P0316

Effect of Cannabidiol on Measured Glomerular Filtration Rate in Healthy Participants: A Phase 1, Open-Label, Single-Site Study

Svetlana Markova,[1] Hongwei Xue,[1] Patricia Chandler,[1] Sujith Madhavan,[2] Cuiping Chen[1]

[1]Jazz Pharmaceuticals, Inc., Palo Alto, CA, USA;
[2]Jazz Pharmaceuticals, UK Ltd., London, UK.

Objective

- To assess the effect of cannabidiol (CBD) on measured glomerular filtration rate (mGFR), using iohexol as a probe compound, in healthy adults

Conclusions

- Multiple doses of CBD 7.5 mg/kg BID for 7 days had no effect on the mGFR and mGFR normalised for body surface area
- Consistent with historical observations, minor increases in serum creatinine were noted, as reflected by minor decreases (5–10%) in creatinine-derived parameters of estimated GFR and creatinine clearance
- The minor increase in serum creatinine following CBD administration was not due to an effect on renal glomerular filtration rate

References: 1. US Food and Drug Administration. Epidiolex® Prescribing Information. 2026. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/210365s024s029s030lbl.pdf (Accessed 19 August 2026). **2.** 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). **3.** 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). **4.** Ebert N, et al. *Kidney Int*. 2024;106(4):583–596. **5.** Pottel H, et al. *Nephrol Dial Transplant*. 2017;32(3):497–507. **6.** Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group 2024. *Kidney Int*. 2024;105(4S): S117–S314. **7.** Inker LA, et al. *N Engl J Med*. 2021;385(19):1737–1749.

Support and Acknowledgements: This study was sponsored by Jazz Pharmaceuticals, Inc. The authors would like to thank all of the study investigators, study staff, and participants for their participation in this research. Writing and editorial assistance were provided to the authors by Vijay Kadasi, MSc, on behalf of Syneos 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. **SvM, HX, PC,** and **CC** are employees of Jazz Pharmaceuticals, Inc., and hold stock and/or stock options in the company. **SuM** is an employee of Jazz Pharmaceuticals, UK Ltd., 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 ID: GWCP18057

POSTER | ANNOTATED POSTER | AUDIO

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

Scan left code to access this poster online.
Scan middle code to access a plain language annotation of this poster.
Scan right code to access an audio narration of this poster.
These codes are not for promotional purposes.

1 Introduction

- Highly purified, plant-derived cannabidiol (CBD; Epidyolex® [EU]/Epidiolex® [US], 100 mg/mL oral solution) is approved for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS), Dravet syndrome (DS), and tuberous sclerosis complex (TSC)[1–3]
- A *post hoc* analysis of safety laboratory results from three double-blind, randomised, placebo-controlled studies of CBD in paediatric and adult patients with LGS or DS, and a phase 1 randomised withdrawal study in healthy participants, showed an ~10% increase in serum creatinine concentration following CBD administration[1–3]
- In healthy participants, the increase was observed within 1 to 2 weeks of initiating CBD, after which it stabilised, and concentrations returned to baseline following CBD discontinuation[1–3]
  - Reversibility of serum creatinine increases was not assessed in LGS or DS CBD studies
- It was unknown whether the observed increase in serum creatinine reflected a reduction in glomerular filtration rate (GFR)[1–3]
- Iohexol is a non-radioactive contrast agent; its plasma clearance is a validated method for measuring GFR and is not affected by limitations of creatinine-based measures[4–6]
- In this phase 1, open-label, single-site study (GWCP18057), the potential cause of the increase in serum creatinine was explored by assessing the effect of repeated-dose CBD administration on measured GFR (mGFR) using iohexol plasma clearance

Methods

Participants

- This study included healthy male and female participants, aged 18–60 years, with a body mass index of 18.5–30.0 kg/m², and a minimum body weight of 50.0 kg from a single centre in the US

Dosing

- **Day −1:** iohexol 5 mL (equivalent to 1.5 g iodine) was administered by intravenous (IV) infusion over a duration of 5 minutes
- **Days 1–6:** CBD 7.5 mg/kg was administered orally twice daily (BID), 30 minutes after starting a standardised meal, at approximately the same times each morning and evening (~12 hours apart [±15 minutes])
- **Day 7:** CBD 7.5 mg/kg was administered 30 minutes after starting a standardised breakfast, followed by iohexol 5 mL IV infusion over 5 minutes
  - Evening dose of CBD was administered ~12 hours after the morning dose (±15 minutes), following a standardised meal (identical to the meal provided on Day −1)

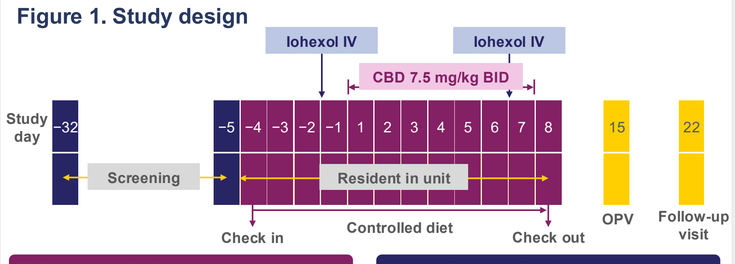
Sample collection and assessments

- On Day −1 and Day 7, 24-hour pooled urine collections were obtained for evaluation of creatinine clearance (CLcr)
  - Water intake was controlled to ensure adequate hydration and reduce variability in renal function parameters
- Blood samples for iohexol analysis were collected on Day −1 and Day 7 from pre-dose (before breakfast) to 12 hours post-dose (prior to the evening CBD dose on Day 7)
- Blood samples for CBD and metabolite analysis were collected on:
  - Days 1, 4, 5, and 6: pre-dose (before breakfast)
  - Day 7: pre-dose to 12 hours post-dose (prior to evening CBD dose)
- This study was conducted with Epidiolex®, and results do not apply to other CBD-containing products

Analyses

- Analysis populations:
  - Pharmacodynamic: all participants who received at least one dose of iohexol and had evaluable pharmacodynamic data
  - Pharmacokinetic: all participants who received at least one dose of CBD and had evaluable pharmacokinetic data
  - Safety: all participants who received at least one dose of study treatment
- Plasma pharmacodynamic and pharmacokinetic parameters were calculated using standard non-compartmental methods
  - Pharmacodynamic parameters were compared by a paired t-test and 2-sided 90% confidence intervals (CIs) for the GMR calculated; pharmacokinetic parameters were summarised descriptively with no formal statistical comparisons performed
  - The primary endpoint mGFR was calculated from the plasma clearance of iohexol and normalised against body surface area (BSA)

Figure 1. Study design



Primary endpoint

- Ratio (Day 7:baseline[a]) of mGFR[b] normalised to BSA (mGFR/BSA), calculated via iohexol plasma clearance

Secondary endpoints

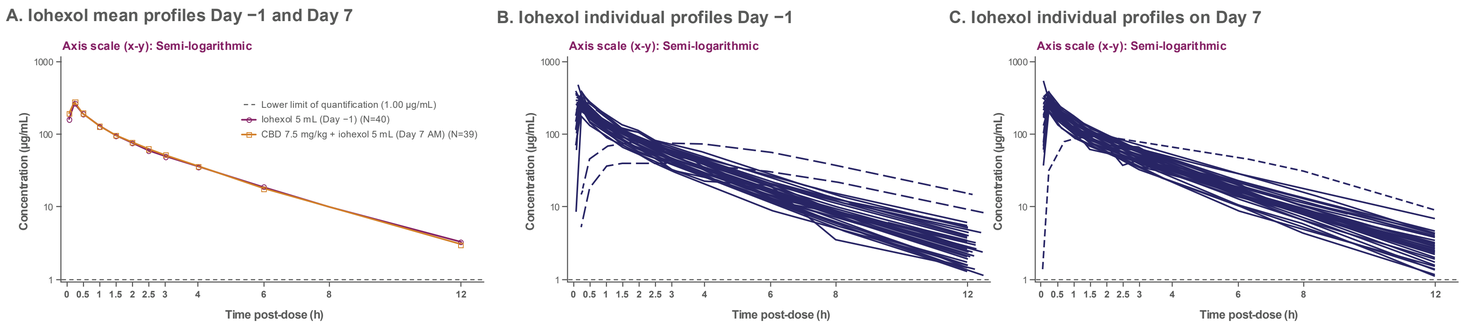
- Ratio (Day 7:baseline[a]) of 24-hour CLcr[c]
- Ratio (Day 7:baseline[a]) of eGFR[d]
- Steady-state pharmacokinetic parameters of CBD and its metabolites 7-OH-CBD, and 7-COOH-CBD
- Treatment-emergent adverse events

[a]Baseline was Day −1. [b]mGFR, calculated via iohexol clearance. [c]CLcr calculated using serum creatinine and 24-hour urine creatinine and volume. [d]eGFR calculated using CKD-EPI Creatinine-Cystatin Equation [2021]).[7]
BID, twice daily; BSA, body surface area; 7-COOH-CBD, 7-carboxy-cannabidiol; 7-OH-CBD, 7-hydroxy-cannabidiol; CBD, cannabidiol; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; CLcr, creatinine clearance; eGFR, estimated glomerular filtration rate; IV, intravenous; mGFR, measured glomerular filtration rate; OPV, outpatient visit.

Results

2 Iohexol concentration–time profiles

Figure 2. Arithmetic mean iohexol concentration–time profiles (pharmacodynamic population)



- Following infusion, the mean plasma iohexol concentrations peaked approximately 15 minutes after infusion start on both Day −1 (no CBD) and Day 7 (after 7 days of CBD 7.5 mg/kg BID)
- Iohexol concentrations then declined rapidly, with similar concentration–time profiles observed on Day −1 and Day 7, indicating no effect of CBD on iohexol pharmacokinetics (**Figure 2**)

3 Pharmacodynamic parameters: mGFR, mGFR/BSA, CLcr, and eGFR

Table 1. Summary of pharmacodynamic parameters

Parameter		mGFR (mL/min)	mGFR/BSA (mL/min/m²)	CLcr (mL/min)	eGFR[a] (mL/min/1.73 m²)
5 mL iohexol (Day −1, morning) [Reference]	N[b]	39	39	26	40
	Mean (SD)	114.0 (21.5)	60.8 (9.6)	120.0 (23.5)	108.0 (12.2)
	Geomean (CV%)	112.0 (18.8)	60.1 (16.1)	118.0 (21.2)	107.0 (11.5)
5 mL iohexol + 7.5 mg/kg CBD (Day 7, AM) [Test]	N[b]	39	39	13[c]	38
	Mean (SD)	112.0 (20.0)	60.2 (9.0)	115.0 (24.8)	103.0 (13.4)
	Geomean (CV%)	111.0 (17.6)	59.5 (15.3)	113.0 (21.2)	103.0 (13.1)
GMR (90% CI) [Test vs Reference][d]		–	–	**0.990 (0.967, 1.014)**	**0.898 (0.871, 0.927)**	**0.953 (0.941, 0.965)**

[a]For eGFR, only data from Day −1, pre-iohexol dose (baseline) and Day 7, pre-iohexol dose were included in the analysis. [b]Number of participants with evaluable data. [c]26 participants were excluded from the CLcr GMR analysis due to a lack of Day −1 and/or Day 7 CLcr data. [d]Data were analysed using a paired t-test and only participants with data at both Day −1 (baseline) and Day 7 were included in the analysis. GMRs and corresponding CIs were obtained by taking the exponential of the differences in means and corresponding CIs on the ln scale.
BSA, body surface area; CBD, cannabidiol; CI, confidence interval; CLcr, creatinine clearance; CV, coefficient of variation; eGFR, estimated glomerular filtration rate; GMR, geometric mean ratio; ln scale, natural logarithmic scale; mGFR, measured glomerular filtration rate; SD, standard deviation.

