Clinical trial results:
Pharmacokinetics and side effects for tetrahydrocannabinol and cannabidiol (Sativex) among patients with chronic kidney disease and patients on dialysis.

Summary

EudraCT number	2019-002786-35
Trial protocol	DK
Global end of trial date	07 February 2024

Results information

Result version number	v1 (current)
This version publication date	23 February 2025
First version publication date	23 February 2025

Trial information

Trial identification

Sponsor protocol code	CUA1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	07 February 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 February 2024
Global end of trial reached?	Yes
Global end of trial date	07 February 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the pharmacokinetics for tetrahydrocannabinol and cannabidiol (Sativex) among patients with chronic kidney disease compared healthy volunteers.

Protection of trial subjects:

Participants were observed at the study unit for 12 hours after administration of study medicine. Vital parameters were controlled 2 hours after administration of study medicine and side effects were assessed at regular time points over 24 hours from administration of study medicine.

Background therapy:

Participants continued their usual treatments for chronic kidney disease and other diseases.

Evidence for comparator:

Kidney healthy controls were used as comparator.

Actual start date of recruitment	29 September 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 66
Worldwide total number of subjects	66
EEA total number of subjects	66

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	44
From 65 to 84 years	22

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants with chronic kidney disease were recruited from Department of Renal Medicine, Aarhus University Hospital, Denmark. Healthy controls were recruited by advertisement. We recruited participants from September 2020 until December 2023.

Pre-assignment

Screening details:

We screened medical records for patients having an appointment at the outpatient clinic at Department of Renal Medicine, Aarhus University Hospital, Denmark, to meet inclusion and exclusion criteria. 257 potential participants were assessed for eligibility of which 66 were included in the study.

Period 1

Period 1 title	Prior to receiving study medicine
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Healthy controls

Arm description:

Kidney healthy controls

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	eGFR <=30 and >15

Arm description:

Participants with chronic kidney disease with eGFR <=30 and >15 ml/min/1.73 m2.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	eGFR <=15

Arm description:

Participants with chronic kidney disease with eGFR <=15 ml/min/1.73 m2

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Haemodialysis

Arm description:

Haemodialysis

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Peritoneal dialysis

Arm description:

Continuous ambulatory peritoneal dialysis and automated peritoneal dialysis with “wet day”

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Healthy controls	eGFR <=30 and >15	eGFR <=15
Started	24	23	11
Completed	20	20	10
Not completed	4	3	1
No longer meeting inclusion/exclusion criteria	-	-	-
Withdrawn consent/no respond/not meeting criteria	4	-	-
Withdrawn consent or problems with venous access	-	3	-
Other (not specified due to n=1)	-	-	1

Number of subjects in period 1	Haemodialysis	Peritoneal dialysis
Started	4	4
Completed	4	1
Not completed	0	3
No longer meeting inclusion/exclusion criteria	-	3
Withdrawn consent/no respond/not meeting criteria	-	-
Withdrawn consent or problems with venous access	-	-
Other (not specified due to n=1)	-	-

Period 2	
Period 2 title	Receiving study medicine
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Healthy controls

Arm description:

Kidney healthy controls

Arm type	Active comparator
Investigational medicinal product name	Sativex
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal spray
Routes of administration	Oromucosal use

Dosage and administration details:

A dose of 5.4 mg of THC and 5.0 mg of CBD, corresponding to 2 sprays of Sativex, were administered to the inside of the cheek after 7 hours of fasting.

Arm title	eGFR <=30 and >15

Arm description:

Participants with chronic kidney disease with eGFR <=15 ml/min/1.73 m2

Arm type	Experimental
Investigational medicinal product name	Sativex
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal spray
Routes of administration	Oromucosal use

Dosage and administration details:

A dose of 5.4 mg of THC and 5.0 mg of CBD, corresponding to 2 sprays of Sativex, were administered to the inside of the cheek after 7 hours of fasting.

Arm title	eGFR <=15

Arm description:

Participants with chronic kidney disease with eGFR <=15 ml/min/1.73 m2

Arm type	Experimental
Investigational medicinal product name	Sativex
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal spray
Routes of administration	Oromucosal use

Dosage and administration details:

A dose of 5.4 mg of THC and 5.0 mg of CBD, corresponding to 2 sprays of Sativex, were administered to the inside of the cheek after 7 hours of fasting.

Arm title	Haemodialysis

Arm description:

Haemodialysis

Arm type	Experimental
Investigational medicinal product name	Sativex
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal spray
Routes of administration	Oromucosal use

Dosage and administration details:

A dose of 5.4 mg of THC and 5.0 mg of CBD, corresponding to 2 sprays of Sativex, were administered to the inside of the cheek after 7 hours of fasting.

Arm title	Peritoneal dialysis

Arm description:

Continuous ambulatory peritoneal dialysis and automated peritoneal dialysis with “wet day”

Arm type	Experimental
Investigational medicinal product name	Sativex
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal spray
Routes of administration	Oromucosal use

Dosage and administration details:

A dose of 5.4 mg of THC and 5.0 mg of CBD, corresponding to 2 sprays of Sativex, were administered to the inside of the cheek after 7 hours of fasting.

Number of subjects in period 2	Healthy controls	eGFR <=30 and >15	eGFR <=15
Started	20	20	10
Completed	20	20	9
Not completed	0	0	1
Other (not specified due to n=1)	-	-	1

Number of subjects in period 2	Haemodialysis	Peritoneal dialysis
Started	4	1
Completed	4	1
Not completed	0	0
Other (not specified due to n=1)	-	-

Period 3

Period 3 title	Completed the study
Is this the baseline period?	Yes[1]
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Healthy controls

Arm description:

Kidney healthy controls

Arm type	Active comparator
Investigational medicinal product name	Sativex
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal spray
Routes of administration	Oromucosal use

Dosage and administration details:

A dose of 5.4 mg of THC and 5.0 mg of CBD, corresponding to 2 sprays of Sativex, were administered to the inside of the cheek after 7 hours of fasting.

Arm title	eGFR <=30 and >15

Arm description:

Participants with chronic kidney disease with eGFR <=30 and >15 ml/min/1.73 m2.

