were 20.9% (–38.0, 1.1) and 13.7% (–38.0, –1.3), respectively
- Effectiveness appears to be consistent with that reported previously in the overall population

Table 1. Summary of treatment-emergent adverse events observed in >10% of patients^a

	OLE CBD (N=116)
Any TEAE, n (%)	112 (96.6)
Diarrhoea	59 (50.9)
Convulsion	43 (37.1)
Pyrexia	33 (28.4)
Somnolence	32 (27.6)
Decreased appetite	30 (25.9)
Upper respiratory tract infection	29 (25.0)
Vomiting	28 (24.1)
Urinary tract infection	24 (20.7)
Decreased weight	23 (19.8)
Nasopharyngitis	16 (13.8)
Sinusitis	16 (13.8)
Cough	16 (13.8)
Sedation	15 (12.9)
Fatigue	14 (12.1)
Pneumonia	14 (12.1)
Influenza	13 (11.2)
Status epilepticus	13 (11.2)
Ear infection	12 (10.3)

^aSafety data were analysed using the OLE and Safety Analysis Set. CBD, cannabidiol; OLE, open-label extension; TEAE, treatment-emergent adverse event.

- The most frequent TEAEs reported were diarrhoea (50.9%), convulsion (37.1%), pyrexia (28.4%), and somnolence (27.6%) (Table 1)
- Safety profile appears to be consistent with that reported previously in the overall safety analysis population

Introduction

- Lennox-Gastaut syndrome (LGS) is a severe developmental and epileptic encephalopathy, characterised by multiple types of drug-resistant seizures, severe cognitive and behavioural impairments, and the presence of slow spike-and-wave complexes and generalised paroxysmal fast activity on electroencephalogram¹
- Onset is most common in children 3–5 years of age; however, LGS continues through to adulthood, with seizures remaining drug resistant¹
- Two randomised, phase 3, double-blind, placebo-controlled trials (GWPCARE3 [NCT02224560] and GWPCARE4 [NCT02224690]) evaluated the efficacy and safety of plant-derived, highly purified cannabidiol (CBD; Epidyolex® [EU]/Epidiolex® [US], 100 mg/mL oral solution) in patients with LGS.²⁻⁶ An open-label extension (OLE; GWPCARE5, NCT02224573) was also conducted in patients who continued on from GWPCARE3 and 4, to assess long-term effectiveness and safety, up to 156 weeks⁷
 - These trials were conducted in mixed-age populations, including paediatric and adult patients^{2-3,7}
- This *post hoc* analysis aimed to evaluate CBD effectiveness and safety specifically in adults with LGS, by analysing a sub-population of adults from the GWPCARE3 and 4, and the subsequent OLE

Methods

- Adults (≥18 years at randomisation) in the randomised controlled trials (RCTs) were analysed using the intent-to-treat (ITT) Analysis Set, which included adults randomised to 10 or 20 mg/kg/day CBD (pooled) or placebo. RCT effectiveness outcomes presented here are for adults who received CBD during the RCTs
- Adults who entered the OLE, including those who had received CBD or placebo during the RCTs, were analysed as OLE CBD; all received CBD during the OLE. OLE effectiveness analyses included adults with seizure data for each analysis period, while OLE safety analyses used the OLE Safety Analysis Set, comprising adults randomised in the RCTs who continued into the OLE (Figure 1)
- Baseline characteristics and demographics were reported; effectiveness was analysed compared with baseline in the RCT and OLE study end (RCT Week 14, OLE Week 156) using descriptive statistics
 - Effectiveness outcomes of this *post hoc* analysis included CBD retention rates after 1 and 3 years of the OLE, reductions in drop and total seizure frequency from baseline, and response rates (≥50% reduction) in drop and total seizures
- Safety data included treatment-emergent adverse events (TEAEs), evaluated throughout the RCT and OLE, and reported at study end (OLE Week 156)
- Although the RCTs were designed to compare CBD with placebo, this *post hoc* analysis of the adult population from the RCT was not powered to confirm a difference between CBD and placebo; thus, subgroup results included in this analysis are descriptive only
- This study used data on Epidyolex®/Epidiolex®, and the results of this *post hoc* analysis do not apply to other CBD-containing products