Main analysis

- The Day 7:baseline geometric mean ratio (GMR; 90% CI) for mGFR/BSA indicated no effect of CBD on glomerular filtration function (**Table 1**)
- Consistent with prior observations, minimal serum creatinine increases reflected in small decreases in creatinine-derived parameters, were noted (**Table 1**)

Sensitivity analysis

- In three participants, iohexol concentration–time profiles were inconsistent with IV infusion (**Figure 2B** and **2C**); however, these were retained in the primary analysis
- Excluding these three participants showed a similar trend for mGFR/BSA (Day 7:baseline GMR [90% CI]: 0.985 [0.962, 1.008])

4 Pharmacokinetic parameters of iohexol

Table 2. Summary of iohexol plasma pharmacokinetic parameters

Parameter[a]		Iohexol 5 mL (Day −1)[b] (N=40)	CBD 7.5 mg/kg + iohexol 5 mL (Day 7, AM)[b] (N=39)
AUC_{0-last} (h·µg/mL)	Mean (SD)	479.0 (86.7)	485.0 (81.6)
	Geomean (CV%)	471.0 (18.7)	478.0 (17.3)
	Median (min–max)	475.0 (313.0–659.0)	471.0 (328.0–673.0)
AUC_{∞} (h·µg/mL)	Mean (SD)	490.0 (90.8)	494.0 (85.1)
	Geomean (CV%)	482.0 (18.8)	487.0 (17.6)
	Median (min–max)	484.0 (316.0–678.0)	481.0 (333.0–687.0)
$\%AUC_{extrap}$	Mean (SD)	2.3 (2.2)	1.9 (0.9)
	Geomean (CV%)	1.8 (65.3)	1.7 (48.5)
	Median (min–max)	1.7 (0.7–11.2)	1.7 (0.7–5.3)
C_{max} (µg/mL)	Mean (SD)	277.0 (77.9)	285.0 (65.4)
	Geomean (CV%)	261.0 (43.8)	277.0 (25.7)
	Median (min–max)	284.0 (40.6–467.0)	274.0 (91.9–542.0)
T_{max} (h)	Mean (SD)	0.4 (0.6)	0.3 (0.2)
	Geomean (CV%)	NC (NC)	NC (NC)
	Median (min–max)	0.3 (0.1–3.0)	0.3 (0.1–1.5)
$t_{1/2}$ (h)	Mean (SD)	2.2 (0.3)	2.2 (0.2)
	Geomean (CV%)	2.2 (14.4)	2.1 (10.7)
	Median (min–max)	2.2 (1.8–3.4)	2.1 (1.8–2.8)

[a]Pharmacokinetic parameters were summarised descriptively; no formal statistical comparisons were performed. [b]40 received at least one dose of iohexol, and 39 received at least one dose of both iohexol and CBD; the participant who only received iohexol was withdrawn from the study after receiving iohexol due to not meeting eligibility criteria.
AUC, area under the plasma concentration–time curve; AUC_{0-last}, AUC from time 0 until the last quantifiable concentration; AUC_{extrap}, AUC that is extrapolated (predicted); AUC_{∞}, AUC from time 0 extrapolated to infinity; CBD, cannabidiol; C_{max}, maximum measured plasma concentration; CV, coefficient of variation; NC, not calculated; SD, standard deviation; T_{max}, time to maximum observed plasma concentration; $t_{1/2}$, terminal elimination half-life.

- The geometric mean values of iohexol maximum measured plasma concentration (C_{max}), area under the curve $(AUC)_{0-last}$, AUC_{∞}, $\%AUC_{extrap}$, and terminal half-life, as well as median time to maximum plasma concentration (T_{max}) values were similar between Day −1 (iohexol alone) and Day 7 (CBD + iohexol; **Table 2**)

Pharmacokinetic parameters of CBD and its metabolites

Table 3. Summary of CBD and CBD metabolite plasma pharmacokinetic parameters

Parameter[a]		CBD 7.5 mg/kg + iohexol 5 mL (Day 7, AM)[b] (N=39)		
		CBD	7-OH-CBD	7-COOH-CBD
AUC_{0-T} (h·ng/mL)	Mean (SD)	1920.0 (691.0)	1140.0 (457.0)	69,200.0 (38,500.0)
	Geomean (CV%)	1800.0 (37.4)	1060.0 (43.1)	58,800.0 (69.5)
C_{max} (ng/mL)	Mean (SD)	412.0 (199.0)	184.0 (60.2)	6800.0 (3530.0)
	Geomean (CV%)	374.0 (45.6)	174.0 (37.2)	5910.0 (63.5)
MR_{AUC}	Mean (SD)	—	0.6 (0.3)	37.2 (22.8)
MR_{Cmax}	Mean (SD)	—	0.5 (0.2)	18.4 (11.2)
T_{max} (h)	Median (min–max)	3.0 (1.5–6.1)	3.0 (1.5–6.1)	4.0 (0–6.1)

[a]Pharmacokinetic parameters were summarised descriptively; no formal statistical comparisons were performed.
[b]38 participants had valid observations.
7-COOH-CBD, 7-carboxy-cannabidiol; 7-OH-CBD, 7-hydroxy-cannabidiol; AUC, area under the plasma concentration–time curve; AUC_{0-T}, AUC over a dosing interval, where tau is the dosing interval; CBD, cannabidiol; C_{max}, maximum measured plasma concentration; CV, coefficient of variation; MR_{AUC}, metabolite-to-parent ratio based on AUC_{0-T}; MR_{Cmax}, metabolite-to-parent ratio based on C_{max}; SD, standard deviation.

- Steady-state plasma CBD, 7-hydroxy-CBD (7-OH-CBD), and 7-carboxy-CBD (7-COOH-CBD) pharmacokinetic parameters (**Table 3**) were consistent with historical data[1,2]
  - Median T_{max} was similar for CBD and 7-OH-CBD (3.0 hours), with a slightly longer T_{max} observed for 7-COOH-CBD (4.0 hours)
  - Metabolite-to-parent ratio (MR) based on AUC_{0-T} (MR_{AUC}) and MR_{Cmax} were higher for 7-COOH-CBD (37.2 and 18.4, respectively) compared with 7-OH-CBD (0.6 and 0.5, respectively)

5 Safety

Table 4. Summary of treatment-emergent adverse events (TEAEs)

TEAEs,[a] n (%)	Iohexol 5 mL (Day −1) (N=40)	CBD 7.5 mg/kg BID (Days 1–6) (N=39)	CBD 7.5 mg/kg + iohexol 5 mL (Day 7, AM) (N=39)	CBD 7.5 mg/kg (Day 7, PM) (N=39)	Overall[b] (N=40)
All-cause TEAEs	**5 (12.5)**	**15 (38.5)**	**3 (7.7)**	**3 (7.7)**	**18 (45.0)**
Iohexol-related TEAEs[c]	1 (2.5)	2 (5.1)	1 (2.6)	0	3 (7.5)
CBD-related TEAEs[c]	NA	3 (7.7)	2 (5.1)	0	5 (12.5)
TEAEs occurring in ≥5% of participants during any treatment period,[d] preferred term					
Diarrhoea	0	5 (12.8)	0	0	5 (12.5)
Nausea	0	3 (7.7)	2 (5.1)	0	5 (12.5)
Abdominal pain	0	3 (7.7)	1 (2.6)	0	3 (7.5)
Headache	1 (2.5)	1 (2.6)	2 (5.1)	0	3 (7.5)
Vomiting	0	0	1 (2.6)	1 (2.6)	2 (5.0)
Lethargy	0	2 (5.1)	0	0	2 (5.0)
Presyncope	0	1 (2.6)	1 (2.6)	0	2 (5.0)
Vessel puncture site haematoma	2 (5.0)	0	0	0	2 (5.0)

[a]Adverse events were coded using the Medical Dictionary for Regulatory Activities Version 27.1. [b]Overall indicates the total number of participants who experienced a TEAE during the study and may not equal the sum across study periods, as participants could have experienced TEAEs in more than one study period. [c]Treatment-related TEAEs were TEAEs with a plausible relationship to the study treatment, as determined by the investigator. [d]Only one (2.5%) renal TEAE (dysuria) was reported.
CBD, cannabidiol; NA, not applicable; TEAEs, treatment-emergent adverse events.

- Overall, 18 participants (45.0%) experienced TEAEs, most frequently during CBD dosing (Days 1–6; **Table 4**)
  - Three participants (7.5%) experienced iohexol-related TEAEs and five participants (12.5%) experienced CBD-related TEAEs
  - All TEAEs were mild in severity, with no serious TEAEs or TEAEs resulting in study discontinuation or death reported

6 Demographics and baseline characteristics

Table 5. Participant demographics

Demographic	Safety and pharmacodynamic population (N=40)	Pharmacokinetic population (N=39)
Age, years		
Mean (SD)	38.7 (10.9)	38.8 (11.0)
Median (range)	37.0 (23.0–60.0)	38.0 (23.0–60.0)
Sex, n (%)		
Female	24 (60.0)	23 (59.0)
Male	16 (40.0)	16 (41.0)
Race, n (%)		
White	26 (65.0)	26 (66.7)
Black or African American	12 (30.0)	11 (28.2)
Asian	2 (5.0)	2 (5.1)
Ethnicity, n (%)		
Hispanic or Latino	6 (15.0)	5 (12.8)
Other	34 (85.0)	34 (87.2)
Body weight, kg		
Mean (SD)	75.2 (13.4)	75.2 (13.6)
Median (range)	74.9 (51.9–103.7)	75.2 (51.9–103.7)

Demographic	Safety and pharmacodynamic population (N=40)	Pharmacokinetic population (N=39)
Body mass index, kg/m²		
Mean (SD)	25.5 (3.0)	25.5 (3.0)
Median (range)	25.9 (18.5–29.9)	25.90 (18.5–29.9)
Body surface area, m²		
Mean (SD)	1.9 (0.2)	1.9 (0.2)
Median (range)	1.9 (1.5–2.3)	1.9 (1.5–2.3)

SD, standard deviation.

- The study enrolled 40 participants; all 40 received at least one dose of iohexol (safety and pharmacodynamic populations), and 39 received at least one dose of both iohexol and CBD (pharmacokinetic population)
  - One participant was withdrawn from the study after receiving iohexol due to not meeting eligibility criteria
  - Overall, 35 completed the study and 5 discontinued (participant withdrawal, n=3; failed to meet continuation criteria, n=1; lost to follow-up, n=1)
- Mean (standard deviation; range) age was 38.7 years (10.9; 23–60; **Table 5**)
- The majority of participants were female or White (**Table 5**)

P0316

Effect of Cannabidiol on Measured Glomerular Filtration Rate in Healthy Participants: A Phase 1, Open-Label, Single-Site Study

Svetlana Markova,[1] Hongwei Xue,[1] Patricia Chandler,[1] Sujith Madhavan,[2] Cuiping Chen[1]

[1]Jazz Pharmaceuticals, Inc., Palo Alto, CA, USA;
[2]Jazz Pharmaceuticals, UK Ltd., London, UK.

Objective

- To assess the effect of cannabidiol (CBD) on measured glomerular filtration rate (mGFR), using iohexol as a probe compound, in healthy adults

Conclusions

- Multiple doses of CBD 7.5 mg/kg BID for 7 days had no effect on the mGFR and mGFR normalised for body surface area
- Consistent with historical observations, minor increases in serum creatinine were noted, as reflected by minor decreases (5–10%) in creatinine-derived parameters of estimated GFR and creatinine clearance
- The minor increase in serum creatinine following CBD administration was not due to an effect on renal glomerular filtration rate

References: 1. US Food and Drug Administration. Epidiolex® Prescribing Information. 2026. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/210365s024s029s030lbl.pdf (Accessed 19 August 2026). **2.** 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). **3.** 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). **4.** Ebert N, et al. *Kidney Int.* 2024;106(4):583–596. **5.** Pottel H, et al. *Nephrol Dial Transplant.* 2017;32(3):497–507. **6.** Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group 2024. *Kidney Int.* 2024;105(4S):S117–S314. **7.** Inker LA, et al. *N Engl J Med.* 2021;385(19):1737–1749.

Support and Acknowledgements: This study was sponsored by Jazz Pharmaceuticals, Inc. The authors would like to thank all of the study investigators, study staff, and participants for their participation in this research. Writing and editorial assistance were provided to the authors by Vijay Kadasi, MSc, on behalf of Syneos 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.

1 Background and study summary

What is cannabidiol (CBD)?

- A highly purified, plant-derived form of **CBD (Epidyolex® [EU]/Epidiolex® [US])** medicine used for **helping control seizures** in some rare forms of epilepsy
  - CBD, is approved for use in seizures associated with **Lennox-Gastaut syndrome, Dravet syndrome, and tuberous sclerosis complex**

What did the study want to research?

- Researchers wanted to understand whether CBD affected how well the kidneys filter waste from the blood

Why was this study done?

- Previous studies have found that **CBD can cause a small increase (~10%) in blood creatinine levels**, a marker often used to check kidney function
  - The small increase was found to occur within 2 weeks of starting CBD, and **went away after stopping CBD** when previously tested in healthy adults

How was the study objective tested?