Arm type	Experimental
Investigational medicinal product name	Sativex
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal spray
Routes of administration	Oromucosal use

Dosage and administration details:

A dose of 5.4 mg of THC and 5.0 mg of CBD, corresponding to 2 sprays of Sativex, were administered to the inside of the cheek after 7 hours of fasting.

Arm title	eGFR <=15

Arm description:	
Participants with chronic kidney disease with eGFR <=15 ml/min/1.73 m2	
Arm type	Experimental
Investigational medicinal product name	Sativex
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal spray
Routes of administration	Oromucosal use
Dosage and administration details:	
A dose of 5.4 mg of THC and 5.0 mg of CBD, corresponding to 2 sprays of Sativex, were administered to the inside of the cheek after 7 hours of fasting.	
Arm title	Haemodialysis
Arm description:	
Haemodialysis	
Arm type	Experimental
Investigational medicinal product name	Sativex
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal spray
Routes of administration	Oromucosal use
Dosage and administration details:	
A dose of 5.4 mg of THC and 5.0 mg of CBD, corresponding to 2 sprays of Sativex, were administered to the inside of the cheek after 7 hours of fasting.	
Arm title	Peritoneal dialysis
Arm description:	
Continuous ambulatory peritoneal dialysis and automated peritoneal dialysis with “wet day”	
Arm type	Experimental
Investigational medicinal product name	Sativex
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal spray
Routes of administration	Oromucosal use
Dosage and administration details:	
A dose of 5.4 mg of THC and 5.0 mg of CBD, corresponding to 2 sprays of Sativex, were administered to the inside of the cheek after 7 hours of fasting.	

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: The 3 periods were needed to fill in correct data, as baseline data is provided for participants who completed the study.

Number of subjects in period 3[2]	Healthy controls	eGFR <=30 and >15	eGFR <=15
Started	20	20	9
Completed	20	20	9

Number of subjects in period 3[2]	Haemodialysis	Peritoneal dialysis
Started	4	1
Completed	4	1

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Baseline data is provided for participants who completed the study.

Baseline characteristics

Reporting groups	
Reporting group title	Healthy controls
Reporting group description:	
Kidney healthy controls	
Reporting group title	eGFR <=30 and >15
Reporting group description:	
Participants with chronic kidney disease with eGFR <=30 and >15 ml/min/1.73 m2.	
Reporting group title	eGFR <=15
Reporting group description:	
Participants with chronic kidney disease with eGFR <=15 ml/min/1.73 m2	
Reporting group title	Haemodialysis
Reporting group description:	
Haemodialysis	
Reporting group title	Peritoneal dialysis
Reporting group description:	
Continuous ambulatory peritoneal dialysis and automated peritoneal dialysis with “wet day”	

Reporting group values	Healthy controls	eGFR <=30 and >15	eGFR <=15
Number of subjects	20	20	9
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
median	27	64	68
inter-quartile range (Q1-Q3)	23 to 54	45 to 74	61 to 73
Gender categorical Units: Subjects			
Female	8	6	1
Male	12	14	8
Smoking			
If there is less than 3 in "yes", the number is set to "0" and all participants are placed in the group "Less than 3 in yes" (not for the group “peritoneal dialysis”).			
Units: Subjects			
Yes	0	5	0
No	0	15	0
Less than 3 in yes	20	0	9
urine albumin-creatinine ratio			

Units: Subjects			
30-299 mg/g	0	12	4
>300 mg/g	0	7	5
Not relevant/other	20	1	0
Comorbidities, diabetes			
If there is less than 3 in "yes", the number is set to "0" and all participants are placed in the group "Less than 3 in yes" (not for the group “peritoneal dialysis”).			
Units: Subjects			
Yes	0	0	0
No	20	20	0
Less than 3 in yes	0	0	9
Comorbidities, hypertension			
If there is less than 3 in "yes", the number is set to "0" and all participants are placed in the group "Less than 3 in yes" (not for the group “peritoneal dialysis”).			
Units: Subjects			
Yes	0	17	9
No	0	3	0
Less than 3 in yes	20	0	0
Comorbidities, Obesity			
If there is less than 3 in "yes", the number is set to "0" and all participants are placed in the group "Less than 3 in yes" (not for the group “peritoneal dialysis”).			
Units: Subjects			
Yes	9	14	7
No	11	6	2
Less than 3 in yes	0	0	0
Comorbidities, ischaemic heart disease			
If there is less than 3 in "yes", the number is set to "0" and all participants are placed in the group "Less than 3 in yes" (not for the group “peritoneal dialysis”).			
Units: Subjects			
Yes	0	5	0
No	20	15	9
Less than 3 in yes	0	0	0
Cause of CKD, hypertension			
If there is less than 3 in "yes", the number is set to "0" and all participants are placed in the group "Not relevant/less than 3 in yes" (not for the group “peritoneal dialysis”).			
Units: Subjects			
Yes	0	0	3
No	0	0	6
Not relevant/less than 3 in yes	20	20	0
Cause of CKD, obstruction			
If there is less than 3 in "yes", the number is set to "0" and all participants are placed in the group "Not relevant/less than 3 in yes" (not for the group “peritoneal dialysis”).			
Units: Subjects			
Yes	0	4	0
No	0	16	0
Not relevant/less than 3 in yes	20	0	9
Cause of CKD, glumerulonephritis			
If there is less than 3 in "yes", the number is set to "0" and all participants are placed in the group "Not relevant/less than 3 in yes" (not for the group “peritoneal dialysis”).			
Units: Subjects			
Yes	0	3	0
No	0	17	0
Not relevant/less than 3 in yes	20	0	9