Figure 1. Study design

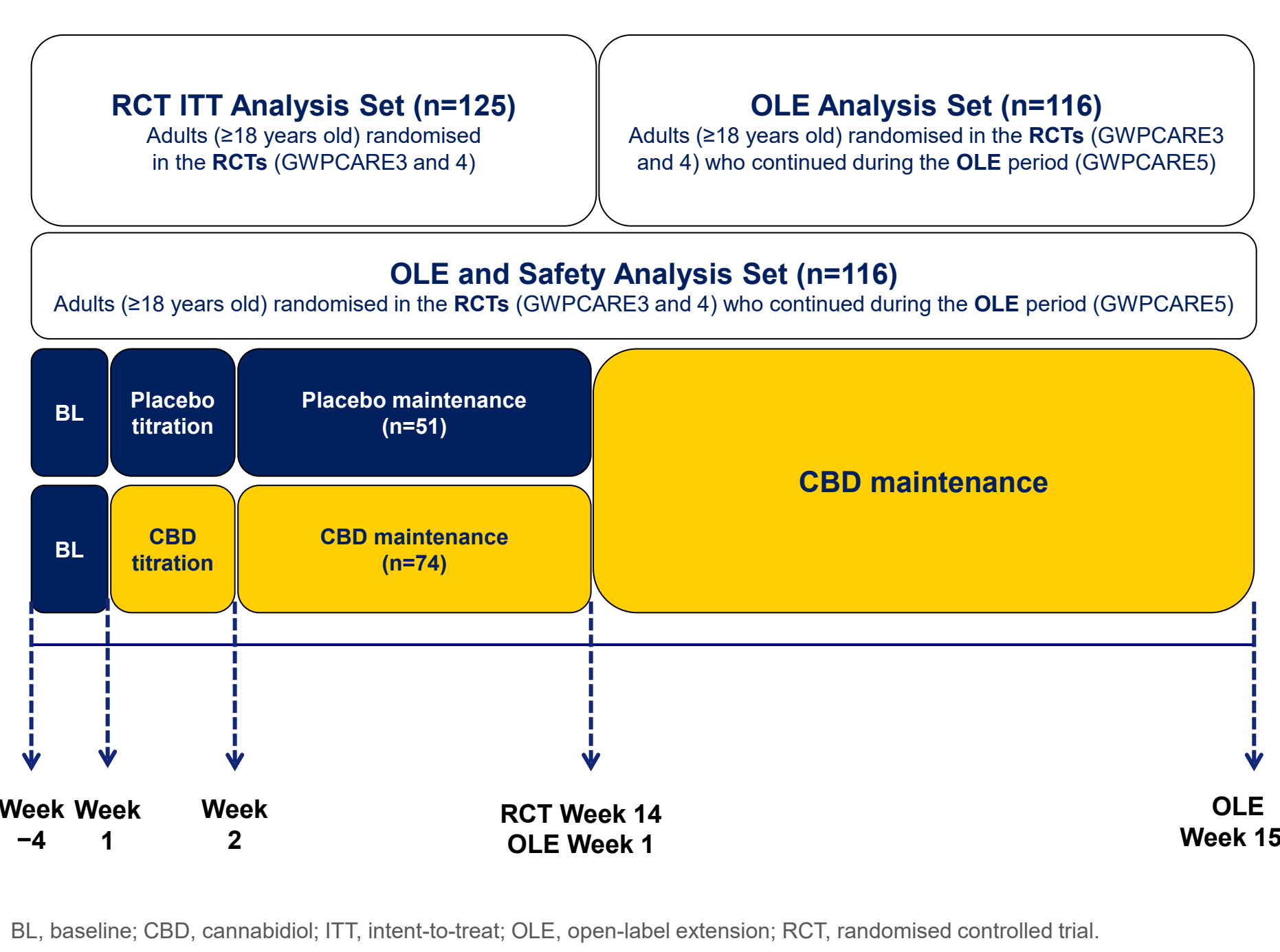
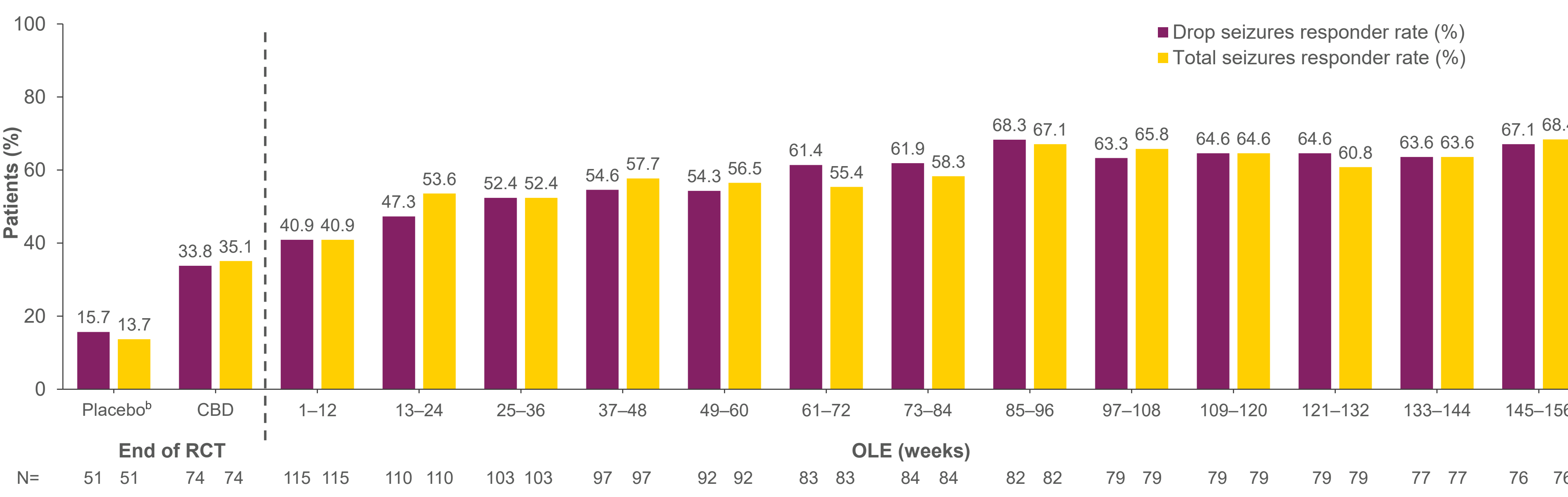