- Healthy adults were treated with CBD and a drug used to measure how well the kidneys can filter material to determine how CBD affected kidney function
  - The study used iohexol, a contrast dye used to help doctors and researchers see inside the body more clearly, to measure how well the kidneys can filter material

Dosing

- **Day −1:** iohexol 5 mL (equivalent to 1.5 g iodine) was administered by intravenous (IV) infusion over a duration of 5 minutes
- **Days 1–6:** CBD 7.5 mg/kg was administered orally twice daily (BID), 30 minutes after starting a standardised meal, at approximately the same times each morning and evening (~12 hours apart [±15 minutes])
- **Day 7:** CBD 7.5 mg/kg was administered 30 minutes after starting a standardised breakfast, followed by iohexol 5 mL IV infusion over 5 minutes
  - Evening dose of CBD was administered ~12 hours after the morning dose (±15 minutes), following a standardised meal (identical to the meal provided on Day −1)

Sample collection and assessments

- On Day −1 and Day 7, 24-hour pooled urine collections were obtained for evaluation of creatinine clearance (CLcr)
  - Water intake was controlled to ensure adequate hydration and reduce variability in renal function parameters
- Blood samples for iohexol analysis were collected on Day −1 and Day 7 from pre-dose (before breakfast) to 12 hours post-dose (prior to the evening CBD dose on Day 7)
- Blood samples for CBD and metabolite analysis were collected on:
  - Days 1, 4, 5, and 6: pre-dose (before breakfast)
  - Day 7: pre-dose to 12 hours post-dose (prior to evening CBD dose)
- This study was conducted with Epidiolex®, and results do not apply to other CBD-containing products

Analyses

- Analysis populations:
  - Pharmacodynamic: all participants who received at least one dose of iohexol and had evaluable pharmacodynamic data
  - Pharmacokinetic: all participants who received at least one dose of CBD and had evaluable pharmacokinetic data
  - Safety: all participants who received at least one dose of study treatment
- Plasma pharmacodynamic and pharmacokinetic parameters were calculated using standard non-compartmental methods
  - Pharmacodynamic parameters were compared by a paired t-test and 2-sided 90% confidence intervals (CIs) for the GMR calculated; pharmacokinetic parameters were summarised descriptively with no formal statistical comparisons performed
  - The primary endpoint mGFR was calculated from the plasma clearance of iohexol and normalised against body surface area (BSA)

Figure 1. Study design

Primary endpoint

- Ratio (Day 7:baseline[a]) of mGFR[b] normalised to BSA (mGFR/BSA), calculated via iohexol plasma clearance

Secondary endpoints

- Ratio (Day 7:baseline[a]) of 24-hour CLcr[c]
- Ratio (Day 7:baseline[a]) of eGFR[d]
- Steady-state pharmacokinetic parameters of CBD and its metabolites 7-OH-CBD, and 7-COOH-CBD
- Treatment-emergent adverse events

[a]Baseline was Day −1. [b]mGFR, calculated via iohexol clearance. [c]CLcr calculated using serum creatinine and 24-hour urine creatinine and volume. [d]eGFR calculated using CKD-EPI Creatinine-Cystatin Equation (2021).[7]
BID, twice daily; BSA, body surface area; 7-COOH-CBD, 7-carboxy-cannabidiol; 7-OH-CBD, 7-hydroxy-cannabidiol; CBD, cannabidiol; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; CLcr, creatinine clearance; eGFR, estimated glomerular filtration rate; IV, intravenous; mGFR, measured glomerular filtration rate; OPV, outpatient visit.

Results

Iohexol concentration–time profiles

Figure 2. Arithmetic mean iohexol concentration–time profiles (pharmacodynamic population)

- Following infusion, the mean plasma iohexol concentrations peaked approximately 15 minutes after infusion start on both Day −1 (no CBD) and Day 7 (after 7 days of CBD 7.5 mg/kg BID)
- Iohexol concentrations then declined rapidly, with similar concentration–time profiles observed on Day −1 and Day 7, indicating no effect of CBD on iohexol pharmacokinetics (**Figure 2**)

Pharmacodynamic parameters: mGFR, mGFR/BSA, CLcr, and eGFR

Table 1. Summary of pharmacodynamic parameters

Parameter		mGFR (mL/min)	mGFR/BSA (mL/min/m²)	CLcr (mL/min)	eGFR[a] (mL/min/1.73 m²)
5 mL iohexol (Day −1, morning) [Reference]	N[b]	39	39	26	40
	Mean (SD)	114.0 (21.5)	60.8 (9.6)	120.0 (23.5)	108.0 (12.2)
	Geomean (CV%)	112.0 (18.8)	60.1 (16.1)	118.0 (21.2)	107.0 (11.5)
5 mL iohexol + 7.5 mg/kg CBD (Day 7, AM) [Test]	N[b]	39	39	13[c]	38
	Mean (SD)	112.0 (20.0)	60.2 (9.0)	115.0 (24.8)	103.0 (13.4)
	Geomean (CV%)	111.0 (17.6)	59.5 (15.3)	113.0 (21.2)	103.0 (13.1)
GMR (90% CI) [Test vs Reference][d]	–	–	**0.990 (0.967, 1.014)**	**0.898 (0.871, 0.927)**	**0.953 (0.941, 0.965)**

[a]For eGFR, only data from Day −1, pre-iohexol dose (baseline) and Day 7, pre-iohexol dose were included in the analysis. [b]Number of participants with evaluable data. [c]26 participants were excluded from the CLcr GMR analysis due to a lack of Day −1 and/or Day 7 CLcr data. [d]Data were analysed using a paired t-test and only participants with data at both Day −1 (baseline) and Day 7 were included in the analysis. GMRs and corresponding CIs were obtained by taking the exponential of the differences in means and corresponding CIs on the ln scale.
BSA, body surface area; CBD, cannabidiol; CI, confidence interval; CLcr, creatinine clearance; CV, coefficient of variation; eGFR, estimated glomerular filtration rate; GMR, geometric mean ratio; ln scale, natural logarithmic scale; mGFR, measured glomerular filtration rate; SD, standard deviation.

Main analysis

- The Day 7:baseline geometric mean ratio (GMR; 90% CI) for mGFR/BSA indicated no effect of CBD on glomerular filtration function (**Table 1**)
- Consistent with prior observations, minimal serum creatinine increases reflected in small decreases in creatinine-derived parameters, were noted (**Table 1**)

Sensitivity analysis

- In three participants, iohexol concentration–time profiles were inconsistent with IV infusion (**Figure 2B** and **2C**); however, these were retained in the primary analysis
- Excluding these three participants showed a similar trend for mGFR/BSA (Day 7:baseline GMR [90% CI]: 0.985 [0.962, 1.008])

Day −1 (iohexol alone) and Day 7 (CBD + iohexol; **Table 2**)

for 7-COOH-CBD (37.2 and 18.4, respectively) compared with 7-OH-CBD (0.6 and 0.5, respectively)

Safety

Table 4. Summary of treatment-emergent adverse events (TEAEs)

TEAEs,[a] n (%)	Iohexol 5 mL (Day −1) (N=40)	CBD 7.5 mg/kg BID (Days 1–6) (N=39)	CBD 7.5 mg/kg + iohexol 5 mL (Day 7, AM) (N=39)	CBD 7.5 mg/kg (Day 7, PM) (N=39)	Overall[b] (N=40)
All-cause TEAEs	**5 (12.5)**	**15 (38.5)**	**3 (7.7)**	**3 (7.7)**	**18 (45.0)**
Iohexol-related TEAEs[c]	1 (2.5)	2 (5.1)	1 (2.6)	0	3 (7.5)
CBD-related TEAEs[c]	NA	3 (7.7)	2 (5.1)	0	5 (12.5)
TEAEs occurring in ≥5% of participants during any treatment period,[d] preferred term					
Diarrhoea	0	5 (12.8)	0	0	5 (12.5)
Nausea	0	3 (7.7)	2 (5.1)	0	5 (12.5)
Abdominal pain	0	3 (7.7)	1 (2.6)	0	3 (7.5)
Headache	1 (2.5)	1 (2.6)	2 (5.1)	0	3 (7.5)
Vomiting	0	0	1 (2.6)	1 (2.6)	2 (5.0)
Lethargy	0	2 (5.1)	0	0	2 (5.0)
Presyncope	0	1 (2.6)	1 (2.6)	0	2 (5.0)
Vessel puncture site haematoma	2 (5.0)	0	0	0	2 (5.0)

[a]Adverse events were coded using the Medical Dictionary for Regulatory Activities Version 27.1. [b]Overall indicates the total number of participants who experienced a TEAE during the study and may not equal the sum across study periods, as participants could have experienced TEAEs in more than one study period. [c]Treatment-related TEAEs were TEAEs with a plausible relationship to the study treatment, as determined by the investigator. [d]Only one (2.5%) renal TEAE (dysuria) was reported.
CBD, cannabidiol; NA, not applicable; TEAEs, treatment-emergent adverse events.

- Overall, 18 participants (45.0%) experienced TEAEs, most frequently during CBD dosing (Days 1–6; **Table 4**)
  - Three participants (7.5%) experienced iohexol-related TEAEs and five participants (12.5%) experienced CBD-related TEAEs
  - All TEAEs were mild in severity, with no serious TEAEs or TEAEs resulting in study discontinuation or death reported

Demographics and baseline characteristics

Table 5. Participant demographics

Demographic	Safety and pharmacodynamic population (N=40)	Pharmacokinetic population (N=39)
Age, years		
Mean (SD)	38.7 (10.9)	38.8 (11.0)
Median (range)	37.0 (23.0–60.0)	38.0 (23.0–60.0)
Sex, n (%)		
Female	24 (60.0)	23 (59.0)
Male	16 (40.0)	16 (41.0)
Race, n (%)		
White	26 (65.0)	26 (66.7)
Black or African American	12 (30.0)	11 (28.2)
Asian	2 (5.0)	2 (5.1)
Ethnicity, n (%)		
Hispanic or Latino	6 (15.0)	5 (12.8)
Other	34 (85.0)	34 (87.2)
Body weight, kg		
Mean (SD)	75.2 (13.4)	75.2 (13.6)
Median (range)	74.9 (51.9–103.7)	75.2 (51.9–103.7)
Body mass index, kg/m²		
Mean (SD)	25.5 (3.0)	25.5 (3.0)
Median (range)	25.9 (18.5–29.9)	25.90 (18.5–29.9)
Body surface area, m²		
Mean (SD)	1.9 (0.2)	1.9 (0.2)
Median (range)	1.9 (1.5–2.3)	1.9 (1.5–2.3)

SD, standard deviation.

- The study enrolled 40 participants; all 40 received at least one dose of iohexol (safety and pharmacodynamic populations), and 39 received at least one dose of both iohexol and CBD (pharmacokinetic population)
  - One participant was withdrawn from the study after receiving iohexol due to not meeting eligibility criteria
  - Overall, 35 completed the study and 5 discontinued (participant withdrawal, n=3; failed to meet continuation criteria, n=1; lost to follow-up, n=1)
- Mean (standard deviation; range) age was 38.7 years (10.9; 23–60; **Table 5**)
- The majority of participants were female or White (**Table 5**)

P0316

Effect of Cannabidiol on Measured Glomerular Filtration Rate in Healthy Participants: A Phase 1, Open-Label, Single-Site Study

Svetlana Markova,[1] Hongwei Xue,[1] Patricia Chandler,[1] Sujith Madhavan,[2] Cuiping Chen[1]

[1]Jazz Pharmaceuticals, Inc., Palo Alto, CA, USA;
[2]Jazz Pharmaceuticals, UK Ltd., London, UK.

Objective

- To assess the effect of cannabidiol (CBD) on measured glomerular filtration rate (mGFR), using iohexol as a probe compound, in healthy adults

Conclusions

- Multiple doses of CBD 7.5 mg/kg BID for 7 days had no effect on the mGFR and mGFR normalised for body surface area
- Consistent with historical observations, minor increases in serum creatinine were noted, as reflected by minor decreases (5–10%) in creatinine-derived parameters of estimated GFR and creatinine clearance
- The minor increase in serum creatinine following CBD administration was not due to an effect on renal glomerular filtration rate

References: 1. US Food and Drug Administration. Epidiolex® Prescribing Information. 2026. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/210365s024s029s030lbl.pdf (Accessed 19 August 2026). **2.** 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). **3.** 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). **4.** Ebert N, et al. *Kidney Int.* 2024;106(4):583–596. **5.** Pottel H, et al. *Nephrol Dial Transplant.* 2017;32(3):497–507. **6.** Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group 2024. *Kidney Int.* 2024;105(4S): S117–S314. **7.** Inker LA, et al. *N Engl J Med.* 2021;385(19):1737–1749.