Cause of CKD, vasculitis			
If there is less than 3 in "yes", the number is set to "0" and all participants are placed in the group "Not relevant/less than 3 in yes" (not for the group “peritoneal dialysis”).			
Units: Subjects			
Yes	0	0	0
No	0	0	9
Not relevant/less than 3 in yes	20	20	0
Cause of CKD, hereditary			
If there is less than 3 in "yes", the number is set to "0" and all participants are placed in the group "Not relevant/less than 3 in yes" (not for the group “peritoneal dialysis”).			
Units: Subjects			
Yes	0	4	3
No	0	16	6
Not relevant/less than 3 in yes	20	0	0
Cause of CKD, other			
If there is less than 3 in "yes", the number is set to "0" and all participants are placed in the group "Not relevant/less than 3 in yes" (not for the group “peritoneal dialysis”).			
Units: Subjects			
Yes	0	3	0
No	0	17	0
Not relevant/less than 3 in yes	20	0	9
Cause of CKD, unknown			
If there is less than 3 in "yes", the number is set to "0" and all participants are placed in the group "Not relevant/less than 3 in yes"(not for the group “peritoneal dialysis”).			
Units: Subjects			
Yes	0	0	0
No	0	0	9
Not relevant/less than 3 in yes	20	20	0
Weight			
Units: kg			
median	83	88	92
inter-quartile range (Q1-Q3)	74 to 96	74 to 97	75 to 96
Height			
Units: cm			
median	181	175	177
inter-quartile range (Q1-Q3)	174 to 188	168 to 180	169 to 180
BMI			
Units: kg/m2			
median	24.6	29.2	27.1
inter-quartile range (Q1-Q3)	21.6 to 27.7	24.0 to 31.5	25.6 to 30.8
Waist measurement			
Units: cm			
median	92	102	103
inter-quartile range (Q1-Q3)	81 to 98	94 to 111	94 to 105
Systolic blood pressure			
Units: mmHg			
median	125	139	137
inter-quartile range (Q1-Q3)	115 to 140	131 to 150	129 to 153
Diastolic blood pressure			
Units: mmHg			
median	80	89	81
inter-quartile range (Q1-Q3)	72 to 89	82 to 93	81 to 90
Heart rate			

Units: bpm			
median	68	74	69
inter-quartile range (Q1-Q3)	61 to 78	64 to 79	62 to 89
Number of drugs			
Units: Number			
median	1	8	7
inter-quartile range (Q1-Q3)	0 to 2	6 to 11	6 to 8
Creatinine			
As a number must be provided, "99" is reported if the value is not relevant.			
Units: micromole(s)/litre			
median	76	256	437
inter-quartile range (Q1-Q3)	66 to 86	234 to 292	381 to 459
Blood urea nitrogen			
As a number must be provided, "99" is reported if the value is not relevant.			
Units: mmol/l			
median	4.6	16.5	17.4
inter-quartile range (Q1-Q3)	4.0 to 5.3	14.0 to 18.3	15.4 to 25.2
Cystatin C			
As a number must be provided, "99" is reported if the value is not relevant.			
Units: mg/l			
median	0.97	2.93	3.72
inter-quartile range (Q1-Q3)	0.80 to 1.08	2.69 to 3.25	3.49 to 3.82
eGFR (creatinine)			
As a number must be provided, "99" is reported if the value is not relevant.			
Units: ml/min/1.73m2			
median	107	21	11
inter-quartile range (Q1-Q3)	95 to 121	18 to 24	11 to 13
eGFR (cystatine C)			
As a number must be provided, "99" is reported if the value is not relevant.			
Units: ml/min/1.73m2			
median	94	18	13
inter-quartile range (Q1-Q3)	79 to 113	16 to 20	12 to 14
eGFR (creatinene and cystatin C)			
As a number must be provided, "99" is reported if the value is not relevant.			
Units: ml/min/1.73m2			
median	98	19	12
inter-quartile range (Q1-Q3)	86 to 114	16 to 20	11 to 12
Absolute eGFR (creatinine)			
As a number must be provided, "99" is reported if the value is not relevant.			
Units: ml/min			
median	127	24	13
inter-quartile range (Q1-Q3)	100 to 139	19 to 26	13 to 14

Reporting group values	Haemodialysis	Peritoneal dialysis	Total
Number of subjects	4	1	54
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0

Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
median	68	70	
inter-quartile range (Q1-Q3)	63 to 76	70 to 70	-
Gender categorical			
Units: Subjects			
Female	2	1	18
Male	2	0	36
Smoking			
If there is less than 3 in "yes", the number is set to "0" and all participants are placed in the group "Less than 3 in yes" (not for the group “peritoneal dialysis”).			
Units: Subjects			
Yes	0	0	5
No	4	1	20
Less than 3 in yes	0	0	29
urine albumin-creatinine ratio			
Units: Subjects			
30-299 mg/g	0	0	16
>300 mg/g	0	0	12
Not relevant/other	4	1	26
Comorbidities, diabetes			
If there is less than 3 in "yes", the number is set to "0" and all participants are placed in the group "Less than 3 in yes" (not for the group “peritoneal dialysis”).			
Units: Subjects			
Yes	0	0	0
No	4	1	45
Less than 3 in yes	0	0	9
Comorbidities, hypertension			
If there is less than 3 in "yes", the number is set to "0" and all participants are placed in the group "Less than 3 in yes" (not for the group “peritoneal dialysis”).			
Units: Subjects			
Yes	0	1	27
No	0	0	3
Less than 3 in yes	4	0	24
Comorbidities, Obesity			
If there is less than 3 in "yes", the number is set to "0" and all participants are placed in the group "Less than 3 in yes" (not for the group “peritoneal dialysis”).			
Units: Subjects			
Yes	3	0	33
No	1	1	21
Less than 3 in yes	0	0	0
Comorbidities, ischaemic heart disease			
If there is less than 3 in "yes", the number is set to "0" and all participants are placed in the group "Less than 3 in yes" (not for the group “peritoneal dialysis”).			
Units: Subjects			
Yes	0	0	5