Figure 4. Response rates (≥50% reduction) for drop and total seizures at the end of the RCTs and OLE^a



^aRCT data were analysed using the RCT ITT Analysis Set, and OLE data were analysed using the OLE Analysis Set. ^bPlacebo data are presented for transparency only; this exploratory *post hoc* analysis was not designed or powered for formal statistical comparisons between CBD and placebo. N values indicate patients with evaluable seizure data at each time point. ITT, intent-to-treat; OLE, open-label extension; RCT, randomised controlled trial.

- At the end of the RCTs (Week 14), 33.8% and 35.1% of patients in the CBD group achieved responses (≥50% reduction from baseline) in drop and total seizures, respectively; corresponding response rates with placebo were 15.7% and 13.7%, respectively (Figure 4)
 - At 156 weeks in the OLE, these response rates were 67.1% and 68.4%, respectively

Strengths and Limitations

- The strengths of this study include adult-specific data across two RCTs with long-term OLE follow-up (up to Week 156) and high retention rates
- Whilst dosage optimisation with sustained retention during longer-term follow-up may explain the greater reductions and increased responder rates observed in the OLE Week 156, these may also be a reflection of survivor bias with the reduction in patient numbers across the OLE
- Results may be limited by selection bias and residual confounders, as estimates were not adjusted for baseline characteristics or time-dependent factors

Table 2. Patient demographics and characteristics at baseline

	RCT CBD (N=74) at baseline	RCT placebo (N=51) at baseline	OLE CBD (N=116) at baseline
Age (years), median (min–max)	25.1 (18–48)	23.6 (18–45)	25.2 (18–48)
Sex (male), n (%)	38 (51.4)	23 (45.1)	56 (48.3)
Race, n (%)			
Asian	1 (1.4)	0	2 (1.7)
Black/African American	3 (4.1)	0	2 (1.7)
White	67 (90.5)	51 (100.0)	109 (94.0)
Other	3 (4.1)	0	3 (2.6)
Region, n (%)			
USA	58 (78.4)	40 (78.4)	90 (77.6)
RoW	16 (21.6)	11 (21.6)	26 (22.4)
BL drop seizures per 28 days, median (Q1–Q3)	65.2 (26.1–113.7)	52.0 (23.0–83.0)	58.8 (24.0–97.5)
Patients experiencing other seizures at BL, n (%)			
Tonic	59 (79.7)	39 (76.5)	89 (76.7)
Clonic	3 (4.1)	5 (9.8)	6 (5.2)
Tonic-clonic	35 (47.3)	32 (62.7)	62 (53.4)
Atonic	36 (48.6)	28 (54.9)	60 (51.7)
Myoclonic	24 (32.4)	22 (43.1)	42 (36.2)

	RCT CBD (N=74) at baseline	RCT placebo (N=51) at baseline	OLE CBD (N=116) at baseline
Patients who received prior ASMs, n (%)	74 (100)	51 (100)	116 (100)
Number of prior ASMs, median (Q1–Q3)	7.5 (5.0–10.0)	8.0 (5.0–12.0)	8.0 (4.5–11.0)
Patients currently receiving ASMs, n (%)	74 (100)	51 (100)	116 (100)
Number of current ASMs, median (Q1–Q3)	3.0 (2.0–4.0)	3.0 (2.0–4.0)	3.0 (2.0–4.0)
ASMs being received, n (%)			
Clobazam	37 (50.0)	14 (27.5)	54 (46.6)
Valproate	33 (44.6)	25 (49.0)	53 (45.7)
Lamotrigine	36 (48.6)	20 (39.2)	53 (45.7)
Levetiracetam	20 (27.0)	15 (29.4)	35 (30.2)
Rufinamide	15 (20.3)	16 (31.4)	31 (26.7)

ASM, antiseizure medication; BL, baseline; CBD, cannabidiol; OLE, open-label extension; Q1–Q3, interquartile range; RCT, randomised controlled trial; RoW, rest of the world.