Support and Acknowledgements: This study was sponsored by Jazz Pharmaceuticals, Inc. The authors would like to thank all of the study investigators, study staff, and participants for their participation in this research. Writing and editorial assistance were provided to the authors by Vijay Kadasi, MSc, on behalf of Syneos 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. **SvM, HX, PC,** and **CC** are employees of Jazz Pharmaceuticals, Inc., and hold stock and/or stock options in the company. **SuM** is an employee of Jazz Pharmaceuticals, UK Ltd., 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

Participants

- This study included healthy male and female participants, aged 18–60 years, with a body mass index of 18.5–30.0 kg/m², and a minimum body weight of 50.0 kg from a single centre in the US

Dosing

- **Day −1:** iohexol 5 mL (equivalent to 1.5 g iodine) was administered by intravenous (IV) infusion over a duration of 5 minutes
- **Days 1–6:** CBD 7.5 mg/kg was administered orally twice daily (BID), 30 minutes after starting a standardised meal, at approximately the same times each morning and evening (~12 hours apart [±15 minutes])
- **Day 7:** CBD 7.5 mg/kg was administered 30 minutes after starting a standardised breakfast, followed by iohexol 5 mL IV infusion over 5 minutes
  - Evening dose of CBD was administered ~12 hours after the morning dose (±15 minutes), following a standardised meal (identical to the meal provided on Day −1)

Sample collection and assessments

- On Day −1 and Day 7, 24-hour pooled urine collections were obtained for evaluation of creatinine clearance (CLcr)
  - Water intake was controlled to ensure adequate hydration and reduce variability in renal function parameters
- Blood samples for iohexol analysis were collected on Day −1 and Day 7 from pre-dose (before breakfast) to 12 hours post-dose (prior to the evening CBD dose on Day 7)
- Blood samples for CBD and metabolite analysis were collected on:
  - Days 1, 4, 5, and 6: pre-dose (before breakfast)
  - Day 7: pre-dose to 12 hours post-dose (prior to evening CBD dose)
- This study was conducted with Epidiolex®, and results do not apply to other CBD-containing products

Analyses

- Analysis populations:
  - Pharmacodynamic: all participants who received at least one dose of iohexol and had evaluable pharmacodynamic data
  - Pharmacokinetic: all participants who received at least one dose of CBD and had evaluable pharmacokinetic data
  - Safety: all participants who received at least one dose of study treatment
- Plasma pharmacodynamic and pharmacokinetic parameters were calculated using standard non-compartmental methods
  - Pharmacodynamic parameters were compared by a paired t-test and 2-sided 90% confidence intervals (CIs) for the GMR calculated; pharmacokinetic parameters were summarised descriptively with no formal statistical comparisons performed
  - The primary endpoint mGFR was calculated from the plasma clearance of iohexol and normalised against body surface area (BSA)

Figure 1. Study design

Primary endpoint

- Ratio (Day 7:baseline[a]) of mGFR[b] normalised to BSA (mGFR/BSA), calculated via iohexol plasma clearance

Secondary endpoints

- Ratio (Day 7:baseline[a]) of 24-hour CLcr[c]
- Ratio (Day 7:baseline[a]) of eGFR[d]
- Steady-state pharmacokinetic parameters of CBD and its metabolites 7-OH-CBD, and 7-COOH-CBD
- Treatment-emergent adverse events

[a]Baseline was Day −1. [b]mGFR, calculated via iohexol clearance. [c]CLcr calculated using serum creatinine and 24-hour urine creatinine and volume. [d]eGFR calculated using CKD-EPI Creatinine-Cystatin Equation (2021).[7]
BID, twice daily; BSA, body surface area; 7-COOH-CBD, 7-carboxy-cannabidiol; 7-OH-CBD, 7-hydroxy-cannabidiol; CBD, cannabidiol; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; CLcr, creatinine clearance; eGFR, estimated glomerular filtration rate; IV, intravenous; mGFR, measured glomerular filtration rate; OPV, outpatient visit.

Results

Iohexol concentration–time profiles

Figure 2. Arithmetic mean iohexol concentration–time profiles (pharmacodynamic population)

- Following infusion, the mean plasma iohexol concentrations peaked approximately 15 minutes after infusion start on both Day −1 (no CBD) and Day 7 (after 7 days of CBD 7.5 mg/kg BID)
- Iohexol concentrations then declined rapidly, with similar concentration–time profiles observed on Day −1 and Day 7, indicating no effect of CBD on iohexol pharmacokinetics (**Figure 2**)

Pharmacodynamic parameters: mGFR, mGFR/BSA, CLcr, and eGFR

Table 1. Summary of pharmacodynamic parameters

Parameter		mGFR (mL/min)	mGFR/BSA (mL/min/m²)	CLcr (mL/min)	eGFR[a] (mL/min/1.73 m²)
5 mL iohexol (Day −1, morning) [Reference]	N[b]	39	39	26	40
	Mean (SD)	114.0 (21.5)	60.8 (9.6)	120.0 (23.5)	108.0 (12.2)
	Geomean (CV%)	112.0 (18.8)	60.1 (16.1)	118.0 (21.2)	107.0 (11.5)
5 mL iohexol + 7.5 mg/kg CBD (Day 7, AM) [Test]	N[b]	39	39	13[c]	38
	Mean (SD)	112.0 (20.0)	60.2 (9.0)	115.0 (24.8)	103.0 (13.4)
	Geomean (CV%)	111.0 (17.6)	59.5 (15.3)	113.0 (21.2)	103.0 (13.1)
GMR (90% CI) [Test vs Reference][d]	–	–	**0.990 (0.967, 1.014)**	**0.898 (0.871, 0.927)**	**0.953 (0.941, 0.965)**

[a]For eGFR, only data from Day −1, pre-iohexol dose (baseline) and Day 7, pre-iohexol dose were included in the analysis. [b]Number of participants with evaluable data. [c]26 participants were excluded from the CLcr GMR analysis due to a lack of Day −1 and/or Day 7 CLcr data. [d]Data were analysed using a paired t-test and only participants with data at both Day −1 (baseline) and Day 7 were included in the analysis. GMRs and corresponding CIs were obtained by taking the exponential of the differences in means and corresponding CIs on the ln scale.
BSA, body surface area; CBD, cannabidiol; CI, confidence interval; CLcr, creatinine clearance; CV, coefficient of variation; eGFR, estimated glomerular filtration rate; GMR, geometric mean ratio; ln scale, natural logarithmic scale; mGFR, measured glomerular filtration rate; SD, standard deviation.

Main analysis

- The Day 7:baseline geometric mean ratio (GMR; 90% CI) for mGFR/BSA indicated no effect of CBD on glomerular filtration function (**Table 1**)
- Consistent with prior observations, minimal serum creatinine increases reflected in small decreases in creatinine-derived parameters, were noted (**Table 1**)

Sensitivity analysis

- In three participants, iohexol concentration–time profiles were inconsistent with IV infusion (**Figure 2B** and **2C**); however, these were retained in the primary analysis
- Excluding these three participants showed a similar trend for mGFR/BSA (Day 7:baseline GMR [90% CI]: 0.985 [0.962, 1.008])

Pharmacokinetic parameters of iohexol

Table 2. Summary of iohexol plasma pharmacokinetic parameters

observed plasma concentration; $t_{1/2}$, terminal elimination half-life.

- The geometric mean values of iohexol maximum measured plasma concentration (C_{max}), area under the curve $(AUC)_{0\text{-}last}$, AUC_{∞}, $\%AUC_{extrap}$, and terminal half-life, as well as median time to maximum plasma concentration (T_{max}) values were similar between Day −1 (iohexol alone) and Day 7 (CBD + iohexol; **Table 2**)

Pharmacokinetic parameters of CBD and its metabolites

Table 3. Summary of CBD and CBD metabolite plasma pharmacokinetic parameters

- Median T_{max} was similar for CBD and 7-OH-CBD (3.0 hours), with a slightly longer T_{max} observed for 7-COOH-CBD (4.0 hours)
  - Metabolite-to-parent ratio (MR) based on $AUC_{0\text{-}T}$ (MR_{AUC}) and MR_{Cmax} were higher for 7-COOH-CBD (37.2 and 18.4, respectively) compared with 7-OH-CBD (0.6 and 0.5, respectively)

Safety

Table 4. Summary of treatment-emergent adverse events (TEAEs)

TEAEs,[a] n (%)	Iohexol 5 mL (Day −1) (N=40)	CBD 7.5 mg/kg BID (Days 1–6) (N=39)	CBD 7.5 mg/kg + iohexol 5 mL (Day 7, AM) (N=39)	CBD 7.5 mg/kg (Day 7, PM) (N=39)	Overall[b] (N=40)
All-cause TEAEs	**5 (12.5)**	**15 (38.5)**	**3 (7.7)**	**3 (7.7)**	**18 (45.0)**
Iohexol-related TEAEs[c]	1 (2.5)	2 (5.1)	1 (2.6)	0	3 (7.5)
CBD-related TEAEs[c]	NA	3 (7.7)	2 (5.1)	0	5 (12.5)
TEAEs occurring in ≥5% of participants during any treatment period,[d] preferred term					
Diarrhoea	0	5 (12.8)	0	0	5 (12.5)
Nausea	0	3 (7.7)	2 (5.1)	0	5 (12.5)
Abdominal pain	0	3 (7.7)	1 (2.6)	0	3 (7.5)
Headache	1 (2.5)	1 (2.6)	2 (5.1)	0	3 (7.5)
Vomiting	0	0	1 (2.6)	1 (2.6)	2 (5.0)
Lethargy	0	2 (5.1)	0	0	2 (5.0)
Presyncope	0	1 (2.6)	1 (2.6)	0	2 (5.0)
Vessel puncture site haematoma	2 (5.0)	0	0	0	2 (5.0)

[a]Adverse events were coded using the Medical Dictionary for Regulatory Activities Version 27.1. [b]Overall indicates the total number of participants who experienced a TEAE during the study and may not equal the sum across study periods, as participants could have experienced TEAEs in more than one study period. [c]Treatment-related TEAEs were TEAEs with a plausible relationship to the study treatment, as determined by the investigator. [d]Only one (2.5%) renal TEAE (dysuria) was reported.
CBD, cannabidiol; NA, not applicable; TEAEs, treatment-emergent adverse events.

- Overall, 18 participants (45.0%) experienced TEAEs, most frequently during CBD dosing (Days 1–6; **Table 4**)
  - Three participants (7.5%) experienced iohexol-related TEAEs and five participants (12.5%) experienced CBD-related TEAEs
  - All TEAEs were mild in severity, with no serious TEAEs or TEAEs resulting in study discontinuation or death reported

Demographics and baseline characteristics

Table 5. Participant demographics

Demographic	Safety and pharmacodynamic population (N=40)	Pharmacokinetic population (N=39)
Age, years		
Mean (SD)	38.7 (10.9)	38.8 (11.0)
Median (range)	37.0 (23.0–60.0)	38.0 (23.0–60.0)
Sex, n (%)		
Female	24 (60.0)	23 (59.0)
Male	16 (40.0)	16 (41.0)
Race, n (%)		
White	26 (65.0)	26 (66.7)
Black or African American	12 (30.0)	11 (28.2)
Asian	2 (5.0)	2 (5.1)
Ethnicity, n (%)		
Hispanic or Latino	6 (15.0)	5 (12.8)
Other	34 (85.0)	34 (87.2)
Body weight, kg		
Mean (SD)	75.2 (13.4)	75.2 (13.6)
Median (range)	74.9 (51.9–103.7)	75.2 (51.9–103.7)

Demographic	Safety and pharmacodynamic population (N=40)	Pharmacokinetic population (N=39)
Body mass index, kg/m²		
Mean (SD)	25.5 (3.0)	25.5 (3.0)
Median (range)	25.9 (18.5–29.9)	25.90 (18.5–29.9)
Body surface area, m²		
Mean (SD)	1.9 (0.2)	1.9 (0.2)
Median (range)	1.9 (1.5–2.3)	1.9 (1.5–2.3)

SD, standard deviation.

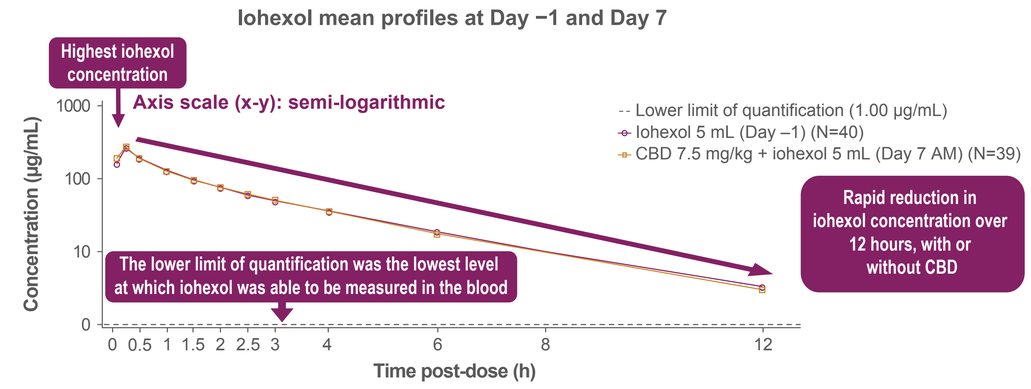
- The study enrolled 40 participants; all 40 received at least one dose of iohexol (safety and pharmacodynamic populations), and 39 received at least one dose of both iohexol and CBD (pharmacokinetic population)
  - One participant was withdrawn from the study after receiving iohexol due to not meeting eligibility criteria
  - Overall, 35 completed the study and 5 discontinued (participant withdrawal, n=3; failed to meet continuation criteria, n=1; lost to follow-up, n=1)
- Mean (standard deviation; range) age was 38.7 years (10.9; 23–60; **Table 5**)
- The majority of participants were female or White (**Table 5**)

2

Mean iohexol concentration–time profiles (pharmacodynamic analysis)

- Concentration–time profiles are graphs showing how the concentration of a medicine in the blood changes over time
- In this study, participants who received iohexol treatments had the **highest concentration of iohexol in their blood after 15 minutes**
  - After the highest concentration was achieved, iohexol concentration in the blood **rapidly decreased over 12 hours**
- When participants received iohexol in combination with CBD, the **same time to highest concentration and rapid decrease** in iohexol concentration was observed
- Data for iohexol alone were a mean from 40 participants, while iohexol and CBD combined was from 39 participants as one participant did not receive CBD
- These data indicated that **CBD had no effect** on the concentration of iohexol or how rapidly the body was able to remove iohexol

Iohexol mean profiles at Day −1 and Day 7



P0316

Effect of Cannabidiol on Measured Glomerular Filtration Rate in Healthy Participants: A Phase 1, Open-Label, Single-Site Study

Svetlana Markova,[1] Hongwei Xue,[1] Patricia Chandler,[1] Sujith Madhavan,[2] Cuiping Chen[1]

[1]Jazz Pharmaceuticals, Inc., Palo Alto, CA, USA;
[2]Jazz Pharmaceuticals, UK Ltd., London, UK.