No	0	1	45
Less than 3 in yes	4	0	4
Cause of CKD, hypertension			
If there is less than 3 in "yes", the number is set to "0" and all participants are placed in the group "Not relevant/less than 3 in yes" (not for the group “peritoneal dialysis”).			
Units: Subjects			
Yes	0	0	3
No	4	1	11
Not relevant/less than 3 in yes	0	0	40
Cause of CKD, obstruction			
If there is less than 3 in "yes", the number is set to "0" and all participants are placed in the group "Not relevant/less than 3 in yes" (not for the group “peritoneal dialysis”).			
Units: Subjects			
Yes	0	0	4
No	4	1	21
Not relevant/less than 3 in yes	0	0	29
Cause of CKD, glumerulonephritis			
If there is less than 3 in "yes", the number is set to "0" and all participants are placed in the group "Not relevant/less than 3 in yes" (not for the group “peritoneal dialysis”).			
Units: Subjects			
Yes	3	0	6
No	1	1	19
Not relevant/less than 3 in yes	0	0	29
Cause of CKD, vasculitis			
If there is less than 3 in "yes", the number is set to "0" and all participants are placed in the group "Not relevant/less than 3 in yes" (not for the group “peritoneal dialysis”).			
Units: Subjects			
Yes	0	0	0
No	4	1	14
Not relevant/less than 3 in yes	0	0	40
Cause of CKD, hereditary			
If there is less than 3 in "yes", the number is set to "0" and all participants are placed in the group "Not relevant/less than 3 in yes" (not for the group “peritoneal dialysis”).			
Units: Subjects			
Yes	0	0	7
No	4	1	27
Not relevant/less than 3 in yes	0	0	20
Cause of CKD, other			
If there is less than 3 in "yes", the number is set to "0" and all participants are placed in the group "Not relevant/less than 3 in yes" (not for the group “peritoneal dialysis”).			
Units: Subjects			
Yes	0	1	4
No	0	0	17
Not relevant/less than 3 in yes	4	0	33
Cause of CKD, unknown			
If there is less than 3 in "yes", the number is set to "0" and all participants are placed in the group "Not relevant/less than 3 in yes"(not for the group “peritoneal dialysis”).			
Units: Subjects			
Yes	0	0	0
No	4	1	14
Not relevant/less than 3 in yes	0	0	40

Weight Units: kg median inter-quartile range (Q1-Q3)	 109 87 to 110	 46 46 to 46	 -
Height Units: cm median inter-quartile range (Q1-Q3)	 176 164 to 192	 148 148 to 148	 -
BMI Units: kg/m2 median inter-quartile range (Q1-Q3)	 30.1 26.4 to 36.2	 21.2 21.2 to 21.2	 -
Waist measurement Units: cm median inter-quartile range (Q1-Q3)	 118 98 to 128	 77 77 to 77	 -
Systolic blood pressure Units: mmHg median inter-quartile range (Q1-Q3)	 155 129 to 165	 138 138 to 138	 -
Diastolic blood pressure Units: mmHg median inter-quartile range (Q1-Q3)	 86 77 to 89	 81 81 to 81	 -
Heart rate Units: bpm median inter-quartile range (Q1-Q3)	 69 63 to 75	 87 87 to 87	 -
Number of drugs Units: Number median inter-quartile range (Q1-Q3)	 14 13 to 18	 14 14 to 14	 -
Creatinine			
As a number must be provided, “99” is reported if the value is not relevant.			
Units: micromole(s)/litre median inter-quartile range (Q1-Q3)	 99 99 to 99	 99 99 to 99	 -
Blood urea nitrogen			
As a number must be provided, “99” is reported if the value is not relevant.			
Units: mmol/l median inter-quartile range (Q1-Q3)	 99 99 to 99	 99 99 to 99	 -
Cystatin C			
As a number must be provided, “99” is reported if the value is not relevant.			
Units: mg/l median inter-quartile range (Q1-Q3)	 99 99 to 99	 99 99 to 99	 -
eGFR (creatinine)			
As a number must be provided, “99” is reported if the value is not relevant.			
Units: ml/min/1.73m2 median inter-quartile range (Q1-Q3)	 99 99 to 99	 99 99 to 99	 -

eGFR (cystatine C)			
As a number must be provided, “99” is reported if the value is not relevant.			
Units: ml/min/1.73m2			
median	99	99	
inter-quartile range (Q1-Q3)	99 to 99	99 to 99	-
eGFR (creatinene and cystatin C)			
As a number must be provided, “99” is reported if the value is not relevant.			
Units: ml/min/1.73m2			
median	99	99	
inter-quartile range (Q1-Q3)	99 to 99	99 to 99	-
Absolute eGFR (creatinine)			
As a number must be provided, “99” is reported if the value is not relevant.			
Units: ml/min			
median	99	99	
inter-quartile range (Q1-Q3)	99 to 99	99 to 99	-

End points

End points reporting groups

Reporting group title	Healthy controls
Reporting group description: Kidney healthy controls	
Reporting group title	eGFR <=30 and >15
Reporting group description: Participants with chronic kidney disease with eGFR <=30 and >15 ml/min/1.73 m2.	
Reporting group title	eGFR <=15
Reporting group description: Participants with chronic kidney disease with eGFR <=15 ml/min/1.73 m2	
Reporting group title	Haemodialysis
Reporting group description: Haemodialysis	
Reporting group title	Peritoneal dialysis
Reporting group description: Continuous ambulatory peritoneal dialysis and automated peritoneal dialysis with “wet day”	
Reporting group title	Healthy controls
Reporting group description: Kidney healthy controls	
Reporting group title	eGFR <=30 and >15
Reporting group description: Participants with chronic kidney disease with eGFR <=15 ml/min/1.73 m2	
Reporting group title	eGFR <=15
Reporting group description: Participants with chronic kidney disease with eGFR <=15 ml/min/1.73 m2	
Reporting group title	Haemodialysis
Reporting group description: Haemodialysis	
Reporting group title	Peritoneal dialysis
Reporting group description: Continuous ambulatory peritoneal dialysis and automated peritoneal dialysis with “wet day”	
Reporting group title	Healthy controls
Reporting group description: Kidney healthy controls	
Reporting group title	eGFR <=30 and >15
Reporting group description: Participants with chronic kidney disease with eGFR <=30 and >15 ml/min/1.73 m2.	
Reporting group title	eGFR <=15
Reporting group description: Participants with chronic kidney disease with eGFR <=15 ml/min/1.73 m2	
Reporting group title	Haemodialysis
Reporting group description: Haemodialysis	
Reporting group title	Peritoneal dialysis
Reporting group description: Continuous ambulatory peritoneal dialysis and automated peritoneal dialysis with “wet day”	

Primary: AUC for THC	
End point title	AUC for THC
End point description: THC: tetrahydrocannabinol	
End point type	Primary
End point timeframe: 24 hours	

End point values	Healthy controls	eGFR <=30 and >15	eGFR <=15	Haemodialysis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	9	4
Units: h*ng/ml				
median (inter-quartile range (Q1-Q3))	2.8 (1.8 to 3.5)	4.2 (3.3 to 5.3)	4.3 (3.2 to 5.4)	2.7 (2.4 to 3.7)

End point values	Peritoneal dialysis			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: h*ng/ml				
median (inter-quartile range (Q1-Q3))	7.7 (7.7 to 7.7)			

