Clinical trial results:
A Phase 1, Open-label, Single-dose Study to Assess the Mass Balance, Route of Elimination, and Metabolic Profile of [14C]-labeled MGCD516 Malate Salt in Healthy Male Subjects

Summary

EudraCT number	2019-003898-26
Trial protocol	NL
Global end of trial date	06 February 2020

Results information

Result version number	v1 (current)
This version publication date	19 September 2021
First version publication date	19 September 2021

Trial information

Trial identification

Sponsor protocol code	516-007

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Mirati Therapeutics, Inc.
Sponsor organisation address	3545 Cray Court, San Diego, CA, United States, 92121
Public contact	Michael Lane, Senior Manager, Regulatory Affairs, Mirati Therapeutics, Inc., +1 619-816-4358, lanem@mirati.com
Scientific contact	Curtis Chin MD PhD, Medical Director, Mirati Therapeutics, Inc., +1 619-816-4272, chinc@mirati.com

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	06 February 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 February 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objectives of the trial were to:
• Characterize the absorption, metabolism, and excretion (AME), and mass balance of a single oral dose of 120 mg MGCD516 (therapeutic dose) containing 3.7 megabecquerel (MBq) of [14C]-labeled MGCD516 in healthy male participants.
• Determine the rate and routes of excretion of MGCD516 in urine and feces.

Protection of trial subjects:

The study was conducted in accordance with the principles of the Declaration of Helsinki in place at the time of study conduct. The study was conducted in compliance with the International Council for Harmonisation (ICH) E6(R2) Guideline for Good Clinical Practice (GCP) (European Medicines Agency [EMA]/Committee for Medicinal Products for Human Use [CHMP]/ICH/135/1995), and compliant with the European Union (EU) Clinical Trial Directive (CTD): Directive 2001/20/EC.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 December 2019
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	Netherlands: 6
Worldwide total number of subjects	6
EEA total number of subjects	6

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)	6

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 6 male participants were enrolled at a single site in the Netherlands.

Pre-assignment

Screening details:

18 participants were screened within 3 weeks prior to dosing for participation in the study. Of these, 7 participants were screening failures and 5 participants were approved but not included in the study. 6 participants were enrolled and received the study drug.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	120 mg MGCD516

Arm description:

Participants were administered a single oral dose of 120 mg MGCD516 containing approximately 3.7 MBq of [14C]-MGCD516 on Day 1 of the treatment period.

Arm type	Experimental
Investigational medicinal product name	MGCD516
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

MGCD516 was administered as an oral capsule.

Number of subjects in period 1	120 mg MGCD516
Started	6
Received Treatment	6
Completed	6

Baseline characteristics

Reporting groups	
Reporting group title	120 mg MGCD516
Reporting group description:	
Participants were administered a single oral dose of 120 mg MGCD516 containing approximately 3.7 MBq of [14C]-MGCD516 on Day 1 of the treatment period.	

Reporting group values	120 mg MGCD516	Total	
Number of subjects	6	6	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	6	6	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	28		
standard deviation	± 6	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	6	6	
Race Units: Subjects			
White	5	5	
Asian	1	1	
Ethnicity Units: Subjects			
Not Hispanic or Latino	6	6	

End points

End points reporting groups

Reporting group title	120 mg MGCD516

Reporting group description:

Participants were administered a single oral dose of 120 mg MGCD516 containing approximately 3.7 MBq of [14C]-MGCD516 on Day 1 of the treatment period.

Primary: Maximum Observed Plasma Concentration (Cmax) of MGCD516 in Plasma

End point title	Maximum Observed Plasma Concentration (Cmax) of MGCD516 in Plasma[1]

End point description:

End point type	Primary

End point timeframe:

Day 1 to Day 16: Predose and 1, 2, 3, 4, 6, 8, 10 and 12 hours postdose on Day 1 and 24, 48, 72, 96, 144, 192, 240, 288, 312, 336, and 360 hours postdose

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	120 mg MGCD516			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: nanograms per milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)				
MGCD516 in Plasma	66.0 (± 15.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Observed Plasma Concentration (Cmax) of Total Radioactivity in Plasma and Whole Blood

End point title	Maximum Observed Plasma Concentration (Cmax) of Total Radioactivity in Plasma and Whole Blood[2]

End point description:

The unit of measurement for Cmax is equivalent nanogram hours per milliliter (h.ngEq/mL).