- The RCT CBD, RCT placebo, and OLE CBD groups included 74, 51, and 116 adults, respectively (51.4%, 45.1%, and 48.3% male; Table 2)
 - The median (min–max) age was 25.1 (18–48), 23.6 (18–45), and 25.2 (18–48) years, respectively
- Patients were predominantly White, and the majority were enrolled at sites in the US
- The median (Q1–Q3) drop seizure frequency was 65.2 (26.1–113.7), 52.0 (23.0–83.0), and 58.8 (24.0–97.5) per 28 days, respectively
- Tonic seizures were the most frequent seizure type at baseline, followed by tonic-clonic, atonic, and myoclonic seizures
- Patients received a median of 7.5–8.0 prior ASMs and three concomitant ASMs (most commonly clobazam, valproate, and lamotrigine)

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What is Lennox-Gastaut syndrome (LGS)?

- LGS is a serious brain disorder that causes seizures and problems with how a child learns and develops^{1,2}
- Although LGS most commonly starts in childhood, it continues into adulthood³
- Medicines for LGS are available, but many children and adults who are being treated with them experience frequent seizures^{1,4}



What is cannabidiol (CBD)?

- A plant-derived, highly purified pharmaceutical formulation of CBD (Epidyolex® [EU]/Epidiolex® [US])⁵ is approved for the treatment of seizures associated with certain rare forms of epilepsy, including LGS^{5,6}
- Two randomised, controlled clinical trials (RCTs), called GWPCARE3 and GWPCARE4, have shown that CBD helps reduce seizures in adults and children with LGS^{2,4}
- The people included in these two studies could continue to receive or switch to treatment with CBD for up to 156 weeks in an open-label extension study (OLE) called GWPCARE5⁷