Objective

- To assess the effect of cannabidiol (CBD) on measured glomerular filtration rate (mGFR), using iohexol as a probe compound, in healthy adults

Conclusions

- Multiple doses of CBD 7.5 mg/kg BID for 7 days had no effect on the mGFR and mGFR normalised for body surface area
- Consistent with historical observations, minor increases in serum creatinine were noted, as reflected by minor decreases (5–10%) in creatinine-derived parameters of estimated GFR and creatinine clearance
- The minor increase in serum creatinine following CBD administration was not due to an effect on renal glomerular filtration rate

References: 1. US Food and Drug Administration. Epidiolex® Prescribing Information. 2026. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/210365s024s029s030lbl.pdf (Accessed 19 August 2026). **2.** 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). **3.** 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). **4.** Ebert N, et al. *Kidney Int.* 2024;106(4):583–596. **5.** Pottel H, et al. *Nephrol Dial Transplant.* 2017;32(3):497–507. **6.** Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group 2024. *Kidney Int.* 2024;105(4S): S117–S314. **7.** Inker LA, et al. *N Engl J Med.* 2021;385(19):1737–1749.

Support and Acknowledgements: This study was sponsored by Jazz Pharmaceuticals, Inc. The authors would like to thank all of the study investigators, study staff, and participants for their participation in this research. Writing and editorial assistance were provided to the authors by Vijay Kadasi, MSc, on behalf of Syneos 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. **SvM, HX, PC,** and **CC** are employees of Jazz Pharmaceuticals, Inc., and hold stock and/or stock options in the company. **SuM** is an employee of Jazz Pharmaceuticals, UK Ltd., 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

Clin

Pa

- This study included healthy male and female participants, aged 18–60 years, with a body mass index of 18.5–30.0 kg/m², and a minimum body weight of 50.0 kg from a single centre in the US

Dosing

- **Day −1:** iohexol 5 mL (equivalent to 1.5 g iodine) was administered by intravenous (IV) infusion over a duration of 5 minutes
- **Days 1–6:** CBD 7.5 mg/kg was administered orally twice daily (BID), 30 minutes after starting a standardised meal, at approximately the same times each morning and evening (~12 hours apart [±15 minutes])
- **Day 7:** CBD 7.5 mg/kg was administered 30 minutes after starting a standardised breakfast, followed by iohexol 5 mL IV infusion over 5 minutes
  - Evening dose of CBD was administered ~12 hours after the morning dose (±15 minutes), following a standardised meal (identical to the meal provided on Day −1)

Sample collection and assessments

- On Day −1 and Day 7, 24-hour pooled urine collections were obtained for evaluation of creatinine clearance (CLcr)
  - Water intake was controlled to ensure adequate hydration and reduce variability in renal function parameters
- Blood samples for iohexol analysis were collected on Day −1 and Day 7 from pre-dose (before breakfast) to 12 hours post-dose (prior to the evening CBD dose on Day 7)
- Blood samples for CBD and metabolite analysis were collected on:
  - Days 1, 4, 5, and 6: pre-dose (before breakfast)
  - Day 7: pre-dose to 12 hours post-dose (prior to evening CBD dose)
- This study was conducted with Epidiolex®, and results do not apply to other CBD-containing products

Analyses

- Analysis populations:
  - Pharmacodynamic: all participants who received at least one dose of iohexol and had evaluable pharmacodynamic data
  - Pharmacokinetic: all participants who received at least one dose of CBD and had evaluable pharmacokinetic data
  - Safety: all participants who received at least one dose of study treatment
- Plasma pharmacodynamic and pharmacokinetic parameters were calculated using standard non-compartmental methods
  - Pharmacodynamic parameters were compared by a paired t-test and 2-sided 90% confidence intervals (CIs) for the GMR calculated; pharmacokinetic parameters were summarised descriptively with no formal statistical comparisons performed
  - The primary endpoint mGFR was calculated from the plasma clearance of iohexol and normalised against body surface area (BSA)

Figure 1. Study design

Primary endpoint

- Ratio (Day 7:baseline[a]) of mGFR[b] normalised to BSA (mGFR/BSA), calculated via iohexol plasma clearance

Secondary endpoints

- Ratio (Day 7:baseline[a]) of 24-hour CLcr[c]
- Ratio (Day 7:baseline[a]) of eGFR[d]
- Steady-state pharmacokinetic parameters of CBD and its metabolites 7-OH-CBD, and 7-COOH-CBD
- Treatment-emergent adverse events

[a]Baseline was Day −1. [b]mGFR, calculated via iohexol clearance. [c]CLcr calculated using serum creatinine and 24-hour urine creatinine and volume. [d]eGFR calculated using CKD-EPI Creatinine-Cystatin Equation (2021).[7]
BID, twice daily; BSA, body surface area; 7-COOH-CBD, 7-carboxy-cannabidiol; 7-OH-CBD, 7-hydroxy-cannabidiol; CBD, cannabidiol; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; CLcr, creatinine clearance; eGFR, estimated glomerular filtration rate; IV, intravenous; mGFR, measured glomerular filtration rate; OPV, outpatient visit.

Results

Iohexol concentration–time profiles

Figure 2. Arithmetic mean iohexol concentration–time profiles (pharmacodynamic population)

- Following infusion, the mean plasma iohexol concentrations peaked approximately 15 minutes after infusion start on both Day −1 (no CBD) and Day 7 (after 7 days of CBD 7.5 mg/kg BID)
- Iohexol concentrations then declined rapidly, with similar concentration–time profiles observed on Day −1 and Day 7, indicating no effect of CBD on iohexol pharmacokinetics (**Figure 2**)

Pharmacodynamic parameters: mGFR, mGFR/BSA, CLcr, and eGFR

Table 1. Summary of pharmacodynamic parameters

Parameter		mGFR (mL/min)	mGFR/BSA (mL/min/m²)	CLcr (mL/min)	eGFR[a] (mL/min/1.73 m²)
5 mL iohexol (Day −1, morning) [Reference]	N[b]	39	39	26	40
	Mean (SD)	114.0 (21.5)	60.8 (9.6)	120.0 (23.5)	108.0 (12.2)
	Geomean (CV%)	112.0 (18.8)	60.1 (16.1)	118.0 (21.2)	107.0 (11.5)
5 mL iohexol + 7.5 mg/kg CBD (Day 7, AM) [Test]	N[b]	39	39	13[c]	38
	Mean (SD)	112.0 (20.0)	60.2 (9.0)	115.0 (24.8)	103.0 (13.4)
	Geomean (CV%)	111.0 (17.6)	59.5 (15.3)	113.0 (21.2)	103.0 (13.1)
GMR (90% CI) [Test vs Reference][d]	–	–	**0.990 (0.967, 1.014)**	**0.898 (0.871, 0.927)**	**0.953 (0.941, 0.965)**

[a]For eGFR, only data from Day −1, pre-iohexol dose (baseline) and Day 7, pre-iohexol dose were included in the analysis. [b]Number of participants with evaluable data. [c]26 participants were excluded from the CLcr GMR analysis due to a lack of Day −1 and/or Day 7 CLcr data. [d]Data were analysed using a paired t-test and only participants with data at both Day −1 (baseline) and Day 7 were included in the analysis. GMRs and corresponding CIs were obtained by taking the exponential of the differences in means and corresponding CIs on the ln scale.
BSA, body surface area; CBD, cannabidiol; CI, confidence interval; CLcr, creatinine clearance; CV, coefficient of variation; eGFR, estimated glomerular filtration rate; GMR, geometric mean ratio; ln scale, natural logarithmic scale; mGFR, measured glomerular filtration rate; SD, standard deviation.

Main analysis

- The Day 7:baseline geometric mean ratio (GMR; 90% CI) for mGFR/BSA indicated no effect of CBD on glomerular filtration function (**Table 1**)
- Consistent with prior observations, minimal serum creatinine increases reflected in small decreases in creatinine-derived parameters, were noted (**Table 1**)

Sensitivity analysis

- In three participants, iohexol concentration–time profiles were inconsistent with IV infusion (**Figure 2B** and **2C**); however, these were retained in the primary analysis
- Excluding these three participants showed a similar trend for mGFR/BSA (Day 7:baseline GMR [90% CI]: 0.985 [0.962, 1.008])

Pharmacokinetic parameters of iohexol

Table 2. Summary of iohexol plasma pharmacokinetic parameters

- The geometric mean values of iohexol maximum measured plasma concentration (C_{max}), area under the curve $(AUC)_{0\text{-}last}$, AUC_{∞}, $\%AUC_{extrap}$, and terminal half-life, as well as median time to maximum plasma concentration (T_{max}) values were similar between Day −1 (iohexol alone) and Day 7 (CBD + iohexol; **Table 2**)

Pharmacokinetic parameters of CBD and its metabolites

Table 3. Summary of CBD and CBD metabolite plasma

observed for 7-COOH-CBD (4.0 hours)

- Metabolite-to-parent ratio (MR) based on $AUC_{0\text{-}t}$ (MR_{AUC}) and MR_{Cmax} were higher for 7-COOH-CBD (37.2 and 18.4, respectively) compared with 7-OH-CBD (0.6 and 0.5, respectively)

Safety

Table 4. Summary of treatment-emergent adverse events (TEAEs)

TEAEs,[a] n (%)	Iohexol 5 mL (Day −1) (N=40)	CBD 7.5 mg/kg BID (Days 1–6) (N=39)	CBD 7.5 mg/kg + iohexol 5 mL (Day 7, AM) (N=39)	CBD 7.5 mg/kg (Day 7, PM) (N=39)	Overall[b] (N=40)
All-cause TEAEs	**5 (12.5)**	**15 (38.5)**	**3 (7.7)**	**3 (7.7)**	**18 (45.0)**
Iohexol-related TEAEs[c]	1 (2.5)	2 (5.1)	1 (2.6)	0	3 (7.5)
CBD-related TEAEs[c]	NA	3 (7.7)	2 (5.1)	0	5 (12.5)
TEAEs occurring in ≥5% of participants during any treatment period,[d] preferred term					
Diarrhoea	0	5 (12.8)	0	0	5 (12.5)
Nausea	0	3 (7.7)	2 (5.1)	0	5 (12.5)
Abdominal pain	0	3 (7.7)	1 (2.6)	0	3 (7.5)
Headache	1 (2.5)	1 (2.6)	2 (5.1)	0	3 (7.5)
Vomiting	0	0	1 (2.6)	1 (2.6)	2 (5.0)
Lethargy	0	2 (5.1)	0	0	2 (5.0)
Presyncope	0	1 (2.6)	1 (2.6)	0	2 (5.0)
Vessel puncture site haematoma	2 (5.0)	0	0	0	2 (5.0)

[a]Adverse events were coded using the Medical Dictionary for Regulatory Activities Version 27.1. [b]Overall indicates the total number of participants who experienced a TEAE during the study and may not equal the sum across study periods, as participants could have experienced TEAEs in more than one study period. [c]Treatment-related TEAEs were TEAEs with a plausible relationship to the study treatment, as determined by the investigator. [d]Only one (2.5%) renal TEAE (dysuria) was reported.
CBD, cannabidiol; NA, not applicable; TEAEs, treatment-emergent adverse events.

- Overall, 18 participants (45.0%) experienced TEAEs, most frequently during CBD dosing (Days 1–6; **Table 4**)
  - Three participants (7.5%) experienced iohexol-related TEAEs and five participants (12.5%) experienced CBD-related TEAEs
  - All TEAEs were mild in severity, with no serious TEAEs or TEAEs resulting in study discontinuation or death reported

Demographics and baseline characteristics

Table 5. Participant demographics

Demographic	Safety and pharmacodynamic population (N=40)	Pharmacokinetic population (N=39)
Age, years		
Mean (SD)	38.7 (10.9)	38.8 (11.0)
Median (range)	37.0 (23.0–60.0)	38.0 (23.0–60.0)
Sex, n (%)		
Female	24 (60.0)	23 (59.0)
Male	16 (40.0)	16 (41.0)
Race, n (%)		
White	26 (65.0)	26 (66.7)
Black or African American	12 (30.0)	11 (28.2)
Asian	2 (5.0)	2 (5.1)
Ethnicity, n (%)		
Hispanic or Latino	6 (15.0)	5 (12.8)
Other	34 (85.0)	34 (87.2)
Body weight, kg		
Mean (SD)	75.2 (13.4)	75.2 (13.6)
Median (range)	74.9 (51.9–103.7)	75.2 (51.9–103.7)
Body mass index, kg/m²		
Mean (SD)	25.5 (3.0)	25.5 (3.0)
Median (range)	25.9 (18.5–29.9)	25.90 (18.5–29.9)
Body surface area, m²		
Mean (SD)	1.9 (0.2)	1.9 (0.2)
Median (range)	1.9 (1.5–2.3)	1.9 (1.5–2.3)

SD, standard deviation.