End point type	Primary

End point timeframe:

Day 1 to Day 16: Predose and 1, 2, 3, 4, 6, 8, 10 and 12 hours postdose on Day 1 and 24, 48, 72, 96, 144, 192, 240, 288, 312, 336, and 360 hours postdose

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	120 mg MGCD516			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: h.ngEq/mL				
geometric mean (geometric coefficient of variation)				
Total Radioactivity in Plasma	251 (± 18.0)			
Total Radioactivity in Whole Blood	186 (± 17.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Time to Attain Maximum Observed Plasma Concentration (tmax) of MGCD516 in Plasma and for Total Radioactivity in Plasma and Whole Blood

End point title	Time to Attain Maximum Observed Plasma Concentration (tmax) of MGCD516 in Plasma and for Total Radioactivity in Plasma and Whole Blood[3]

End point description:

End point type	Primary

End point timeframe:

Day 1 to Day 16: Predose and 1, 2, 3, 4, 6, 8, 10 and 12 hours postdose on Day 1 and 24, 48, 72, 96, 144, 192, 240, 288, 312, 336, and 360 hours postdose

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	120 mg MGCD516			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: hours				
median (full range (min-max))				
MGCD516 in Plasma	11.01 (8.00 to 12.20)			
Total Radioactivity in Plasma	18.01 (8.00 to 24.00)			
Total Radioactivity in Whole Blood	10.00 (8.00 to 12.20)			

Statistical analyses

No statistical analyses for this end point

Primary: Terminal Phase Rate Constant (kel) of MGCD516 in Plasma and for Total Radioactivity in Plasma and Whole Blood

End point title	Terminal Phase Rate Constant (kel) of MGCD516 in Plasma and for Total Radioactivity in Plasma and Whole Blood[4]

End point description:

Kel was calculated by linear regression of the terminal log-linear portion of the concentration vs time curve. Linear regression of at least 3 points was required to obtain a reliable kel.

End point type	Primary

End point timeframe:

Day 1 to Day 16: Predose and 1, 2, 3, 4, 6, 8, 10 and 12 hours postdose on Day 1 and 24, 48, 72, 96, 144, 192, 240, 288, 312, 336, and 360 hours postdose

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	120 mg MGCD516			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: per hour (/h)				
geometric mean (geometric coefficient of variation)				
MGCD516 in Plasma	0.0141 (± 4.2)			
Total Radioactivity in Plasma	0.00760 (± 2.6)			
Total Radioactivity in Whole Blood	0.0145 (± 2.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Terminal Elimination Half-life (t1/2) of MGCD516 in Plasma and for Total Radioactivity in Plasma and Whole Blood

End point title	Terminal Elimination Half-life (t1/2) of MGCD516 in Plasma and for Total Radioactivity in Plasma and Whole Blood[5]

End point description:

t1/2 was calculated as 0.693/kel.

End point type	Primary

End point timeframe:

Day 1 to Day 16: Predose and 1, 2, 3, 4, 6, 8, 10 and 12 hours postdose on Day 1 and 24, 48, 72, 96, 144, 192, 240, 288, 312, 336, and 360 hours postdose

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	120 mg MGCD516			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: hours (h)				
geometric mean (geometric coefficient of variation)				
MGCD516 in Plasma	49.3 (± 14.2)			
Total Radioactivity in Plasma	91.2 (± 22.6)			
Total Radioactivity in Whole Blood	47.7 (± 22.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Time of Last Observed Plasma Concentration (tlast) of MGCD516 in Plasma and for Total Radioactivity in Plasma and Whole Blood

End point title	Time of Last Observed Plasma Concentration (tlast) of MGCD516 in Plasma and for Total Radioactivity in Plasma and Whole Blood[6]

End point description:

End point type	Primary

End point timeframe:

Day 1 to Day 16: Predose and 1, 2, 3, 4, 6, 8, 10 and 12 hours postdose on Day 1 and 24, 48, 72, 96, 144, 192, 240, 288, 312, 336, and 360 hours postdose