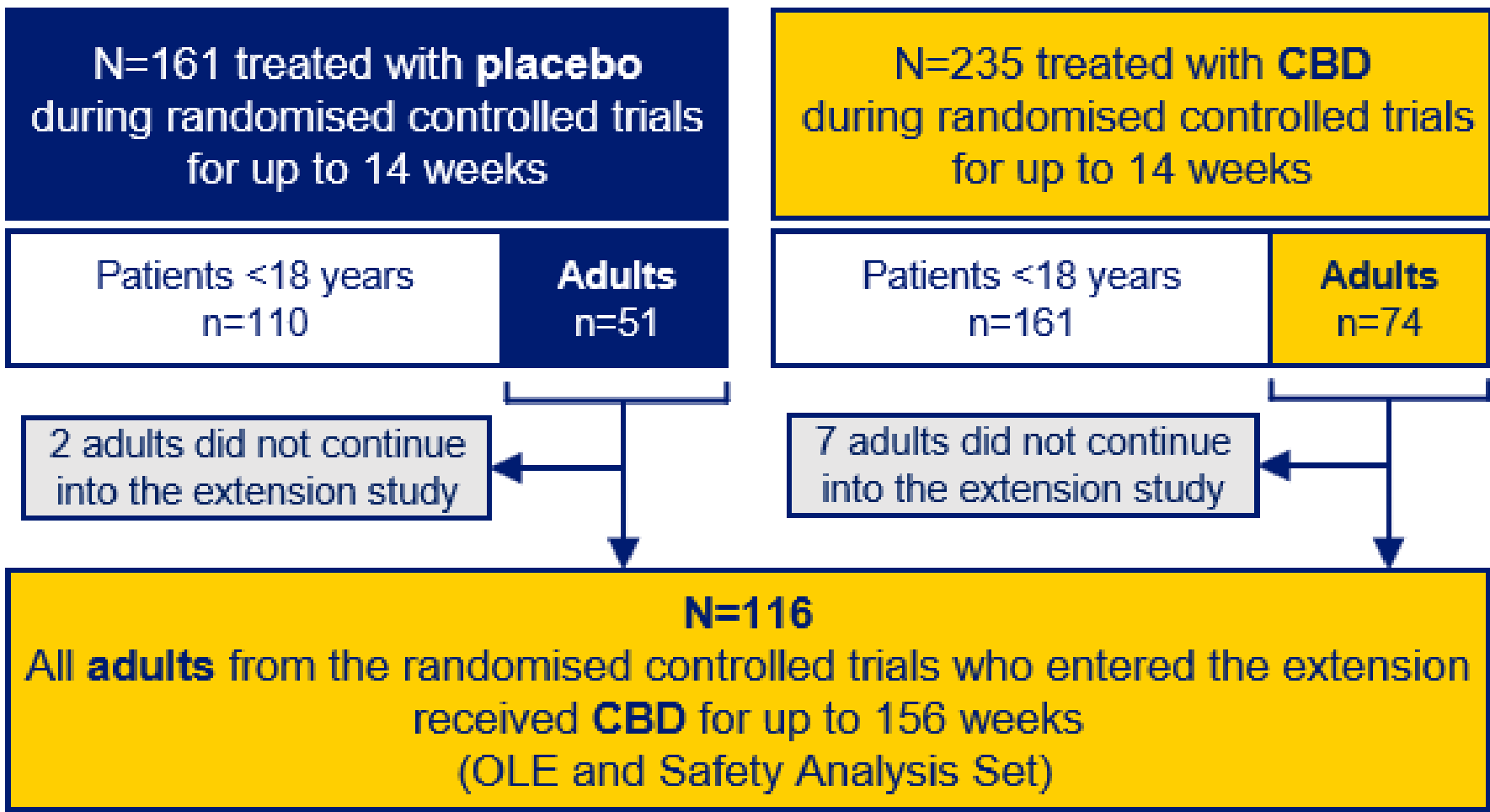


Why was this analysis done?

- Although adult patients were included in the two RCTs and the subsequent OLE, neither analysed seizure reduction specifically in adult participants alone
- This analysis therefore used only the adult data to assess whether the response in the adult participants alone was broadly consistent with the overall population



How was the analysis designed?



^aDrop seizure: Includes attacks or spells (atonic, tonic, or tonic-clonic) involving the entire body, trunk, or head that led or could have led to a fall, injury, slumping in a chair, or hitting the patient's head on a surface.^{2,4}

^bTotal seizures: Any countable seizure. LGS is associated with several different types of seizure, including tonic, clonic, tonic-clonic, atonic, and myoclonic.^{2,4}

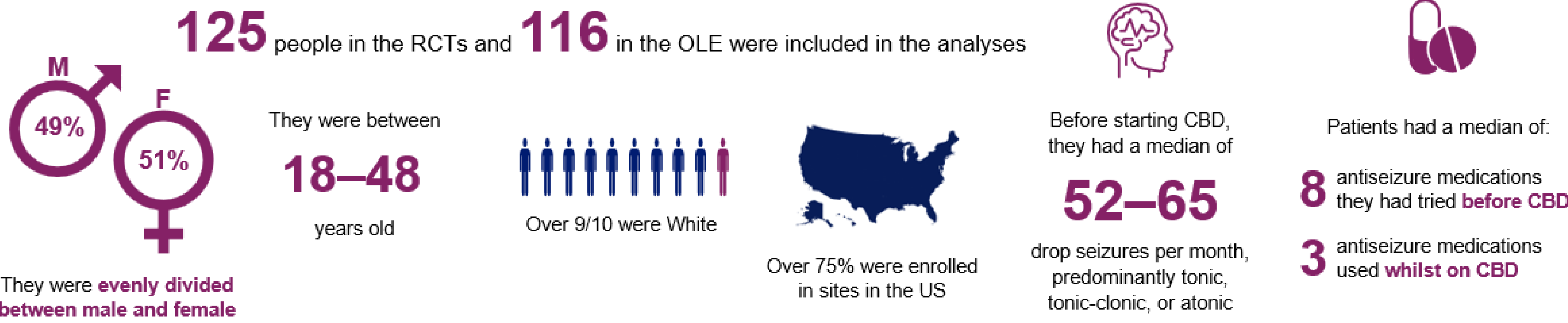


What did it evaluate?