Statistical analyses

Statistical analysis title	Kruskal-Wallis test
Comparison groups	eGFR <=30 and >15 v eGFR <=15 v Healthy controls
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.004
Method	Kruskal-wallis

Notes:

[1] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
Non-parametric test used to compare three or more distributions

Statistical analysis title	Dunns test corrected with Bonferroni
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 0.004 [3]
Method	Kruskal-wallis

Notes:

[2] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
A post-hoc pairwise comparison test used after a significant Kruskal-Wallis test to determine which specific groups differ.
[3] - Significant differences between CKD groups and healthy controls

Secondary: AUC for CBD

End point title	AUC for CBD

End point description:

CBD: cannabidiol

End point type	Secondary

End point timeframe:

24 hours

End point values	Healthy controls	eGFR <=30 and >15	eGFR <=15	Haemodialysis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	9	4
Units: h*ng/ml				
median (inter-quartile range (Q1-Q3))	1.3 (0.49 to 1.8)	2.8 (2.5 to 3.7)	3.6 (2.2 to 4.7)	2.0 (1.7 to 2.5)

End point values	Peritoneal dialysis			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: h*ng/ml				
median (inter-quartile range (Q1-Q3))	6.6 (6.6 to 6.6)			

Statistical analyses

Statistical analysis title	Kruskal Wallis test
Comparison groups	eGFR <=30 and >15 v Healthy controls v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	= 0
Method	Kruskal-wallis

Notes:

[4] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
Non-parametric test used to compare three or more distributions

Statistical analysis title	Dunns test corrected with Bonferroni
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15

Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	= 0 [6]
Method	Kruskal-wallis

Notes:

[5] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
A post-hoc pairwise comparison test used after a significant Kruskal-Wallis test to determine which specific groups differ.
[6] - Significant differences between CKD groups and healthy controls

Secondary: AUC for THC-OH

End point title	AUC for THC-OH

End point description:

THC-OH: 11-hydroxy-Δ9-tetrahydrocannabinol

End point type	Secondary

End point timeframe:

24 hours

End point values	Healthy controls	eGFR <=30 and >15	eGFR <=15	Haemodialysis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	9	4
Units: h*ng/ml				
median (inter-quartile range (Q1-Q3))	4.9 (2.9 to 7.0)	19 (15 to 23)	18 (16 to 36)	9.2 (6.7 to 13)

End point values	Peritoneal dialysis			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: h*ng/ml				
median (inter-quartile range (Q1-Q3))	36 (36 to 36)			

Statistical analyses

Statistical analysis title	Kruskal Wallis test
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[7]
P-value	= 0
Method	Kruskal-wallis

Notes:

[7] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
Non-parametric test used to compare three or more distributions

Statistical analysis title	Dunns test corrected with Bonferroni
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[8]
P-value	= 0 [9]
Method	Kruskal-wallis

Notes:

[8] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
A post-hoc pairwise comparison test used after a significant Kruskal-Wallis test to determine which specific groups differ.
[9] - Significant differences between CKD groups and healthy controls

Secondary: AUC for THC-COOH

End point title	AUC for THC-COOH

End point description:

THC-COOH: 11-nor-9-carboxy-Δ9-tetrahydrocannabinol

End point type	Secondary

End point timeframe:

24 hours

End point values	Healthy controls	eGFR <=30 and >15	eGFR <=15	Haemodialysis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	9	4
Units: h*ng/ml				
median (inter-quartile range (Q1-Q3))	85 (69 to 130)	150 (110 to 190)	130 (120 to 170)	66 (36 to 120)

End point values	Peritoneal dialysis			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: h*ng/ml				
median (inter-quartile range (Q1-Q3))	190 (190 to 190)			

Statistical analyses

Statistical analysis title	Kruskal Wallis test
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15

Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[10]
P-value	= 0.019
Method	Kruskal-wallis

Notes:

[10] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
Non-parametric test used to compare three or more distributions

Statistical analysis title	Dunns test corrected with Bonferroni
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[11]
P-value	= 0.019 [12]
Method	Kruskal-wallis

Notes:

[11] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
A post-hoc pairwise comparison test used after a significant Kruskal-Wallis test to determine which
[12] - Significant difference between eGFR <=30 and >15 and healthy controls

Secondary: AUC for THC-COOH-glucuronide

End point title	AUC for THC-COOH-glucuronide

End point description:

THC-COOH: 11-nor-9-carboxy-Δ9-tetrahydrocannabinol

End point type	Secondary

End point timeframe:

24 hours

End point values	Healthy controls	eGFR <=30 and >15	eGFR <=15	Haemodialysis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	9	4
Units: h*ng/ml				
median (inter-quartile range (Q1-Q3))	400 (250 to 460)	710 (600 to 1100)	940 (720 to 1200)	680 (390 to 930)

End point values	Peritoneal dialysis			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: h*ng/ml				
median (inter-quartile range (Q1-Q3))	1300 (1300 to 1300)			

Statistical analyses

Statistical analysis title	Kruskal Wallis test
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[13]
P-value	= 0
Method	Kruskal-wallis

Notes:

[13] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
Non-parametric test used to compare three or more distributions

Statistical analysis title	Dunns test corrected with Bonferroni
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[14]
P-value	= 0 [15]
Method	Kruskal-wallis

Notes:

[14] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
A post-hoc pairwise comparison test used after a significant Kruskal-Wallis test to determine which specific groups differ.
[15] - Significant differences between CKD groups and healthy controls

Secondary: Cmax for THC

End point title	Cmax for THC

End point description:

THC: Δ9-tetrahydrocannabinol
Cmax: maximum concentration

End point type	Secondary

End point timeframe:

24 hours

End point values	Healthy controls	eGFR <=30 and >15	eGFR <=15	Haemodialysis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	9	4
Units: ng/ml				
median (inter-quartile range (Q1-Q3))	0.62 (0.37 to 0.98)	0.94 (0.73 to 1.5)	1.1 (0.70 to 2.0)	0.56 (0.34 to 0.95)

End point values	Peritoneal dialysis			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: ng/ml				

median (inter-quartile range (Q1-Q3))	2.1 (2.1 to 2.1)			

Statistical analyses

Statistical analysis title	Kruskal Wallis test
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[16]
P-value	= 0.014
Method	Kruskal-wallis

Notes:

[16] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
Non-parametric test used to compare three or more distributions.