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	120 mg MGCD516			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: hours (h)				
median (full range (min-max))				
MGCD516 in Plasma	360.00 (336.00 to 360.13)			
Total Radioactivity in Plasma	240.00 (192.00 to 336.00)			
Total Radioactivity in Whole Blood	96.00 (96.00 to 144.00)			

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-time Curve Over an Interval of 0-12 Hours (AUC0-12) of Total Radioactivity in Plasma and Whole Blood

End point title	Area Under the Plasma Concentration-time Curve Over an Interval of 0-12 Hours (AUC0-12) of Total Radioactivity in Plasma and Whole Blood[7]

End point description:

The unit of measurement for AUC0-12 is equivalent nanogram hours per milliliter (h.ngEq/mL).

End point type	Primary

End point timeframe:

Day 1: Predose, and 1, 2, 3, 4, 6, 8, 10 and 12 hours postdose

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	120 mg MGCD516			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: h.ngEq/mL				
geometric mean (geometric coefficient of variation)				
Total Radioactivity in Plasma	2015 (± 19.8)			
Total Radioactivity in Whole Blood	1529 (± 20.1)			

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-time Curve Over an Interval of 0-24 Hours (AUC0-24) of Total Radioactivity in Plasma and Whole Blood

End point title	Area Under the Plasma Concentration-time Curve Over an Interval of 0-24 Hours (AUC0-24) of Total Radioactivity in Plasma and Whole Blood[8]

End point description:

The unit of measurement for AUC0-24 is equivalent nanogram hours per milliliter (h.ngEq/mL).

End point type	Primary

End point timeframe:

Day 1 to Day 2: Predose and 1, 2, 3, 4, 6, 8, 10 and 12 postdose on Day 1 and 24 hours postdose

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	120 mg MGCD516			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: h.ngEq/mL				
geometric mean (geometric coefficient of variation)				
Total Radioactivity in Plasma	4933 (± 18.3)			
Total Radioactivity in Whole Blood	3629 (± 16.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-time Curve up to Time t (AUC0-t) for MGCD516 in Plasma

End point title	Area Under the Plasma Concentration-time Curve up to Time t (AUC0-t) for MGCD516 in Plasma[9]

End point description:

Time t was defined as the last point with concentrations above the lower limit of quantitation.

End point type	Primary

End point timeframe:

Day 1 to Day 16: Predose and 1, 2, 3, 4, 6, 8, 10 and 12 hours postdose on Day 1 and 24, 48, 72, 96, 144, 192, 240, 288, 312, 336, and 360 hours postdose

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	120 mg MGCD516			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: nanogram hours per milliliter (h.ng/mL)				
geometric mean (geometric coefficient of variation)				
MGCD516 in Plasma	3253 (± 13.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-time Curve up to Time t (AUC0-t) of Total Radioactivity in Plasma and Whole Blood

End point title	Area Under the Plasma Concentration-time Curve up to Time t (AUC0-t) of Total Radioactivity in Plasma and Whole Blood[10]

End point description:

Time t was defined as the last point with concentrations above the lower limit of quantitation. The unit of measurement for AUC0-t is equivalent nanogram hours per milliliter (h.ngEq/mL).

End point type	Primary

End point timeframe:

Day 1 to Day 16: Predose and 1, 2, 3, 4, 6, 8, 10 and 12 hours postdose on Day 1 and 24, 48, 72, 96, 144, 192, 240, 288, 312, 336, and 360 hours postdose

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	120 mg MGCD516			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: h.ngEq/mL				
geometric mean (geometric coefficient of variation)				
Total Radioactivity in Plasma	22053 (± 18.5)			

Total Radioactivity in Whole Blood	11211 (± 12.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-time Curve from Time 0 to Infinity (AUC0-inf) of MGCD516 in Plasma

End point title	Area Under the Plasma Concentration-time Curve from Time 0 to Infinity (AUC0-inf) of MGCD516 in Plasma[11]

End point description:

AUC0-inf was calculated as AUC0-inf = AUC0-t + Clast/kel, where Clast is the last measurable plasma concentration and kel is the terminal elimination rate constant.

End point type	Primary

End point timeframe:

Day 1 to Day 16: Predose and 1, 2, 3, 4, 6, 8, 10 and 12 hours postdose on Day 1 and 24, 48, 72, 96, 144, 192, 240, 288, 312, 336, and 360 hours postdose

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	120 mg MGCD516			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: nanogram hours per milliliter (h.ng/mL)				
geometric mean (geometric coefficient of variation)				
MGCD516 in Plasma	3260 (± 14.0)			

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-time Curve from Time 0 to Infinity (AUC0-inf) of Total Radioactivity in Plasma and Whole Blood

End point title	Area Under the Plasma Concentration-time Curve from Time 0 to Infinity (AUC0-inf) of Total Radioactivity in Plasma and Whole Blood[12]

End point description:

AUC0-inf was calculated as AUC0-inf = AUC0-t + Clast/kel, where Clast is the last measurable plasma concentration and kel is the terminal elimination rate constant. The unit of measurement for AUC0-inf is equivalent nanogram hours per milliliter (h.ngEq/mL).

End point type	Primary

End point timeframe:

Day 1 to Day 16: Predose and 1, 2, 3, 4, 6, 8, 10 and 12 hours postdose on Day 1 and 24, 48, 72, 96, 144, 192, 240, 288, 312, 336, and 360 hours postdose

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	120 mg MGCD516			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: h.ngEq/mL				
geometric mean (geometric coefficient of variation)				
Total Radioactivity in Plasma	25113 (± 18.6)			
Total Radioactivity in Whole Blood	14863 (± 12.1)			

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-time Curve Over an Interval of 0-144 Hours (AUC0-144) of MGCD516 in Plasma

End point title	Area Under the Plasma Concentration-time Curve Over an Interval of 0-144 Hours (AUC0-144) of MGCD516 in Plasma[13]

End point description:

End point type	Primary

End point timeframe:

Day 1 to Day 7: Predose and 1, 2, 3, 4, 6, 8, 10, and 12 hours postdose on Day 1 and 24, 48, 72, 96 and 144 hours postdose

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	120 mg MGCD516			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: nanogram hours per milliliter (h.ng/mL)				
geometric mean (geometric coefficient of variation)				
MGCD516 in Plasma	3110 (± 12.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-time Curve Over an Interval of 0-144 Hours (AUC0-144) of Total Radioactivity in Plasma and Whole Blood

End point title	Area Under the Plasma Concentration-time Curve Over an Interval of 0-144 Hours (AUC0-144) of Total Radioactivity in Plasma and Whole Blood[14]

End point description:

The unit of measurement for AUC0-144 is equivalent nanogram hours per milliliter (h.ngEq/mL).

End point type	Primary

End point timeframe:

Day 1 to Day 7: Predose and 1, 2, 3, 4, 6, 8, 10, and 12 hours postdose on Day 1 and 24, 48, 72, 96 and 144 hours postdose

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	120 mg MGCD516			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: h.ngEq/mL				
geometric mean (geometric coefficient of variation)				
Total Radioactivity in Plasma	18282 (± 13.3)			
Total Radioactivity in Whole Blood	12325 (± 10.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Oral Clearance (CL/F) of MGCD516 in Plasma

End point title	Apparent Oral Clearance (CL/F) of MGCD516 in Plasma[15]

End point description:

CL/F was calculated as dose/AUC0-inf.

End point type	Primary

End point timeframe:

Day 1 to Day 16: Predose and 1, 2, 3, 4, 6, 8, 10 and 12 hours postdose on Day 1 and 24, 48, 72, 96, 144, 192, 240, 288, 312, 336, and 360 hours postdose

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	120 mg MGCD516			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: liters per hour (L/h)				
geometric mean (geometric coefficient of variation)	36.8 (± 14.0)			

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Volume of Distribution at Terminal Phase (Vz/F) of MGCD516 in Plasma

End point title	Apparent Volume of Distribution at Terminal Phase (Vz/F) of MGCD516 in Plasma[16]

End point description:

End point type	Primary

End point timeframe:

Day 1 to Day 16: Predose and 1, 2, 3, 4, 6, 8, 10 and 12 hours postdose on Day 1 and 24, 48, 72, 96, 144, 192, 240, 288, 312, 336, and 360 hours postdose

Notes:

[16] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	120 mg MGCD516			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: liters (L)				
geometric mean (geometric coefficient of variation)	2619 (± 10.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-time Curve Over a Dosing Interval of 0-12 hours (AUC0-12) Whole Blood to Plasma Ratio for Total Radioactivity

End point title	Area Under the Plasma Concentration-time Curve Over a Dosing Interval of 0-12 hours (AUC0-12) Whole Blood to Plasma Ratio for Total Radioactivity[17]

End point description:

Calculated as AUC0-12,blood / AUC0-12,plasma.

End point type	Primary

End point timeframe:

Day 1: Predose, and 1, 2, 3, 4, 6, 8, 10 and 12 hours postdose

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	120 mg MGCD516			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: ratio				
geometric mean (geometric coefficient of variation)	0.76 (± 3.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-time Curve Over a Dosing Interval of 0-24 hours (AUC0-24) Whole Blood to Plasma Ratio for Total Radioactivity

End point title	Area Under the Plasma Concentration-time Curve Over a Dosing Interval of 0-24 hours (AUC0-24) Whole Blood to Plasma Ratio for Total Radioactivity[18]

End point description:

Calculated as AUC0-24,blood / AUC0-24,plasma.

End point type	Primary

End point timeframe:

Day 1 to Day 2: Predose and 1, 2, 3, 4, 6, 8, 10, 12 postdose on Day 1 and 24 hours postdose

Notes:

[18] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	120 mg MGCD516			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: ratio				
geometric mean (geometric coefficient of variation)	0.74 (± 3.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-time Curve Over a Dosing Interval of 0-96 hours (AUC0-96) Whole Blood to Plasma Ratio for Total Radioactivity

End point title	Area Under the Plasma Concentration-time Curve Over a Dosing Interval of 0-96 hours (AUC0-96) Whole Blood to Plasma Ratio for Total Radioactivity[19]

End point description:

Calculated as AUC0-96,blood / AUC0-96,plasma

End point type	Primary

End point timeframe:

Day 1: Predose and 1, 2, 3, 4, 6, 8, 10 and 12 hours postdose on Day 1 and 24, 48, 72 and 96 hours postdose

Notes:

[19] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	120 mg MGCD516			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: ratio				
geometric mean (geometric coefficient of variation)	0.71 (± 3.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-time Curve Over a Dosing Interval of 0-144 hours (AUC0-144) Whole Blood to Plasma Ratio for Total Radioactivity

End point title	Area Under the Plasma Concentration-time Curve Over a Dosing Interval of 0-144 hours (AUC0-144) Whole Blood to Plasma Ratio for Total Radioactivity[20]

End point description:

Calculated as AUC0-144,blood / AUC0-144,plasma

End point type	Primary

End point timeframe:

Day 1 to Day 7: Predose and 1, 2, 3, 4, 6, 8, 10, and 12 hours postdose on Day 1 and 24, 48, 72, 96 and 144 hours postdose

Notes:

[20] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	120 mg MGCD516			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: ratio				
geometric mean (geometric coefficient of variation)	0.67 (± 5.1)			

Statistical analyses

No statistical analyses for this end point

Primary: Cumulative Amount of MGCD516 Excreted Unchanged in Urine up to the Last Quantifiable Concentration (Aeurine)

End point title	Cumulative Amount of MGCD516 Excreted Unchanged in Urine up to the Last Quantifiable Concentration (Aeurine)[21]

End point description:

End point type	Primary

End point timeframe:

Day 1 to Day 16: Predose on Day 1 to 360 hours postdose

Notes:

[21] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	120 mg MGCD516			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: micrograms (µg)				
arithmetic mean (standard deviation)	62.7 (± 30.0)			

Statistical analyses

No statistical analyses for this end point

Primary: Cumulative Percentage of Total MGCD516 Excreted Unchanged in Urine (feurine) up to the Last Quantifiable Concentration

End point title	Cumulative Percentage of Total MGCD516 Excreted Unchanged in Urine (feurine) up to the Last Quantifiable Concentration[22]

End point description:

End point type	Primary

End point timeframe:

Day 1 to Day 16: Predose on Day 1 to 360 hours postdose

Notes:

[22] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	120 mg MGCD516			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: percentage of MGCD516				
arithmetic mean (standard deviation)	0.05 (± 0.03)			

Statistical analyses

No statistical analyses for this end point

Primary: Renal Clearance of MGCD516 (CLR)

End point title	Renal Clearance of MGCD516 (CLR)[23]

End point description:

Calculated as cumulative Aeurine / AUC0-t.

End point type	Primary

End point timeframe:

Day 1 to Day 16: Predose on Day 1 to 360 hours postdose

Notes:

[23] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	120 mg MGCD516			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: liters per hour (L/h)				
arithmetic mean (standard deviation)	0.0190 (± 0.00726)			

Statistical analyses

No statistical analyses for this end point

Primary: Cumulative Amount of Total Radioactivity Excreted Unchanged in Urine (Aeurine), Feces (Aefeces) and Total Urine and Feces (Aetotal) up to the Last Quantifiable Concentration

End point title	Cumulative Amount of Total Radioactivity Excreted Unchanged in Urine (Aeurine), Feces (Aefeces) and Total Urine and Feces (Aetotal) up to the Last Quantifiable Concentration[24]

End point description:

Aetotal was calculated as cumulative Aeurine + cumulative Aefeces

End point type	Primary

End point timeframe:

Day 1 to Day 16: Predose on Day 1 to 360 hours postdose

Notes:

[24] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	120 mg MGCD516			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: equivalent milligrams (mgEq)				
arithmetic mean (standard deviation)				
Aeurine 0-144 hours	3.99 (± 0.973)			
Aefeces 0-144 hours	154 (± 11.7)			
Aetotal 0-144 hours	158 (± 12.1)			
Aeurine 0-360 hours	4.52 (± 1.09)			
Aefeces 0-360 hours	168 (± 13.1)			
Aetotal 0-360 hours	172 (± 13.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Cumulative Percentage of Total Radioactivity Excreted Unchanged in Urine (feurine), Feces (fefeces) and Total Urine and Feces (fetotal) up to the Last Quantifiable Concentration

End point title	Cumulative Percentage of Total Radioactivity Excreted Unchanged in Urine (feurine), Feces (fefeces) and Total Urine and Feces (fetotal) up to the Last Quantifiable Concentration[25]

End point description:

Fetotal was calculated as cumulative feurine + cumulative fefeces / dose

End point type	Primary

End point timeframe:

Day 1 to Day 16: Predose on Day 1 to 360 hours postdose

Notes:

[25] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned for this endpoint.

End point values	120 mg MGCD516			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: percentage of total radioactivity				
arithmetic mean (standard deviation)				
Feurine 0-144 hours	2.6 (± 0.6)			
Fefeces 0-144 hours	98.9 (± 7.8)			
Fetotal 0-144 hours	101.5 (± 8.3)			
Feurine 0-360 hours	2.9 (± 0.7)			
Fefeces 0-360 hours	108.1 (± 8.7)			
Fetotal 0-360 hours	111.0 (± 9.3)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Day 1 to end of follow-up (maximum time to follow-up was 20 days)	
Adverse event reporting additional description:	
Mortality, serious adverse events and non-serious adverse events are reported for all participants who enrolled in the study.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups	
Reporting group title	120 mg MGCD516
Reporting group description:	
Participants were administered a single oral dose of 120 mg MGCD516 containing approximately 3.7 MBq of [14C]-MGCD516 on Day 1 of the treatment period.	

Serious adverse events	120 mg MGCD516		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	120 mg MGCD516		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)		
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Paraesthesia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Presyncope			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		

General disorders and administration site conditions			
Influenza Like Illness			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Injection Site Haematoma			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Injection Site Irritation			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Gastrointestinal disorders			
Gastrointestinal Sounds Abnormal			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Abdominal Discomfort			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Oropharyngeal Pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Skin Irritation			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		

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

None reported