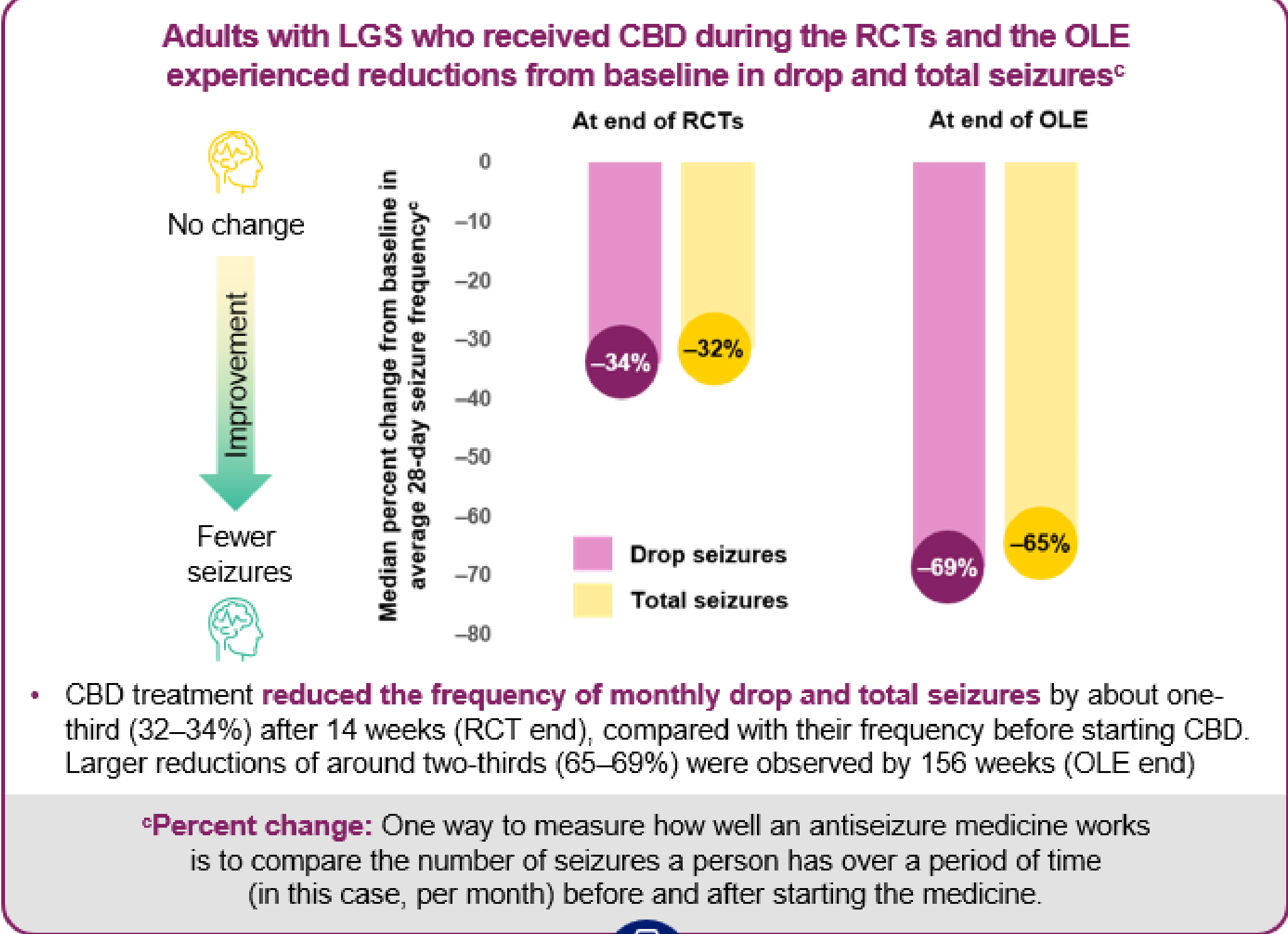
- Drop^a and total^b seizures**
 - How many adults experienced a reduction in these seizure types after finishing the RCT period or the OLE period, compared with before CBD treatment?
 - How many adults experienced at least 50% fewer seizures compared with baseline at the end of the RCT or at 12-week intervals throughout the OLE?
- Other assessments:**
 - Treatment retention:** how many patients kept taking CBD throughout the OLE
 - Safety:** how many patients experienced side effects



What were the key characteristics of the people who were included?