Statistical analysis title	Dunns test corrected with Bonferroni
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[17]
P-value	= 0.014 [18]
Method	Kruskal-wallis

Notes:

[17] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
A post-hoc pairwise comparison test used after a significant Kruskal-Wallis test to determine which specific groups differ.

[18] - Significant differences between CKD groups and healthy controls

Secondary: Cmax for CBD

End point title	Cmax for CBD

End point description:

Cmax: maximum concentration
CBD: cannabidiol

End point type	Secondary

End point timeframe:

24 hours

End point values	Healthy controls	eGFR <=30 and >15	eGFR <=15	Haemodialysis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	9	4
Units: ng/ml				
median (inter-quartile range (Q1-Q3))	0.18 (0.12 to 0.45)	0.68 (0.57 to 0.87)	0.86 (0.47 to 1.3)	0.45 (0.36 to 0.63)

End point values	Peritoneal dialysis			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: ng/ml				
median (inter-quartile range (Q1-Q3))	2.0 (2.0 to 2.0)			

Statistical analyses

Statistical analysis title	Kruskal Wallis test
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[19]
P-value	= 0
Method	Kruskal-wallis

Notes:

[19] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
Non-parametric test used to compare three or more distributions.

Statistical analysis title	Dunns test corrected with Bonferroni
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[20]
P-value	= 0 [21]
Method	Kruskal-wallis

Notes:

[20] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
A post-hoc pairwise comparison test used after a significant Kruskal-Wallis test to determine which specific groups differ.
[21] - Significant differences between CKD groups and healthy controls

Secondary: Cmax for THC-OH

End point title	Cmax for THC-OH

End point description:

Cmax: maximum concentration
THC-OH: 11-hydroxy-Δ9-tetrahydrocannabinol

End point type	Secondary

End point timeframe:
24 hours

End point values	Healthy controls	eGFR <=30 and >15	eGFR <=15	Haemodialysis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	9	4
Units: ng/ml				
median (inter-quartile range (Q1-Q3))	0.91 (0.73 to 1.3)	3.0 (2.1 to 3.9)	2.9 (2.7 to 5.7)	1.8 (1.2 to 2.7)

End point values	Peritoneal dialysis			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: ng/ml				
median (inter-quartile range (Q1-Q3))	5.5 (5.5 to 5.5)			

Statistical analyses

Statistical analysis title	Kruskal Wallis test
Comparison groups	eGFR <=30 and >15 v Healthy controls v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[22]
P-value	= 0
Method	Kruskal-wallis

Notes:

[22] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
Non-parametric test used to compare three or more distributions.

Statistical analysis title	Dunns test corrected with
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[23]
P-value	= 0 [24]
Method	Kruskal-wallis

Notes:

[23] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
A post-hoc pairwise comparison test used after a significant Kruskal-Wallis test to determine which specific groups differ.
[24] - Significant differences between CKD groups and healthy controls

Secondary: Cmax for THC-COOH

End point title	Cmax for THC-COOH
End point description: Cmax: maximum concentration THC-COOH: 11-nor-9-carboxy-Δ9-tetrahydrocannabinol	
End point type	Secondary
End point timeframe: 24 hours	

End point values	Healthy controls	eGFR <=30 and >15	eGFR <=15	Haemodialysis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	9	4
Units: ng/ml				
median (inter-quartile range (Q1-Q3))	12 (8.1 to 14)	16 (11 to 18)	14 (12 to 17)	7.1 (4.0 to 12)

End point values	Peritoneal dialysis			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: ng/ml				
median (inter-quartile range (Q1-Q3))	25 (25 to 25)			

Statistical analyses

Statistical analysis title	Kruskal Wallis test
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[25]
P-value	= 0.02
Method	Kruskal-wallis

Notes:

[25] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
Non-parametric test used to compare three or more distributions.

Statistical analysis title	Dunns test corrected with Bonferroni
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[26]
P-value	= 0.02 [27]
Method	Kruskal-wallis

Notes:

[26] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
A post-hoc pairwise comparison test used after a significant Kruskal-Wallis test to determine which specific groups differ.
[27] - Significant difference between eGFR <=30 and >15 and healthy controls

Secondary: Cmax for THC-COOH-glucuronide

End point title	Cmax for THC-COOH-glucuronide

End point description:

Cmax: maximum concentration
THC-COOH: 11-nor-9-carboxy-Δ9-tetrahydrocannabinol

End point type	Secondary

End point timeframe:

24 hours

End point values	Healthy controls	eGFR <=30 and >15	eGFR <=15	Haemodialysis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	9	4
Units: ng/ml				
median (inter-quartile range (Q1-Q3))	33 (21 to 38)	49 (40 to 61)	59 (44 to 69)	44 (28 to 61)

End point values	Peritoneal dialysis			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: ng/ml				
median (inter-quartile range (Q1-Q3))	83 (83 to 83)			

Statistical analyses

Statistical analysis title	Kruskal Wallis test
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[28]
P-value	= 0
Method	Kruskal-wallis

Notes:

[28] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
Non-parametric test used to compare three or more distributions.

Statistical analysis title	Dunns test corrected with Bonferroni
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15

Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[29]
P-value	= 0 [30]
Method	Kruskal-wallis

Notes:

[29] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
A post-hoc pairwise comparison test used after a significant Kruskal-Wallis test to determine which specific groups differ.

[30] - Significant differences between CKD groups and healthy controls

Secondary: Tmax for THC

End point title	Tmax for THC

End point description:

Tmax: time to maximum concentration
THC: Δ9-tetrahydrocannabinol

End point type	Secondary

End point timeframe:

24 hours

End point values	Healthy controls	eGFR <=30 and >15	eGFR <=15	Haemodialysis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	9	4
Units: hours				
median (inter-quartile range (Q1-Q3))	1.75 (1.00 to 2.50)	1.50 (1.00 to 2.00)	1.00 (0.75 to 1.00)	0.88 (0.63 to 1.25)

End point values	Peritoneal dialysis			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: hours				
median (inter-quartile range (Q1-Q3))	0.75 (0.75 to 0.75)			

Statistical analyses

Statistical analysis title	Kruskal Wallis test
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15

Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[31]
P-value	= 0.041
Method	Kruskal-wallis

Notes:

[31] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
Non-parametric test used to compare three or more distributions.