- The study enrolled 40 participants; all 40 received at least one dose of iohexol (safety and pharmacodynamic populations), and 39 received at least one dose of both iohexol and CBD (pharmacokinetic population)
  - One participant was withdrawn from the study after receiving iohexol due to not meeting eligibility criteria
  - Overall, 35 completed the study and 5 discontinued (participant withdrawal, n=3; failed to meet continuation criteria, n=1; lost to follow-up, n=1)
- Mean (standard deviation; range) age was 38.7 years (10.9; 23–60; **Table 5**)
- The majority of participants were female or White (**Table 5**)

3 Additional pharmacodynamic analyses

- Pharmacodynamic parameters are measures indicating how a medicine affects the body (eg, change in symptoms or body functions)
- Geometric mean ratios are used to compare two values over time, with values <0.80 considered to be a potentially substantial decrease
- In this study, the geometric mean ratio was used to compare multiple measures of kidney function at **baseline (before CBD treatment)** and on the **seventh day of CBD treatment**

The main measure of kidney function in this study was measured glomerular filtration rate (a direct measure of how well the kidneys filter blood) after participant's body surface area was taken into account	**The geometric mean ratio was 0.99 after CBD treatment, indicating CBD did not substantially affect glomerular filtration function or kidney filtering**
Additionally, the geometric mean ratios were **0.90 for creatinine clearance** (how well kidneys can filter creatinine) and **0.95 for estimated glomerular filtration rate** (an estimate of how well kidneys filter blood)	**These represented ~5–10% reductions in the body's ability to filter creatinine (ie, a 5–10% increase in blood creatinine levels)**

Taken together, these data reflect the previously reported creatinine increases, but do not suggest any concern regarding reduced kidney filtering when participants received CBD

P0316

Effect of Cannabidiol on Measured Glomerular Filtration Rate in Healthy Participants: A Phase 1, Open-Label, Single-Site Study

Svetlana Markova,[1] Hongwei Xue,[1] Patricia Chandler,[1] Sujith Madhavan,[2] Cuiping Chen[1]

[1]Jazz Pharmaceuticals, Inc., Palo Alto, CA, USA;
[2]Jazz Pharmaceuticals, UK Ltd., London, UK.

Objective

- To assess the effect of cannabidiol (CBD) on measured glomerular filtration rate (mGFR), using iohexol as a probe compound, in healthy adults

Conclusions

- Multiple doses of CBD 7.5 mg/kg BID for 7 days had no effect on the mGFR and mGFR normalised for body surface area
- Consistent with historical observations, minor increases in serum creatinine were noted, as reflected by minor decreases (5–10%) in creatinine-derived parameters of estimated GFR and creatinine clearance
- The minor increase in serum creatinine following CBD administration was not due to an effect on renal glomerular filtration rate

References:
1. https://
2. Es
http
g
e
7
S
s
s
(
D
w
S
E
c
tu
C

– Evening dose of CBD was administered ~12 hours after the morning dose (±15 minutes), following a standardised meal (identical to the meal provided on Day −1)

Sample collection and assessments

- On Day −1 and Day 7, 24-hour pooled urine collections were obtained for evaluation of creatinine clearance (CLcr)
  – Water intake was controlled to ensure adequate hydration and reduce variability in renal function parameters
- Blood samples for iohexol analysis were collected on Day −1 and Day 7 from pre-dose (before breakfast) to 12 hours post-dose (prior to the evening CBD dose on Day 7)
- Blood samples for CBD and metabolite analysis were collected on:
  – Days 1, 4, 5, and 6: pre-dose (before breakfast)
  – Day 7: pre-dose to 12 hours post-dose (prior to evening CBD dose)
- This study was conducted with Epidiolex®, and results do not apply to other CBD-containing products

Analyses

- Analysis populations:
  – Pharmacodynamic: all participants who received at least one dose of iohexol and had evaluable pharmacodynamic data
  – Pharmacokinetic: all participants who received at least one dose of CBD and had evaluable pharmacokinetic data
  – Safety: all participants who received at least one dose of study treatment
- Plasma pharmacodynamic and pharmacokinetic parameters were calculated using standard non-compartmental methods
  – Pharmacodynamic parameters were compared by a paired t-test and 2-sided 90% confidence intervals (CIs) for the GMR calculated; pharmacokinetic parameters were summarised descriptively with no formal statistical comparisons performed
  – The primary endpoint mGFR was calculated from the plasma clearance of iohexol and normalised against body surface area (BSA)

Figure 1. Study design

Primary endpoint

- Ratio (Day 7:baseline[a]) of mGFR[b] normalised to BSA (mGFR/BSA), calculated via iohexol plasma clearance

Secondary endpoints

- Ratio (Day 7:baseline[a]) of 24-hour CLcr[c]
- Ratio (Day 7:baseline[a]) of eGFR[d]
- Steady-state pharmacokinetic parameters of CBD and its metabolites 7-OH-CBD, and 7-COOH-CBD
- Treatment-emergent adverse events

[a]Baseline was Day −1. [b]mGFR, calculated via iohexol clearance. [c]CLcr calculated using serum creatinine and 24-hour urine creatinine and volume. [d]eGFR calculated using CKD-EPI Creatinine-Cystatin Equation (2021).[7]
BID, twice daily; BSA, body surface area; 7-COOH-CBD, 7-carboxy-cannabidiol; 7-OH-CBD, 7-hydroxy-cannabidiol; CBD, cannabidiol; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; CLcr, creatinine clearance; eGFR, estimated glomerular filtration rate; IV, intravenous; mGFR, measured glomerular filtration rate; OPV, outpatient visit.

Results

Iohexol concentration–time profiles

Figure 2. Arithmetic mean iohexol concentration–time profiles (pharmacodynamic population)

- Following infusion, the mean plasma iohexol concentrations peaked approximately 15 minutes after infusion start on both Day −1 (no CBD) and Day 7 (after 7 days of CBD 7.5 mg/kg BID)
- Iohexol concentrations then declined rapidly, with similar concentration–time profiles observed on Day −1 and Day 7, indicating no effect of CBD on iohexol pharmacokinetics (**Figure 2**)

Pharmacodynamic parameters: mGFR, mGFR/BSA, CLcr, and eGFR

Table 1. Summary of pharmacodynamic parameters

Parameter		mGFR (mL/min)	mGFR/BSA (mL/min/m²)	CLcr (mL/min)	eGFR[a] (mL/min/1.73 m²)
5 mL iohexol (Day −1, morning) [Reference]	N[b]	39	39	26	40
	Mean (SD)	114.0 (21.5)	60.8 (9.6)	120.0 (23.5)	108.0 (12.2)
	Geomean (CV%)	112.0 (18.8)	60.1 (16.1)	118.0 (21.2)	107.0 (11.5)
5 mL iohexol + 7.5 mg/kg CBD (Day 7, AM) [Test]	N[b]	39	39	13[c]	38
	Mean (SD)	112.0 (20.0)	60.2 (9.0)	115.0 (24.8)	103.0 (13.4)
	Geomean (CV%)	111.0 (17.6)	59.5 (15.3)	113.0 (21.2)	103.0 (13.1)
GMR (90% CI) [Test vs Reference][d]	–	–	0.990 (0.967, 1.014)	0.898 (0.871, 0.927)	0.953 (0.941, 0.965)

[a]For eGFR, only data from Day −1, pre-iohexol dose (baseline) and Day 7, pre-iohexol dose were included in the analysis. [b]Number of participants with evaluable data. [c]26 participants were excluded from the CLcr GMR analysis due to a lack of Day −1 and/or Day 7 CLcr data. [d]Data were analysed using a paired t-test and only participants with data at both Day −1 (baseline) and Day 7 were included in the analysis. GMRs and corresponding CIs were obtained by taking the exponential of the differences in means and corresponding CIs on the ln scale.
BSA, body surface area; CBD, cannabidiol; CI, confidence interval; CLcr, creatinine clearance; CV, coefficient of variation; eGFR, estimated glomerular filtration rate; GMR, geometric mean ratio; ln scale, natural logarithmic scale; mGFR, measured glomerular filtration rate; SD, standard deviation.

Main analysis

- The [illegible] GMR [illegible] 0.990 (0.967, 1.014) [illegible] 0.953 (0.941, 0.965) [illegible] of mGFR

4 Pharmacokinetic analysis

- Pharmacokinetic parameters are measures indicating what happens to a medicine after it is taken (eg, how fast it is absorbed)
- This study measured pharmacokinetic parameters of iohexol and CBD:
  – Parameters for iohexol were analysed by comparing pharmacokinetic parameters when receiving just iohexol (Baseline at Day −1) with those when receiving iohexol and CBD after 6 days of CBD treatment (Day 7, AM)
  – Parameters for CBD were analysed by comparing pharmacokinetic parameters for CBD and its metabolites (materials formed when a medicine has been processed by the body) when receiving iohexol and CBD after 6 days of CBD treatment (Day 7, AM)
- The pharmacokinetic parameters assessed across the study included the following:

Parameter	Definition	Parameters for each study
AUC	**Area under the curve (AUC)** is a measure of the body's total exposure to a medicine over time	Both
AUC_{0-last}	AUC_{0-last} is the total drug exposure from before the first dose up to the last reliable measurement	Iohexol
AUC_{∞}	AUC_{∞} is the estimated total drug exposure from before the first dose up to infinity (includes estimation of drug exposure after the last reliable measurement)	Iohexol
$\%AUC_{extrap}$	$\%AUC_{extrap}$ is the proportion of AUC_{∞} that was estimated rather than directly measured (a lower value generally indicates increased reliability)	Iohexol
$AUC_{0-\tau}$	$AUC_{0-\tau}$ is the total drug exposure from before the first dose up to a specific timepoint; in this study, this was the end of each dosing interval (~12 hours)	CBD
C_{max}	C_{max} is the highest concentration of a medicine measured in the blood	Both
MR_{AUC}	MR_{AUC} is the ratio comparing the overall exposure of a metabolite with the original medicine based on AUC	CBD
MR_{Cmax}	MR_{Cmax} is the ratio comparing the highest concentration of a metabolite with the original medicine based on C_{max}	CBD
$t_{1/2}$	$t_{1/2}$, or half-life, is the time it takes for the concentration of a medicine in the body to decrease by half (50%)	Iohexol
T_{max}	T_{max} is the time it takes to reach the highest concentration of a medicine measured in the blood	Iohexol

Iohexol

Iohexol pharmacokinetic parameters were similar between Day −1 (iohexol alone) and Day 7 (CBD + iohexol)

CBD (Day 7, AM; CBD plus iohexol)

CBD pharmacokinetic parameters were consistent with historic data for CBD and CBD metabolites 7-hydroxy-CBD (7-OH-CBD) and 7-carboxy-CBD (7-COOH-CBD)

TEAEs,[a] n (%)	5 mL iohexol (Day −1) (N=40)	7.5 mg/kg CBD (Days 1–6) (N=39)	5 mL (Day 7, AM) (N=39)	(Day 7, PM) (N=39)	[illegible] (N=40)
All-cause TEAEs	5 (12.5)	15 (38.5)	3 (7.7)	3 (7.7)	18 (45.0)
Iohexol-related TEAEs[c]	1 (2.5)	2 (5.1)	1 (2.6)	0	3 (7.5)
CBD-related TEAEs[c]	NA	3 (7.7)	2 (5.1)	0	5 (12.5)
TEAEs occurring in ≥5% of participants during any treatment period,[d] preferred term					
Diarrhoea	0	5 (12.8)	0	0	5 (12.5)
Nausea	0	3 (7.7)	2 (5.1)	0	5 (12.5)
Abdominal pain	0	3 (7.7)	1 (2.6)	0	3 (7.5)
Headache	1 (2.5)	1 (2.6)	2 (5.1)	0	3 (7.5)
Vomiting	0	0	1 (2.6)	1 (2.6)	2 (5.0)
Lethargy	0	2 (5.1)	0	0	2 (5.0)
Presyncope	0	1 (2.6)	1 (2.6)	0	2 (5.0)
Vessel puncture site haematoma	2 (5.0)	0	0	0	2 (5.0)

[a]Adverse events were coded using the Medical Dictionary for Regulatory Activities Version 27.1. [b]Overall indicates the total number of participants who experienced a TEAE during the study and may not equal the sum across study periods, as participants could have experienced TEAEs in more than one study period. [c]Treatment-related TEAEs were TEAEs with a plausible relationship to the study treatment, as determined by the investigator. [d]Only one (2.5%) renal TEAE (dysuria) was reported.
CBD, cannabidiol; NA, not applicable; TEAEs, treatment-emergent adverse events.

- Overall, 18 participants (45.0%) experienced TEAEs, most frequently during CBD dosing (Days 1–6; **Table 4**)
  – Three participants (7.5%) experienced iohexol-related TEAEs and five participants (12.5%) experienced CBD-related TEAEs
  – All TEAEs were mild in severity, with no serious TEAEs or TEAEs resulting in study discontinuation or death reported

Demographics and baseline characteristics

Table 5. Participant demographics

Demographic	Safety and pharmacodynamic population (N=40)	Pharmacokinetic population (N=39)
Age, years		
Mean (SD)	38.7 (10.9)	38.8 (11.0)
Median (range)	37.0 (23.0–60.0)	38.0 (23.0–60.0)
Sex, n (%)		
Female	24 (60.0)	23 (59.0)
Male	16 (40.0)	16 (41.0)
Race, n (%)		
White	26 (65.0)	26 (66.7)
Black or African American	12 (30.0)	11 (28.2)
Asian	2 (5.0)	2 (5.1)
Ethnicity, n (%)		
Hispanic or Latino	6 (15.0)	5 (12.8)
Other	34 (85.0)	34 (87.2)
Body weight, kg		
Mean (SD)	75.2 (13.4)	75.2 (13.6)
Median (range)	74.9 (51.9–103.7)	75.2 (51.9–103.7)
Body mass index, kg/m²		
Mean (SD)	25.5 (3.0)	25.5 (3.0)
Median (range)	25.9 (18.5–29.9)	25.90 (18.5–29.9)
Body surface area, m²		
Mean (SD)	1.9 (0.2)	1.9 (0.2)
Median (range)	1.9 (1.5–2.3)	1.9 (1.5–2.3)

SD, standard deviation.

- The study enrolled 40 participants; all 40 received at least one dose of iohexol (safety and pharmacodynamic populations), and 39 received at least one dose of both iohexol and CBD (pharmacokinetic population)
  – One participant was withdrawn from the study after receiving iohexol due to not meeting eligibility criteria
  – Overall, 35 completed the study and 5 discontinued (participant withdrawal, n=3; failed to meet continuation criteria, n=1; lost to follow-up, n=1)
- Mean (standard deviation; range) age was 38.7 years (10.9; 23–60; **Table 5**)
- The majority of participants were female or White (**Table 5**)

P0316

Effect of Cannabidiol on Measured Glomerular Filtration Rate in Healthy Participants: A Phase 1, Open-Label, Single-Site Study

Svetlana Markova,[1] Hongwei Xue,[1] Patricia Chandler,[1] Sujith Madhavan,[2] Cuiping Chen[1]

[1]Jazz Pharmaceuticals, Inc., Palo Alto, CA, USA;
[2]Jazz Pharmaceuticals, UK Ltd., London, UK.

Objective

- To assess the effect of cannabidiol (CBD) on measured glomerular filtration rate (mGFR), using iohexol as a probe compound, in healthy adults

Conclusions

- Multiple doses of CBD 7.5 mg/kg BID for 7 days had no effect on the mGFR and mGFR normalised for body surface area
- Consistent with historical observations, minor increases in serum creatinine were noted, as reflected by minor decreases (5–10%) in creatinine-derived parameters of estimated GFR and creatinine clearance
- The minor increase in serum creatinine following CBD administration was not due to an effect on renal glomerular filtration rate

References: 1. US Food and Drug Administration. Epidiolex® Prescribing Information. 2026. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/210365s024s029s030lbl.pdf (Accessed 19 August 2026). **2.** 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). **3.** 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). **4.** Ebert N, et al. *Kidney Int*. 2024;106(4):583–596. **5.** Pottel H, et al. *Nephrol Dial Transplant*. 2017;32(3):497–507. **6.** Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group 2024. *Kidney Int*. 2024;105(4S): S117–S314. **7.** Inker LA, et al. *N Engl J Med*. 2021;385(19):1737–1749.

Support and Acknowledgements: This study was sponsored by Jazz Pharmaceuticals, Inc. The authors would like to thank all of the study investigators, study staff, and participants for their participation in this research. Writing and editorial assistance were provided to the authors by Vijay Kadasi, MSc, on behalf of Syneos 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

Dosing

- **Day −1:** iohexol 5 mL (equivalent to 1.5 g iodine) was administered by intravenous (IV) infusion over a duration of 5 minutes
- **Days 1–6:** CBD 7.5 mg/kg was administered orally twice daily (BID), 30 minutes after starting a standardised meal, at approximately the same times each morning and evening (~12 hours apart [±15 minutes])
- **Day 7:** CBD 7.5 mg/kg was administered 30 minutes after starting a standardised breakfast, followed by iohexol 5 mL IV infusion over 5 minutes
  - Evening dose of CBD was administered ~12 hours after the morning dose (±15 minutes), following a standardised meal (identical to the meal provided on Day −1)

Sample collection and assessments

- On Day −1 and Day 7, 24-hour pooled urine collections were obtained for evaluation of creatinine clearance (CLcr)
  - Water intake was controlled to ensure adequate hydration and reduce variability in renal function parameters
- Blood samples for iohexol analysis were collected on Day −1 and Day 7 from pre-dose (before breakfast) to 12 hours post-dose (prior to the evening CBD dose on Day 7)
- Blood samples for CBD and metabolite analysis were collected on:
  - Days 1, 4, 5, and 6: pre-dose (before breakfast)
  - Day 7: pre-dose to 12 hours post-dose (prior to evening CBD dose)
- This study was conducted with Epidiolex®, and results do not apply to other CBD-containing products

Analyses

- Analysis populations:
  - Pharmacodynamic: all participants who received at least one dose of iohexol and had evaluable pharmacodynamic data
  - Pharmacokinetic: all participants who received at least one dose of CBD and had evaluable pharmacokinetic data
  - Safety: all participants who received at least one dose of study treatment
- Plasma pharmacodynamic and pharmacokinetic parameters were calculated using standard non-compartmental methods
  - Pharmacodynamic parameters were compared by a paired t-test and 2-sided 90% confidence intervals (CIs) for the GMR calculated; pharmacokinetic parameters were summarised descriptively with no formal statistical comparisons performed
  - The primary endpoint mGFR was calculated from the plasma clearance of iohexol and normalised against body surface area (BSA)

Figure 1. Study design

Primary endpoint

- Ratio (Day 7:baseline[a]) of mGFR[b] normalised to BSA (mGFR/BSA), calculated via iohexol plasma clearance

Secondary endpoints

- Ratio (Day 7:baseline[a]) of 24-hour CLcr[c]
- Ratio (Day 7:baseline[a]) of eGFR[d]
- Steady-state pharmacokinetic parameters of CBD and its metabolites 7-OH-CBD, and 7-COOH-CBD
- Treatment-emergent adverse events

[a]Baseline was Day −1. [b]mGFR, calculated via iohexol clearance. [c]CLcr calculated using serum creatinine and 24-hour urine creatinine and volume. [d]eGFR calculated using CKD-EPI Creatinine-Cystatin Equation (2021).[7]
BID, twice daily; BSA, body surface area; 7-COOH-CBD, 7-carboxy-cannabidiol; 7-OH-CBD, 7-hydroxy-cannabidiol; CBD, cannabidiol; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; CLcr, creatinine clearance; eGFR, estimated glomerular filtration rate; IV, intravenous; mGFR, measured glomerular filtration rate; OPV, outpatient visit.

Results

Iohexol concentration–time profiles

Figure 2. Arithmetic mean iohexol concentration–time profiles (pharmacodynamic population)

- Following infusion, the mean plasma iohexol concentrations peaked approximately 15 minutes after infusion start on both Day −1 (no CBD) and Day 7 (after 7 days of CBD 7.5 mg/kg BID)
- Iohexol concentrations then declined rapidly, with similar concentration–time profiles observed on Day −1 and Day 7, indicating no effect of CBD on iohexol pharmacokinetics (**Figure 2**)

Pharmacodynamic parameters: mGFR, mGFR/BSA, CLcr, and eGFR

Table 1. Summary of pharmacodynamic parameters

Parameter		mGFR (mL/min)	mGFR/BSA (mL/min/m²)	CLcr (mL/min)	eGFR[a] (mL/min/1.73 m²)
5 mL iohexol (Day −1, morning) [Reference]	N[b]	39	39	26	40
	Mean (SD)	114.0 (21.5)	60.8 (9.6)	120.0 (23.5)	108.0 (12.2)
	Geomean (CV%)	112.0 (18.8)	60.1 (16.1)	118.0 (21.2)	107.0 (11.5)
5 mL iohexol + 7.5 mg/kg CBD (Day 7, AM) [Test]	N[b]	39	39	13[c]	38
	Mean (SD)	112.0 (20.0)	60.2 (9.0)	115.0 (24.8)	103.0 (13.4)
	Geomean (CV%)	111.0 (17.6)	59.5 (15.3)	113.0 (21.2)	103.0 (13.1)
GMR (90% CI) [Test vs Reference][d]	–	–	**0.990 (0.967, 1.014)**	**0.898 (0.871, 0.927)**	**0.953 (0.941, 0.965)**

[a]For eGFR, only data from Day −1, pre-iohexol dose (baseline) and Day 7, pre-iohexol dose were included in the analysis. [b]Number of participants with evaluable data. [c]26 participants were excluded from the CLcr GMR analysis due to a lack of Day −1 and/or Day 7 CLcr data. [d]Data were analysed using a paired t-test and only participants with data at both Day −1 (baseline) and Day 7 were included in the analysis. GMRs and corresponding CIs were obtained by taking the exponential of the differences in means and corresponding CIs on the ln scale.
BSA, body surface area; CBD, cannabidiol; CI, confidence interval; CLcr, creatinine clearance; CV, coefficient of variation; eGFR, estimated glomerular filtration rate; GMR, geometric mean ratio; ln scale, natural logarithmic scale; mGFR, measured glomerular filtration rate; SD, standard deviation.

Main analysis

- The Day 7:baseline geometric mean ratio (GMR; 90% CI) for mGFR/BSA indicated no effect of CBD on glomerular filtration function (**Table 1**)
- Consistent with prior observations, minimal serum creatinine increases reflected in small decreases in creatinine-derived parameters, were noted (**Table 1**)

Sensitivity analysis

- In three participants, iohexol concentration–time profiles were inconsistent with IV infusion (**Figure 2B** and **2C**); however, these were retained in the primary analysis
- Excluding these three participants showed a similar trend for mGFR/BSA (Day 7:baseline GMR [90% CI]: 0.985 [0.962, 1.008])

Pharmacokinetic parameters of iohexol

- Median time to maximum plasma concentration (Tmax) values were similar between Day −1 (iohexol alone) and Day 7 (CBD + iohexol; **Table 2**)

Pharmacokinetic parameters of CBD and its metabolites

- Median Tmax values were similar for 7-COOH-CBD (37.2 and 18.4, respectively) compared with 7-OH-CBD (0.6 and 0.5, respectively)

Safety

Table 4. Summary of treatment-emergent adverse events (TEAEs)

TEAEs,[a] n (%)	Iohexol 5 mL (Day −1) (N=40)	CBD 7.5 mg/kg BID (Days 1–6) (N=39)	CBD 7.5 mg/kg + iohexol 5 mL (Day 7, AM) (N=39)	CBD 7.5 mg/kg (Day 7, PM) (N=39)	Overall[b] (N=40)
All-cause TEAEs	**5 (12.5)**	**15 (38.5)**	**3 (7.7)**	**3 (7.7)**	**18 (45.0)**
Iohexol-related TEAEs[c]	1 (2.5)	2 (5.1)	1 (2.6)	0	3 (7.5)
CBD-related TEAEs[c]	NA	3 (7.7)	2 (5.1)	0	5 (12.5)
TEAEs occurring in ≥5% of participants during any treatment period,[d] preferred term					
Diarrhoea	0	5 (12.8)	0	0	5 (12.5)
Nausea	0	3 (7.7)	2 (5.1)	0	5 (12.5)
Abdominal pain	0	3 (7.7)	1 (2.6)	0	3 (7.5)
Headache	1 (2.5)	1 (2.6)	2 (5.1)	0	3 (7.5)
Vomiting	0	0	1 (2.6)	1 (2.6)	2 (5.0)
Lethargy	0	2 (5.1)	0	0	2 (5.0)
Presyncope	0	1 (2.6)	1 (2.6)	0	2 (5.0)
Vessel puncture site haematoma	2 (5.0)	0	0	0	2 (5.0)

[a]Adverse events were coded using the Medical Dictionary for Regulatory Activities Version 27.1. [b]Overall indicates the total number of participants who experienced a TEAE during the study and may not equal the sum across study periods, as participants could have experienced TEAEs in more than one study period. [c]Treatment-related TEAEs were TEAEs with a plausible relationship to the study treatment, as determined by the investigator. [d]Only one (2.5%) renal TEAE (dysuria) was reported.
CBD, cannabidiol; NA, not applicable; TEAEs, treatment-emergent adverse events.

- Overall, 18 participants (45.0%) experienced TEAEs, most frequently during CBD dosing (Days 1–6; **Table 4**)
  - Three participants (7.5%) experienced iohexol-related TEAEs and five participants (12.5%) experienced CBD-related TEAEs
  - All TEAEs were mild in severity, with no serious TEAEs or TEAEs resulting in study discontinuation or death reported

Demographics and baseline characteristics

Table 5. Participant demographics

Demographic	Safety and pharmacodynamic population (N=40)	Pharmacokinetic population (N=39)
Age, years		
Mean (SD)	38.7 (10.9)	38.8 (11.0)
Median (range)	37.0 (23.0–60.0)	38.0 (23.0–60.0)
Sex, n (%)		
Female	24 (60.0)	23 (59.0)
Male	16 (40.0)	16 (41.0)
Race, n (%)		
White	26 (65.0)	26 (66.7)
Black or African American	12 (30.0)	11 (28.2)
Asian	2 (5.0)	2 (5.1)
Ethnicity, n (%)		
Hispanic or Latino	6 (15.0)	5 (12.8)
Other	34 (85.0)	34 (87.2)
Body weight, kg		
Mean (SD)	75.2 (13.4)	75.2 (13.6)
Median (range)	74.9 (51.9–103.7)	75.2 (51.9–103.7)

Demographic	Safety and pharmacodynamic population (N=40)	Pharmacokinetic population (N=39)
Body mass index, kg/m²		
Mean (SD)	25.5 (3.0)	25.5 (3.0)
Median (range)	25.9 (18.5–29.9)	25.90 (18.5–29.9)
Body surface area, m²		
Mean (SD)	1.9 (0.2)	1.9 (0.2)
Median (range)	1.9 (1.5–2.3)	1.9 (1.5–2.3)

SD, standard deviation.

- The study enrolled 40 participants; all 40 received at least one dose of iohexol (safety and pharmacodynamic populations), and 39 received at least one dose of both iohexol and CBD (pharmacokinetic population)
  - One participant was withdrawn from the study after receiving iohexol due to not meeting eligibility criteria
  - Overall, 35 completed the study and 5 discontinued (participant withdrawal, n=3; failed to meet continuation criteria, n=1; lost to follow-up, n=1)
- Mean (standard deviation; range) age was 38.7 years (10.9; 23–60; **Table 5**)
- The majority of participants were female or White (**Table 5**)

5

Safety analysis

18 (45%) participants experienced a side effect during the study

3 (7.5%) Had side effects related to iohexol

5 (12.5%) Had side effects related to CBD

The most common side effects across all treatment groups were:

- **Diarrhoea in 5 (12.5%) participants**
- **Nausea in 5 (12.5%) participants**
- **Abdominal pain in 3 (7.5%) participants**
- **Headache in 3 (7.5%) participants**

All side effects were mild

No side effects were serious

No side effects resulted in a participant needing to stop iohexol or CBD

P0316

Effect of Cannabidiol on Measured Glomerular Filtration Rate in Healthy Participants: A Phase 1, Open-Label, Single-Site Study

Svetlana Markova,[1] Hongwei Xue,[1] Patricia Chandler,[1] Sujith Madhavan,[2] Cuiping Chen[1]
[1]Jazz Pharmaceuticals, Inc., Palo Alto, CA, USA;
[2]Jazz Pharmaceuticals, UK Ltd., London, UK.

Objective

- To assess the effect of cannabidiol (CBD) on measured glomerular filtration rate (mGFR), using iohexol as a probe compound, in healthy adults

Conclusions

- Multiple doses of CBD 7.5 mg/kg BID for 7 days had no effect on the mGFR and mGFR normalised for body surface area
- Consistent with historical observations, minor increases in serum creatinine were noted, as reflected by minor decreases (5–10%) in creatinine-derived parameters of estimated GFR and creatinine clearance
- The minor increase in serum creatinine following CBD administration was not due to an effect on renal glomerular filtration rate

Results

Iohexol concentration–time profiles

Figure 2. Arithmetic mean iohexol concentration–time profiles (pharmacodynamic population)

- Following infusion, the mean plasma iohexol concentrations peaked approximately 15 minutes after infusion start on both Day −1 (no CBD) and Day 7 (after 7 days of CBD 7.5 mg/kg BID)
- Iohexol concentrations then declined rapidly, with similar concentration–time profiles observed on Day −1 and Day 7, indicating no effect of CBD on iohexol pharmacokinetics (**Figure 2**)

Pharmacodynamic parameters: mGFR, mGFR/BSA, CLcr, and eGFR

Table 1. Summary of pharmacodynamic parameters

Parameter		mGFR (mL/min)	mGFR/BSA (mL/min/m²)	CLcr (mL/min)	eGFR[a] (mL/min/1.73 m²)
5 mL iohexol (Day −1, morning) [Reference]	N[b]	39	39	26	40
	Mean (SD)	114.0 (21.5)	60.8 (9.6)	120.0 (23.5)	108.0 (12.2)
	Geomean (CV%)	112.0 (18.8)	60.1 (16.1)	118.0 (21.2)	107.0 (11.5)
5 mL iohexol + 7.5 mg/kg CBD (Day 7, AM) [Test]	N[b]	39	39	13[c]	38
	Mean (SD)	112.0 (20.0)	60.2 (9.0)	115.0 (24.8)	103.0 (13.4)
	Geomean (CV%)	111.0 (17.6)	59.5 (15.3)	113.0 (21.2)	103.0 (13.1)
GMR (90% CI) [Test vs Reference][d]	–	–	**0.990 (0.967, 1.014)**	**0.898 (0.871, 0.927)**	**0.953 (0.941, 0.965)**

[a]For eGFR, only data from Day −1, pre-iohexol dose (baseline) and Day 7, pre-iohexol dose were included in the analysis. [b]Number of participants with evaluable data. [c]26 participants were excluded from the CLcr GMR analysis due to a lack of Day −1 and/or Day 7 CLcr data. [d]Data were analysed using a paired t-test and only participants with data at both Day −1 (baseline) and Day 7 were included in the analysis. GMRs and corresponding CIs were obtained by taking the exponential of the differences in means and corresponding CIs on the ln scale. BSA, body surface area; CBD, cannabidiol; CI, confidence interval; CLcr, creatinine clearance; CV, coefficient of variation; eGFR, estimated glomerular filtration rate; GMR, geometric mean ratio; ln scale, natural logarithmic scale; mGFR, measured glomerular filtration rate; SD, standard deviation.

Main analysis

6

Participants and participant demographics

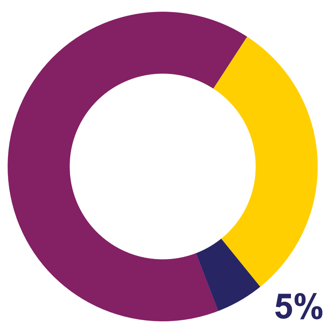
- **40** participants were included in the study
- **39** participants received both iohexol and CBD
- **35** participants completed the study

All participants were 23–60 years old

23 (minimum) — 37 Median age, years — 60 (maximum)

There were more female than male participants: 60% female, 40% male

The majority were White



65% were White; 30% were Black or African American; 5% were Asian

The average participant:

- Weighed 75 kg
- Had a body mass index of 25.5 kg/m²

The analyses performed in this study used three different populations, based on which analysis was done:

Pharmacodynamic analysis	Included all participants who received at least one dose of iohexol and had available data
Pharmacokinetic analysis	Included all participants who received at least one dose of CBD and had available data
Safety analysis	Included all participants who received at least one dose of iohexol or CBD

Sample collection and assessments

- On Day −1 and Day 7, 24-hour pooled urine collections were obtained for evaluation of creatinine clearance (CLcr)
  - Water intake was controlled to ensure adequate hydration and reduce variability in renal function parameters
- Blood samples for iohexol analysis were collected on Day −1 and Day 7 from pre-dose (before breakfast) to 12 hours post-dose (prior to the evening CBD dose on Day 7)
- Blood samples for CBD and metabolite analysis were collected on:
  - Days 1, 4, 5, and 6: pre-dose (before breakfast)
  - Day 7: pre-dose to 12 hours post-dose (prior to evening CBD dose)
- This study was conducted with Epidiolex®, and results do not apply to other CBD-containing products

Analyses

- Analysis populations:
  - Pharmacodynamic: all participants who received at least one dose of iohexol and had evaluable pharmacodynamic data
  - Pharmacokinetic: all participants who received at least one dose of CBD and had evaluable pharmacokinetic data
  - Safety: all participants who received at least one dose of study treatment
- Plasma pharmacodynamic and pharmacokinetic parameters were calculated using standard non-compartmental methods
  - Pharmacodynamic parameters were compared by a paired t-test and 2-sided 90% confidence intervals (CIs) for the GMR calculated; pharmacokinetic parameters were summarised descriptively with no formal statistical comparisons performed
  - The primary endpoint mGFR was calculated from the plasma clearance of iohexol and normalised against body surface area (BSA)

Figure 1. Study design

Primary endpoint
- Ratio (Day 7:baseline[a]) of mGFR[b] normalised to BSA (mGFR/BSA), calculated via iohexol plasma clearance

Secondary endpoints
- Ratio (Day 7:baseline[a]) of 24-hour CLcr[c]
- Ratio (Day 7:baseline[a]) of eGFR[d]
- Steady-state pharmacokinetic parameters of CBD and its metabolites 7-OH-CBD, and 7-COOH-CBD
- Treatment-emergent adverse events

[a]Baseline was Day −1. [b]mGFR, calculated via iohexol clearance. [c]CLcr calculated using serum creatinine and 24-hour urine creatinine and volume. [d]eGFR calculated using CKD-EPI Creatinine-Cystatin Equation (2021).[7]
BID, twice daily; BSA, body surface area; 7-COOH-CBD, 7-carboxy-cannabidiol; 7-OH-CBD, 7-hydroxy-cannabidiol; CBD, cannabidiol; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; CLcr, creatinine clearance; eGFR, estimated glomerular filtration rate; IV, intravenous; mGFR, measured glomerular filtration rate; OPV, outpatient visit.

			(N=39)	(N=39)	
All-cause TEAEs	**5 (12.5)**	**15 (38.5)**	**3 (7.7)**	**3 (7.7)**	**18 (45.0)**
Iohexol-related TEAEs[c]	1 (2.5)	2 (5.1)	1 (2.6)	0	3 (7.5)
CBD-related TEAEs[c]	NA	3 (7.7)	2 (5.1)	0	5 (12.5)
TEAEs occurring in ≥5% of participants during any treatment period,[d] preferred term					
Diarrhoea	0	5 (12.8)	0	0	5 (12.5)
Nausea	0	3 (7.7)	2 (5.1)	0	5 (12.5)
Abdominal pain	0	3 (7.7)	1 (2.6)	0	3 (7.5)
Headache	1 (2.5)	1 (2.6)	2 (5.1)	0	3 (7.5)
Vomiting	0	0	1 (2.6)	1 (2.6)	2 (5.0)
Lethargy	0	2 (5.1)	0	0	2 (5.0)
Presyncope	0	1 (2.6)	1 (2.6)	0	2 (5.0)
Vessel puncture site haematoma	2 (5.0)	0	0	0	2 (5.0)

[a]Adverse events were coded using the Medical Dictionary for Regulatory Activities Version 27.1. [b]Overall indicates the total number of participants who experienced a TEAE during the study and may not equal the sum across study periods, as participants could have experienced TEAEs in more than one study period. [c]Treatment-related TEAEs were TEAEs with a plausible relationship to the study treatment, as determined by the investigator. [d]Only one (2.5%) renal TEAE (dysuria) was reported.
CBD, cannabidiol; NA, not applicable; TEAEs, treatment-emergent adverse events.

- Overall, 18 participants (45.0%) experienced TEAEs, most frequently during CBD dosing (Days 1–6; **Table 4**)
  - Three participants (7.5%) experienced iohexol-related TEAEs and five participants (12.5%) experienced CBD-related TEAEs
  - All TEAEs were mild in severity, with no serious TEAEs or TEAEs resulting in study discontinuation or death reported

Demographics and baseline characteristics

Table 5. Participant demographics

Demographic	Safety and pharmacodynamic population (N=40)	Pharmacokinetic population (N=39)
Age, years		
Mean (SD)	38.7 (10.9)	38.8 (11.0)
Median (range)	37.0 (23.0–60.0)	38.0 (23.0–60.0)
Sex, n (%)		
Female	24 (60.0)	23 (59.0)
Male	16 (40.0)	16 (41.0)
Race, n (%)		
White	26 (65.0)	26 (66.7)
Black or African American	12 (30.0)	11 (28.2)
Asian	2 (5.0)	2 (5.1)
Ethnicity, n (%)		
Hispanic or Latino	6 (15.0)	5 (12.8)
Other	34 (85.0)	34 (87.2)
Body weight, kg		
Mean (SD)	75.2 (13.4)	75.2 (13.6)
Median (range)	74.9 (51.9–103.7)	75.2 (51.9–103.7)

Demographic	Safety and pharmacodynamic population (N=40)	Pharmacokinetic population (N=39)
Body mass index, kg/m²		
Mean (SD)	25.5 (3.0)	25.5 (3.0)
Median (range)	25.9 (18.5–29.9)	25.90 (18.5–29.9)
Body surface area, m²		
Mean (SD)	1.9 (0.2)	1.9 (0.2)
Median (range)	1.9 (1.5–2.3)	1.9 (1.5–2.3)

SD, standard deviation.

- The study enrolled 40 participants; all 40 received at least one dose of iohexol (safety and pharmacodynamic populations), and 39 received at least one dose of both iohexol and CBD (pharmacokinetic population)
  - One participant was withdrawn from the study after receiving iohexol due to not meeting eligibility criteria
  - Overall, 35 completed the study and 5 discontinued (participant withdrawal, n=3; failed to meet continuation criteria, n=1; lost to follow-up, n=1)
- Mean (standard deviation; range) age was 38.7 years (10.9; 23–60; **Table 5**)
- The majority of participants were female or White (**Table 5**)