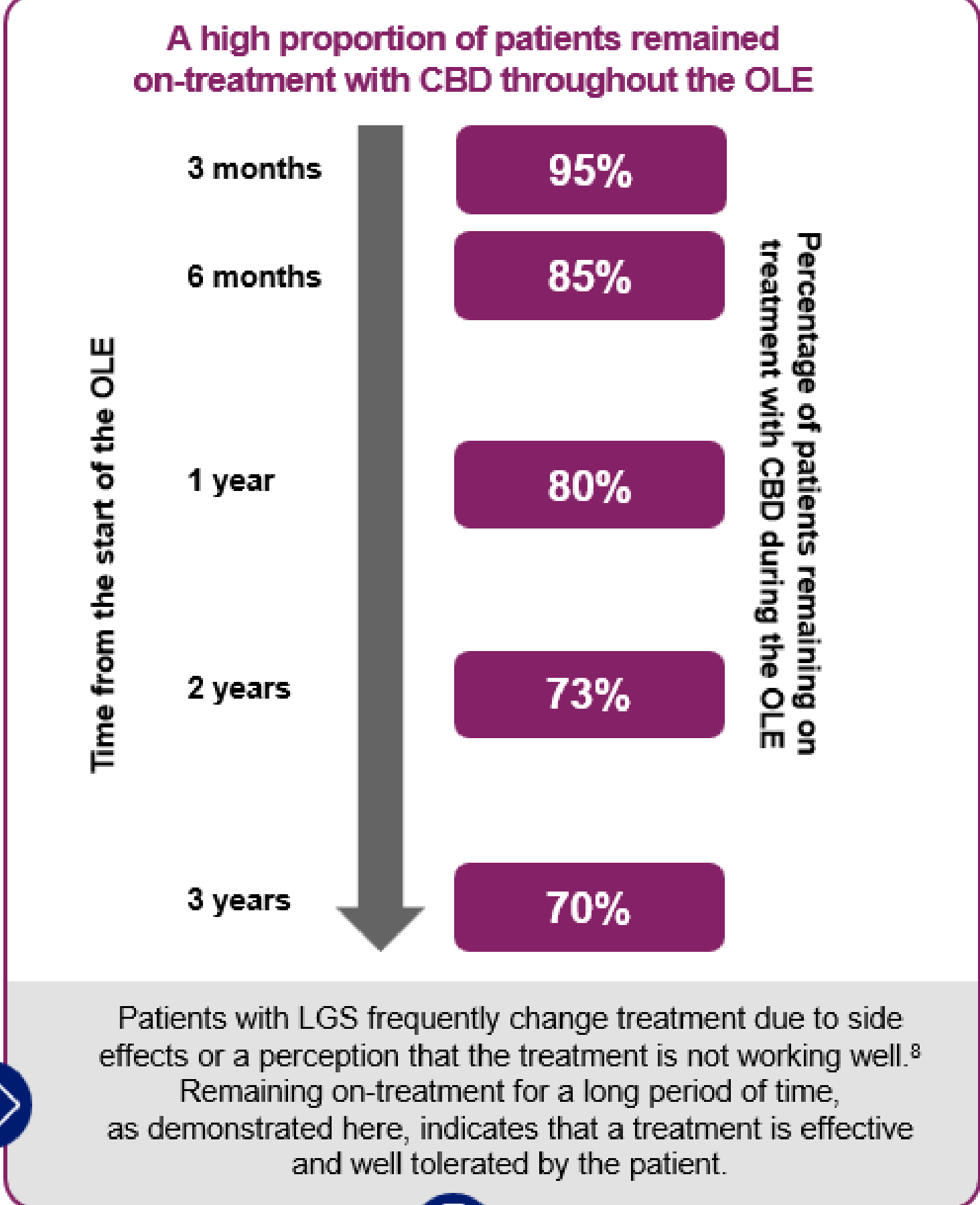


What were the key results from the analysis?

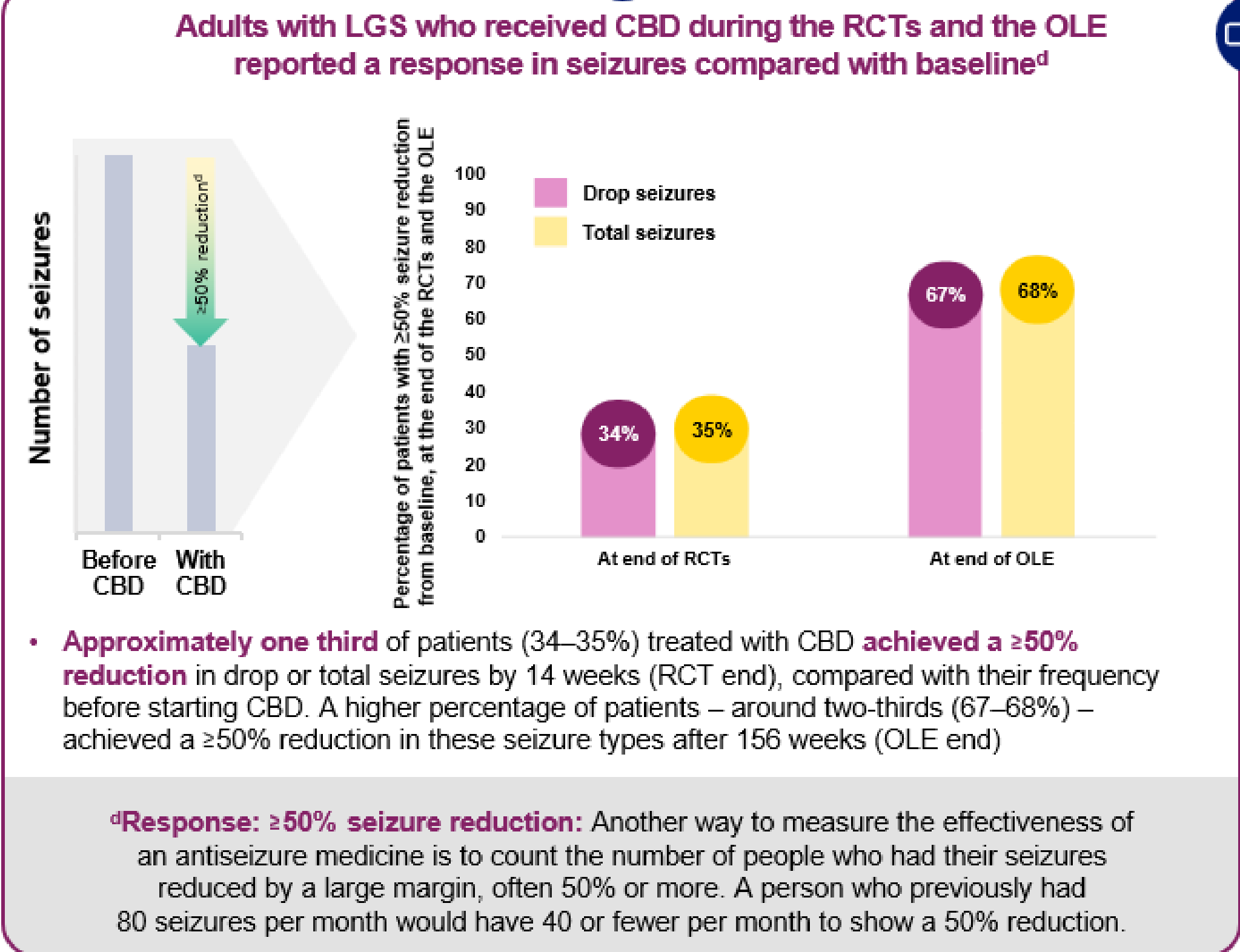


- CBD treatment reduced the frequency of monthly drop and total seizures by about one-third (32–34%) after 14 weeks (RCT end), compared with their frequency before starting CBD. Larger reductions of around two-thirds (65–69%) were observed by 156 weeks (OLE end)

^cPercent change: One way to measure how well an antiseizure medicine works is to compare the number of seizures a person has over a period of time (in this case, per month) before and after starting the medicine.



Patients with LGS frequently change treatment due to side effects or a perception that the treatment is not working well.⁸ Remaining on-treatment for a long period of time, as demonstrated here, indicates that a treatment is effective and well tolerated by the patient.



- Approximately one third of patients (34–35%) treated with CBD achieved a ≥50% reduction in drop or total seizures by 14 weeks (RCT end), compared with their frequency before starting CBD. A higher percentage of patients – around two-thirds (67–68%) – achieved a ≥50% reduction in these seizure types after 156 weeks (OLE end)

^dResponse: ≥50% seizure reduction: Another way to measure the effectiveness of an antiseizure medicine is to count the number of people who had their seizures reduced by a large margin, often 50% or more. A person who previously had 80 seizures per month would have 40 or fewer per month to show a 50% reduction.



Safety

The most common side effects reported were:

- Diarrhoea** (stomach icon)
- Convulsions** (uncontrollable shaking or movements) (person shaking icon)
- Pyrexia** (fever) (head with thermometer icon)
- Somnolence** (sleepiness) (person sleeping icon)

- Side effects in this adult population appeared similar to the overall population (adults and children) studied in the RCTs and OLE^{2,4,7}



What do these results mean?

- The results show that CBD treatment helped reduce seizures in adults with LGS, with a high proportion of patients staying on-treatment over a 3-year period
- These data indicate that CBD effectiveness in adults is similar to the overall population from the RCTs and OLE^{2,4,7}
- Together, the data presented on seizure reduction, treatment retention and safety in adults with LGS, suggest that CBD is effective and demonstrates a safety profile consistent with the overall population

Epidyolex® is approved in the EU for the adjunctive treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome, in conjunction with clobazam, in patients ≥2 years of age; it is additionally approved in the EU for the adjunctive treatment of seizures associated with tuberous sclerosis complex in patients ≥2 years of age.

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References: 1. Cross JH, et al. *Front Neurol*. 2017;8:505. 2. Devinsky O, et al. *N Engl J Med*. 2018;378(20):1888–1897. 3. Specchio N, et al. *Epilepsia*. 2022;63(13):1936–42. 4. Thiele EA, et al. *Lancet*. 2018;391(10125):1035–1036. 5. US Food and Drug Administration. Epidiolex® Prescribing Information. 2026. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/210365s024s029s030bl.pdf (Accessed 19 August 2026). 6. European Medicines Agency. Epidyolex® 100 mg/ml oral solution: summary of product characteristics. 2026. Available from: https://www.ema.europa.eu/en/documents/product-information/epidyolex-epar-product-information_en.pdf (Accessed 19 August 2026). 7. Patel AD, et al. *Epilepsia*. 2021;62(9):2228–2239. 8. Lu M, et al. *Heliyon*. 2026;12:e44489.

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POSTER



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