Statistical analysis title	Dunns test corrected with Bonferroni
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[32]
P-value	= 0.041 [33]
Method	Kruskal-wallis

Notes:

[32] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
A post-hoc pairwise comparison test used after a significant Kruskal-Wallis test to determine which specific groups differ.

[33] - Significant difference between eGFR <=15 and healthy controls and between the two CKD groups

Secondary: Tmax for CBD

End point title	Tmax for CBD

End point description:

Tmax: time to maximum concentration
CBD: cannabidiol

End point type	Secondary

End point timeframe:

24 hours

End point values	Healthy controls	eGFR <=30 and >15	eGFR <=15	Haemodialysis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	9	4
Units: hours				
median (inter-quartile range (Q1-Q3))	2.00 (0.88 to 2.75)	1.50 (1.00 to 2.00)	1.00 (0.75 to 1.00)	0.88 (0.63 to 1.25)

End point values	Peritoneal dialysis			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: hours				
median (inter-quartile range (Q1-Q3))	0.75 (0.75 to			

	0.75)

Statistical analyses

Statistical analysis title	Kruskal Wallis test
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[34]
P-value	= 0.017
Method	Kruskal-wallis

Notes:

[34] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
Non-parametric test used to compare three or more distributions.

Statistical analysis title	Dunns test corrected with Bonferroni
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[35]
P-value	= 0.017 [36]
Method	Kruskal-wallis

Notes:

[35] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
A post-hoc pairwise comparison test used after a significant Kruskal-Wallis test to determine which specific groups differ.
[36] - Significant difference between eGFR <=15 and healthy controls

Secondary: Tmax for THC-OH

End point title	Tmax for THC-OH

End point description:

Tmax: time to maximum concentration
THC-OH: 11-hydroxy-Δ9-tetrahydrocannabinol

End point type	Secondary

End point timeframe:

24 hours

End point values	Healthy controls	eGFR <=30 and >15	eGFR <=15	Haemodialysis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	9	4
Units: hours				
median (inter-quartile range (Q1-Q3))	3.00 (2.00 to 3.50)	2.50 (2.00 to 2.50)	1.50 (1.50 to 1.50)	1.25 (0.88 to 1.75)

End point values	Peritoneal dialysis			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: hours				
median (inter-quartile range (Q1-Q3))	2.00 (2.00 to 2.00)			

Statistical analyses

Statistical analysis title	Kruskal Wallis test
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[37]
P-value	= 0.002
Method	Kruskal-wallis

Notes:

[37] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
Non-parametric test used to compare three or more distributions.

Statistical analysis title	Dunns test corrected with Bonferroni
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[38]
P-value	= 0.002 [39]
Method	Kruskal-wallis

Notes:

[38] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
A post-hoc pairwise comparison test used after a significant Kruskal-Wallis test to determine which specific groups differ.
[39] - Significant difference between eGFR <=15 and healthy controls and between the two CKD groups

Secondary: Tmax for THC-COOH

End point title	Tmax for THC-COOH

End point description:

Tmax: time to maximum concentration
THC-COOH: 11-nor-9-carboxy-Δ9-tetrahydrocannabinol

End point type	Secondary

End point timeframe:

24 hours

End point values	Healthy controls	eGFR <=30 and >15	eGFR <=15	Haemodialysis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	9	4
Units: hours				
median (inter-quartile range (Q1-Q3))	2.75 (2.00 to 3.50)	2.50 (2.00 to 2.50)	2.00 (1.50 to 2.50)	2.00 (1.25 to 2.75)

End point values	Peritoneal dialysis			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: hours				
median (inter-quartile range (Q1-Q3))	2.00 (2.00 to 2.00)			

Statistical analyses

Statistical analysis title	Kruskal Wallis test
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[40]
P-value	= 0.066
Method	Kruskal-wallis

Notes:

[40] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
Non-parametric test used to compare three or more distributions.

Secondary: Tmax for THC-COOH-glucuronide

End point title	Tmax for THC-COOH-glucuronide

End point description:

Tmax: time to maximum concentration
THC-COOH: 11-nor-9-carboxy-Δ9-tetrahydrocannabinol

End point type	Secondary

End point timeframe:

24 hours

End point values	Healthy controls	eGFR <=30 and >15	eGFR <=15	Haemodialysis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	9	4
Units: hours				
median (inter-quartile range (Q1-Q3))	5.00 (3.50 to 6.00)	6.00 (5.00 to 6.00)	6.00 (4.00 to 6.00)	5.00 (3.75 to 6.00)

End point values	Peritoneal dialysis			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: hours				
median (inter-quartile range (Q1-Q3))	3.00 (3.00 to 3.00)			

Statistical analyses

Statistical analysis title	Kruskal Wallis test
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[41]
P-value	= 0.181
Method	Kruskal-wallis

Notes:

[41] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
Non-parametric test used to compare three or more distributions.

Secondary: Excretion of THC-COOH in 24-hour urine

End point title	Excretion of THC-COOH in 24-hour urine

End point description:

THC-COOH: 11-nor-9-carboxy-Δ9-tetrahydrocannabinol

End point type	Secondary

End point timeframe:

24 hours

End point values	Healthy controls	eGFR <=30 and >15	eGFR <=15	Haemodialysis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	9	3
Units: microgram(s)				
median (inter-quartile range (Q1-Q3))	2.4 (1.5 to 4.1)	1.3 (0.34 to 2.0)	0.79 (0.43 to 0.92)	0 (0 to 0.21)

End point values	Peritoneal dialysis			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: microgram(s)				

median (inter-quartile range (Q1-Q3))	0.16 (0.16 to 0.16)			

Statistical analyses

Statistical analysis title	Kruskal Wallis test
Comparison groups	eGFR <=30 and >15 v Healthy controls v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[42]
P-value	= 0.002
Method	Kruskal-wallis

Notes:

[42] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
Non-parametric test used to compare three or more distributions.

Statistical analysis title	Dunns test corrected with Bonferroni
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[43]
P-value	= 0.002 [44]
Method	Kruskal-wallis

Notes:

[43] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
A post-hoc pairwise comparison test used after a significant Kruskal-Wallis test to determine which specific groups differ.
[44] - Significant differences between CKD groups and healthy controls

Secondary: Excretion of THC-COOH-glucuronide in 24-hour urine

End point title	Excretion of THC-COOH-glucuronide in 24-hour urine

End point description:

THC-COOH: 11-nor-9-carboxy-Δ9-tetrahydrocannabinol

End point type	Secondary

End point timeframe:

24 hours

End point values	Healthy controls	eGFR <=30 and >15	eGFR <=15	Haemodialysis
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	9	3
Units: microgram(s)				
median (inter-quartile range (Q1-Q3))	76 (49 to 110)	21 (12 to 40)	26 (21 to 27)	2.6 (0.072 to 8.0)

End point values	Peritoneal dialysis			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: microgram(s)				
median (inter-quartile range (Q1-Q3))	12 (12 to 12)			

Statistical analyses

Statistical analysis title	Kruskal Wallis test
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[45]
P-value	= 0
Method	Kruskal-wallis

Notes:

[45] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
Non-parametric test used to compare three or more distributions.

Statistical analysis title	Dunns test corrected with Bonferroni
Comparison groups	Healthy controls v eGFR <=30 and >15 v eGFR <=15
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other[46]
P-value	= 0 [47]
Method	Kruskal-wallis

Notes:

[46] - Comparison between groups was prespecified, and the most appropriate statistical test was chosen later.
A post-hoc pairwise comparison test used after a significant Kruskal-Wallis test to determine which specific groups differ.
[47] - Significant differences between CKD groups and healthy controls

Secondary: Excretion of THC-COOH in dialysate

End point title	Excretion of THC-COOH in dialysate[48]

End point description:

THC-COOH: 11-nor-9-carboxy-Δ9-tetrahydrocannabinol
No THC-COOH was detected in dialysate from haemodialysis

End point type	Secondary

End point timeframe:

4 hours

Notes:

[48] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Excretion in dialysate is only reported for participants on dialysis

End point values	Haemodialysis	Peritoneal dialysis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	1		
Units: microgram(s)				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	0.48 (0.48 to 0.48)		

Statistical analyses

No statistical analyses for this end point

Secondary: Excretion of THC-COOH-glucuronide in dialysate

End point title	Excretion of THC-COOH-glucuronide in dialysate[49]

End point description:

THC-COOH: 11-nor-9-carboxy-Δ9-tetrahydrocannabinol
No THC-COOH-glucuronide was detected in dialysate from haemodialysis

End point type	Secondary

End point timeframe:

4 hours

Notes:

[49] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Excretion in dialysate is only reported for participants on dialysis

End point values	Haemodialysis	Peritoneal dialysis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	1		
Units: microgram(s)				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	0.94 (0.94 to 0.94)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse events were reported over 24 hours from administration of study medicine.	
Adverse event reporting additional description:	
Numeric rating scale (NRS) questionnaires with common side effects were collected at regular time points.	
Assessment type	Systematic

Dictionary used	
Dictionary name	CTCAE
Dictionary version	5.0

Reporting groups	
Reporting group title	Healthy controls
Reporting group description:	
Kidney healthy controls	
Reporting group title	eGFR <=30 and >15
Reporting group description:	
Participants with chronic kidney disease with eGFR <=30 and >15 ml/min/1.73 m2.	
Reporting group title	eGFR <=15
Reporting group description:	
Participants with chronic kidney disease with eGFR <=15 ml/min/1.73 m2	
Reporting group title	Haemodialysis
Reporting group description:	
Haemodialysis	
Reporting group title	Peritoneal dialysis
Reporting group description:	
Continuous ambulatory peritoneal dialysis and automated peritoneal dialysis with “wet day”	

Serious adverse events	Healthy controls	eGFR <=30 and >15	eGFR <=15
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	0 / 10 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	Haemodialysis	Peritoneal dialysis	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Healthy controls	eGFR <=30 and >15	eGFR <=15
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 20 (90.00%)	13 / 20 (65.00%)	8 / 10 (80.00%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	10 / 20 (50.00%)	10 / 20 (50.00%)	6 / 10 (60.00%)
occurrences (all)	10	10	6
Intoxicated/high			
subjects affected / exposed	9 / 20 (45.00%)	8 / 20 (40.00%)	5 / 10 (50.00%)
occurrences (all)	9	8	5
Concentration impairment			
subjects affected / exposed	8 / 20 (40.00%)	6 / 20 (30.00%)	2 / 10 (20.00%)
occurrences (all)	8	6	2
Headache			
subjects affected / exposed	3 / 20 (15.00%)	4 / 20 (20.00%)	1 / 10 (10.00%)
occurrences (all)	3	4	1
Sleepiness			
subjects affected / exposed	3 / 20 (15.00%)	3 / 20 (15.00%)	2 / 10 (20.00%)
occurrences (all)	3	3	2
Confusion			
subjects affected / exposed	1 / 20 (5.00%)	4 / 20 (20.00%)	2 / 10 (20.00%)
occurrences (all)	1	4	2
Affection of vision and hearing			
subjects affected / exposed	4 / 20 (20.00%)	1 / 20 (5.00%)	1 / 10 (10.00%)
occurrences (all)	4	1	1
Affection of body movement control			
subjects affected / exposed	1 / 20 (5.00%)	4 / 20 (20.00%)	1 / 10 (10.00%)
occurrences (all)	1	4	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 20 (15.00%)	3 / 20 (15.00%)	2 / 10 (20.00%)
occurrences (all)	3	3	2

Non-serious adverse events	Haemodialysis	Peritoneal dialysis	
Total subjects affected by non-serious			

adverse events			
subjects affected / exposed	3 / 4 (75.00%)	1 / 1 (100.00%)	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 4 (25.00%)	1 / 1 (100.00%)	
occurrences (all)	1	1	
Intoxicated/high			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Concentration impairment			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Headache			
subjects affected / exposed	1 / 4 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Sleepiness			
subjects affected / exposed	1 / 4 (25.00%)	1 / 1 (100.00%)	
occurrences (all)	1	1	
Confusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Affection of vision and hearing			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Affection of body movement control			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 4 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The intended number of participants could not be included. Baseline data varied considerable between groups. Healthy controls were significantly younger than other groups. Only a single-dose study with a low dose of both THC and CBD.

Notes: