Clinical trial results:
An open-label, mass balance study to investigate the absorption, distribution, metabolism and excretion of [14C]-etripamil nasal spray after a single dose to healthy male subjects

Summary

EudraCT number	2019-004979-39
Trial protocol	NL
Global end of trial date	09 November 2020

Results information

Result version number	v1 (current)
This version publication date	24 June 2022
First version publication date	24 June 2022

Trial information

Trial identification

Sponsor protocol code	MSP-2017-1220

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Milestone Pharmaceuticals Inc.
Sponsor organisation address	1111 Dr.-Frederik-Philips Blvd, Ste. 420, Montreal, Canada, H4M 2X6
Public contact	Guy Rousseau, Milestone Pharmaceuticals Inc. , +1 5143360444228, grousseau@milestonepharma.com
Scientific contact	Guy Rousseau, Milestone Pharmaceuticals Inc. , +1 5143360444228, grousseau@milestonepharma.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002303-PIP01-17
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	03 June 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 November 2020
Global end of trial reached?	Yes
Global end of trial date	09 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the ratio of parent drug to metabolites in the circulation.
Profiling of [14C]-etripamil metabolites in blood, urine and feces.
To determine the mass balance of drug-related materials following intranasal administration.
To determine the primary route of excretion of drug-related materials.
To determine the total radioactivity versus time profile in plasma and whole blood.

Protection of trial subjects:

To safeguard the study subjects and the site staff, testing for COVID-19 was performed. A SARS-CoV-2 PCR was performed on nasal and/or throat swabs. The testing was performed one day prior to the scheduled study admittance day of the treatment period (Day -2). An extra residence day and night in the clinic was added for the treatment period where subjects came in one day prior to the scheduled study admittance day.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 October 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	Netherlands: 7
Worldwide total number of subjects	7
EEA total number of subjects	7

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)	7
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited in Netherlands and signed inform consent form between 02-Oct-2020 and 16-Oct-2020.

Pre-assignment

Screening details:

The subject population included healthy male subjects who satisfied all entry criteria (Inclusion and exclusion criteria met).

Period 1

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

Blinding implementation details:

This study was not blinded

Arms

Arm title	Overall study

Arm description:

Only 1 arm for this study

Arm type	Experimental
Investigational medicinal product name	Etripamil Nasal Spray
Investigational medicinal product code	MSP-2017
Other name	
Pharmaceutical forms	Nasal spray, solution in single-dose container
Routes of administration	Intranasal use

Dosage and administration details:

A single dose of 70 mg etripamil nasal spray containing 96.9 µCi of radioactivity was administered to the subjects. The formulation of the radiolabeled etripamil nasal spray consisted of etripamil, [14C]-etripamil, water, acetic acid, disodium ethylene-diamine-tetra-acetic acid (EDTA), and sulfuric acid to adjust pH to 4.4.

Number of subjects in period 1	Overall study
Started	7
Completed	7

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	7	7	
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)	7	7	
From 65-84 years	0	0	
85 years and over	0	0	
Adults	0	0	
Age continuous Units: years			
arithmetic mean	32.7		
standard deviation	± 16.00	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	7	7	

Subject analysis sets

Subject analysis set title	Pharmacokinetics set
Subject analysis set type	Per protocol

Subject analysis set description:

This analysis set comprised all subjects who received the study drug, had no major protocol deviation associated with inclusion and exclusion criteria, and did not violate the protocol in a way that could affect the evaluation of the primary endpoints, i.e., without major protocol violations or deviations. The Pharmacokinetics set was employed in the analysis of PK and radioactivity endpoints.

Subject analysis set title	Safety set
Subject analysis set type	Safety analysis

Subject analysis set description:

This analysis set included all subjects who received the study drug. The Safety set was employed in the analysis of tolerability and safety variables

Subject analysis set title	Metabolite profiling set
Subject analysis set type	Per protocol

Subject analysis set description:

This analysis set comprised all subjects who received the study drug, had no major protocol deviation associated with inclusion and exclusion criteria, and did not violate the protocol in a way that could affect the evaluation of the primary endpoints, i.e., without major protocol violations or deviations.

Reporting group values	Pharmacokinetics set	Safety set	Metabolite profiling set
Number of subjects	7	7	7
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	7	7	7
From 65-84 years	0	0	0
85 years and over	0	0	0
Adults	0	0	0
Age continuous Units: years			
arithmetic mean	32.7	32.7	32.7
standard deviation	± 16.00	± 16.00	± 16.00
Gender categorical Units: Subjects			
Female	0	0	0
Male	7	7	7

End points

End points reporting groups

Reporting group title	Overall study

Reporting group description:

Only 1 arm for this study

Subject analysis set title	Pharmacokinetics set
Subject analysis set type	Per protocol

Subject analysis set description:

This analysis set comprised all subjects who received the study drug, had no major protocol deviation associated with inclusion and exclusion criteria, and did not violate the protocol in a way that could affect the evaluation of the primary endpoints, i.e., without major protocol violations or deviations. The Pharmacokinetics set was employed in the analysis of PK and radioactivity endpoints.

Subject analysis set title	Safety set
Subject analysis set type	Safety analysis

Subject analysis set description:

This analysis set included all subjects who received the study drug. The Safety set was employed in the analysis of tolerability and safety variables

Subject analysis set title	Metabolite profiling set
Subject analysis set type	Per protocol

Subject analysis set description:

This analysis set comprised all subjects who received the study drug, had no major protocol deviation associated with inclusion and exclusion criteria, and did not violate the protocol in a way that could affect the evaluation of the primary endpoints, i.e., without major protocol violations or deviations.

Primary: Whole blood - Area under the total radioactivity-time curve from time zero to the last measurable concentration (AUC0-t)

End point title	Whole blood - Area under the total radioactivity-time curve from time zero to the last measurable concentration (AUC0-t)[1]

End point description:

End point type	Primary

End point timeframe:

Pre-dose, 0.5, 1.5, 3. 5, 7, 10, 15, 25, 50, 90, 240, 360, 720 min post-dose on Day 1, Day 2, Day 3, Day 4

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: Study was not designed to be powered for statistical analysis

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: h*ng/mL				
arithmetic mean (standard deviation)	890 (± 949)			

Statistical analyses

No statistical analyses for this end point

Primary: Whole blood - Area under the total radioactivity-time curve from time zero to infinity (AUC0-inf)

End point title	Whole blood - Area under the total radioactivity-time curve from time zero to infinity (AUC0-inf)[2]

End point description:

End point type	Primary

End point timeframe:

Pre-dose, 0.5, 1.5, 3. 5, 7, 10, 15, 25, 50, 90, 240, 360, 720 min post-dose on Day 1, Day 2, Day 3, Day 4

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: Study was not designed to be powered for statistical analysis

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	0[3]			
Units: h*ng-Eq/mL				
arithmetic mean (standard deviation)	()			

Notes:

[3] - This parameter was not estimated as the AUC0-t / AUC0-inf ratio was less than 0.80.

Statistical analyses

No statistical analyses for this end point

Primary: Plasma - Maximum observed total radioactivity (Cmax)

End point title	Plasma - Maximum observed total radioactivity (Cmax)[4]

End point description:

End point type	Primary

End point timeframe:

Pre-dose, 0.5, 1.5, 3. 5, 7, 10, 15, 25, 50, 90, 240, 360, 720 min post-dose on Day 1, Day 2, Day 3, Day 4

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: Study was not designed to be powered for statistical analysis.

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: ng/mL				
arithmetic mean (standard deviation)	67.3 (± 23.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Plasma - Time from time zero to peak total radioactivity (tmax)

End point title	Plasma - Time from time zero to peak total radioactivity

End point description:

End point type	Primary

End point timeframe:

Pre-dose, 0.5, 1.5, 3. 5, 7, 10, 15, 25, 50, 90, 240, 360, 720 min post-dose on Day 1, Day 2, Day 3, Day 4

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: Study was not designed to be powered for statistical analysis.

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: hour				
arithmetic mean (standard deviation)	1.21 (± 0.36)			

Statistical analyses

No statistical analyses for this end point

Primary: Plasma - Area under the total radioactivity-time curve from time zero to the last measurable concentration of total radioactivity (AUC0-t)

End point title	Plasma - Area under the total radioactivity-time curve from time zero to the last measurable concentration of total radioactivity (AUC0-t)[6]

End point description:

End point type	Primary

End point timeframe:

Pre-dose, 0.5, 1.5, 3. 5, 7, 10, 15, 25, 50, 90, 240, 360, 720 min post-dose on Day 1, Day 2, Day 3, Day 4

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: Study was not designed to be powered for statistical analysis.

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: h*ng-Eq/mL				
arithmetic mean (standard deviation)	2230 (± 1590)			

Statistical analyses

No statistical analyses for this end point

Primary: Plasma - Area under the total radioactivity-time curve from time zero to infinity (AUC0-inf)

End point title	Plasma - Area under the total radioactivity-time curve from time zero to infinity (AUC0-inf)[7]

End point description:

End point type	Primary

End point timeframe:

Pre-dose, 0.5, 1.5, 3. 5, 7, 10, 15, 25, 50, 90, 240, 360, 720 min post-dose on Day 1, Day 2, Day 3, Day 4

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: Study was not designed to be powered for statistical analysis.

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	0[8]			
Units: h*ng-Eq/mL				
arithmetic mean (standard deviation)	()			

Notes:

[8] - The AUC0-inf could not be determined, as the AUC0-t / AUC0-inf ratio was l

Statistical analyses

No statistical analyses for this end point

Primary: Plasma - Total radioactivity half-life (t1/2)

End point title	Plasma - Total radioactivity half-life (t1/2)[9]

End point description:

End point type	Primary

End point timeframe:

Pre-dose, 0.5, 1.5, 3. 5, 7, 10, 15, 25, 50, 90, 240, 360, 720 min post-dose on Day 1, Day 2, Day 3, Day 4

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: Study was not designed to be powered for statistical analysis.

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	0[10]			
Units: hour				
arithmetic mean (standard deviation)	()			

Notes:

[10] - The t1/2 could not be determined, as the AUC0-t / AUC0-inf ratio was less than 0.8.

Statistical analyses

No statistical analyses for this end point

Primary: Plasma - Apparent total radioactivity clearance (CL/F)

End point title	Plasma - Apparent total radioactivity clearance (CL/F)[11]

End point description:

End point type	Primary

End point timeframe:

Pre-dose, 0.5, 1.5, 3. 5, 7, 10, 15, 25, 50, 90, 240, 360, 720 min post-dose on Day 1, Day 2, Day 3, Day 4

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: Study was not designed to be powered for statistical analysis.

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	0[12]			
Units: L/h				
arithmetic mean (standard deviation)	()			

Notes:

[12] - The CL/F could not be determined, as the AUC0-t / AUC0-inf ratio was less than 0.8

Statistical analyses

No statistical analyses for this end point

Primary: Plasma - volume of distribution (Vz/F)

End point title	Plasma - volume of distribution (Vz/F)[13]

End point description:

End point type	Primary

End point timeframe:

Pre-dose, 0.5, 1.5, 3. 5, 7, 10, 15, 25, 50, 90, 240, 360, 720 min post-dose on Day 1, Day 2, Day 3, Day 4

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: Study was not designed to be powered for statistical analysis.

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	0[14]			
Units: Liter				
arithmetic mean (standard deviation)	()			

Notes:

[14] - The Vz/F could not be determined, as the AUC0-t / AUC0-inf ratio was less than 0.8.

Statistical analyses

No statistical analyses for this end point

Primary: Urine - Total radioactivity amount excreted in urine (Aeu)

End point title	Urine - Total radioactivity amount excreted in urine (Aeu)[15]

End point description:

End point type	Primary

End point timeframe:

Pre-dose and 0-120, 120-240, 240-360, 360-720, 720-1440 minutes post-dose, Day 2, Day 3, Day 4

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: Study was not designed to be powered for statistical analysis.

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: mg				
arithmetic mean (standard deviation)	0.00873 (± 0.00804)			

Statistical analyses

No statistical analyses for this end point

Primary: Urine - Total radioactivity excreted as a percentage of the radioactive dose.

End point title	Urine - Total radioactivity excreted as a percentage of the radioactive dose.[16]

End point description:

End point type	Primary

End point timeframe:

Pre-dose and 0-120, 120-240, 240-360, 360-720, 720-1440 minutes post-dose, Day 2, Day 3, Day 4

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: Study was not designed to be powered for statistical analysis.

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: Percentage of dose				
arithmetic mean (standard deviation)	28.9 (± 12.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Plasma - 14C]-metabolic profile and identification of metabolites

End point title	Plasma - 14C]-metabolic profile and identification of metabolites[17]

End point description:

End point type	Primary

End point timeframe:

0.0833, 0.117, 0.167, 0.25, 0.417, 0.833, 1.5, 6 hours

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: Study was not designed to be powered for statistical analysis.

End point values	Metabolite profiling set			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: major metabolite (>10%)				
number (not applicable)	3			

Statistical analyses

No statistical analyses for this end point

Primary: Urine - [14C]-metabolic profile and identification of metabolites

End point title	Urine - [14C]-metabolic profile and identification of

End point description:

End point type	Primary

End point timeframe:

0-2, 2-4, 2-6, 6-12, 12-24, 24-48, 48-72

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: Study was not designed to be powered for statistical analysis.

End point values	Metabolite profiling set			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: Major metabolite (>10% of total)				
number (not applicable)	1			

Statistical analyses

No statistical analyses for this end point

Primary: Urine - Major radioactive peak/metabolite(s) in radiochromatogram(s) as a percentage of the radioactive dose

End point title	Urine - Major radioactive peak/metabolite(s) in radiochromatogram(s) as a percentage of the radioactive dose[19]

End point description:

End point type	Primary

End point timeframe:

0-2, 2-4, 2-6, 6-12, 12-24, 24-48, 48-72

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: Study was not designed to be powered for statistical analysis.

End point values	Metabolite profiling set			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: % of dose				
number (not applicable)	18.8			

Statistical analyses

No statistical analyses for this end point

Primary: Feces - Total radioactivity percentage dose excreted

End point title	Feces - Total radioactivity percentage dose excreted[20]

End point description:

End point type	Primary

End point timeframe:

Day 1 (dosing), Day 2, Day 3, Day 4

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: Study was not designed to be powered for statistical analysis.

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: % dose				
number (not applicable)	25.6			

Statistical analyses

No statistical analyses for this end point

Primary: Feces - [14C]-metabolic profile and identification of metabolites

End point title	Feces - [14C]-metabolic profile and identification of

End point description:

End point type	Primary

End point timeframe:

Day 1 (dosing), Day 2, Day 3, Day 4

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: Study was not designed to be powered for statistical analysis.

End point values	Metabolite profiling set			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: Major metabolite (>10%)				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Primary: Feces - Major radioactive peak/metabolite(s) in radiochromatogram(s) as a percentage of the radioactive dose.

End point title	Feces - Major radioactive peak/metabolite(s) in radiochromatogram(s) as a percentage of the radioactive dose.[22]

End point description:

End point type	Primary

End point timeframe:

Day 1 (dosing), Day 2, Day 3, Day 4

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: Study was not designed to be powered for statistical analysis.

End point values	Metabolite profiling set			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: major metabolite - % of dose				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Primary: Whole blood - Maximum observed total radioactivity (Cmax)

End point title	Whole blood - Maximum observed total radioactivity (Cmax)[23]

End point description:

End point type	Primary

End point timeframe:

Pre-dose, 0.5, 1.5, 3. 5, 7, 10, 15, 25, 50, 90, 240, 360, 720 min post-dose on Day 1, Day 2, Day 3, Day 4

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: Study was not designed to be powered for statistical analysis.

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: ng-Eq/mL				
arithmetic mean (standard deviation)	311 (± 252)			

Statistical analyses

No statistical analyses for this end point

Primary: Whole blood - Time from time zero to peak total radioactivity (tmax)

End point title	Whole blood - Time from time zero to peak total radioactivity (tmax)[24]

End point description:

End point type	Primary

End point timeframe:

Pre-dose, 0.5, 1.5, 3. 5, 7, 10, 15, 25, 50, 90, 240, 360, 720 min post-dose on Day 1, Day 2, Day 3, Day 4

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: Study was not designed to be powered for statistical analysis.

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: hour				
arithmetic mean (standard deviation)	1.28 (± 0.35)			

Statistical analyses

No statistical analyses for this end point

Secondary: Safety and Tolerability - Number of SAE

End point title	Safety and Tolerability - Number of SAE

End point description:

End point type	Secondary

End point timeframe:

Continuous monitoring from signature of inform consent to end-of-study (EOS). Adverse events were followed until resolution, or to a maximum of 28 days after the EOS.

End point values	Safety set			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: Number of SAE				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum observed concentration (Cmax) - Etripamil plasma

End point title	Maximum observed concentration (Cmax) - Etripamil plasma

End point description:

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1.5, 3. 5, 7, 10, 15, 25, 50, 90, 240, 360, 720 min post-dose on Day 1, Day 2, Day 3, Day 4

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: ng/mL				
arithmetic mean (standard deviation)	67.3 (± 23.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum observed concentration (Cmax) - MSP-2030 plasma

End point title	Maximum observed concentration (Cmax) - MSP-2030 plasma

End point description:

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1.5, 3. 5, 7, 10, 15, 25, 50, 90, 240, 360, 720 min post-dose on Day 1, Day 2, Day 3, Day 4

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: ng/mL				
arithmetic mean (standard deviation)	59.9 (± 14.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time from time zero to peak concentration (tmax) - etripamil plasma

End point title	Time from time zero to peak concentration (tmax) - etripamil plasma

End point description:

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1.5, 3. 5, 7, 10, 15, 25, 50, 90, 240, 360, 720 min post-dose on Day 1, Day 2, Day 3, Day 4

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: hour				
arithmetic mean (standard deviation)	0.10 (± 0.04)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time from time zero to peak concentration (tmax) - MSP-2030 plasma

End point title	Time from time zero to peak concentration (tmax) - MSP-2030 plasma

End point description:

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1.5, 3. 5, 7, 10, 15, 25, 50, 90, 240, 360, 720 min post-dose on Day 1, Day 2, Day 3, Day 4

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: hour				
arithmetic mean (standard deviation)	0.34 (± 0.11)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the concentration-time curve from time zero to the last measurable concentration (AUC0-t) - etripamil plasma

End point title	Area under the concentration-time curve from time zero to the last measurable concentration (AUC0-t) - etripamil plasma

End point description:

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1.5, 3. 5, 7, 10, 15, 25, 50, 90, 240, 360, 720 min post-dose on Day 1, Day 2, Day 3, Day 4

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: h*ng/mL				
arithmetic mean (standard deviation)	78.6 (± 45.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the concentration-time curve from time zero to the last measurable concentration (AUC0-t) - MSP-2030 plasma

End point title	Area under the concentration-time curve from time zero to the last measurable concentration (AUC0-t) - MSP-2030 plasma

End point description:

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1.5, 3. 5, 7, 10, 15, 25, 50, 90, 240, 360, 720 min post-dose on Day 1, Day 2, Day 3, Day 4

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: h*ng/mL				
arithmetic mean (standard deviation)	288 (± 103)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the concentration-time curve from time zero to infinity (AUC0-inf) - etripamil plasma

End point title	Area under the concentration-time curve from time zero to infinity (AUC0-inf) - etripamil plasma

End point description:

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1.5, 3. 5, 7, 10, 15, 25, 50, 90, 240, 360, 720 min post-dose on Day 1, Day 2, Day 3, Day 4

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: h*ng/mL				
arithmetic mean (standard deviation)	84.5 (± 52.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the concentration-time curve from time zero to infinity (AUC0-inf) - MSP-2030 plasma

End point title	Area under the concentration-time curve from time zero to infinity (AUC0-inf) - MSP-2030 plasma

End point description:

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1.5, 3. 5, 7, 10, 15, 25, 50, 90, 240, 360, 720 min post-dose on Day 1, Day 2, Day 3, Day 4

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: h*ng/mL				
arithmetic mean (standard deviation)	318 (± 121)			

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal half-life (t1/2) - etripamil plasma

End point title	Terminal half-life (t1/2) - etripamil plasma

End point description:

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1.5, 3. 5, 7, 10, 15, 25, 50, 90, 240, 360, 720 min post-dose on Day 1, Day 2, Day 3, Day 4

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: hour				
arithmetic mean (standard deviation)	2.92 (± 2.26)			

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal half-life (t1/2) - MSP-2030 plasma

End point title	Terminal half-life (t1/2) - MSP-2030 plasma

End point description:

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1.5, 3. 5, 7, 10, 15, 25, 50, 90, 240, 360, 720 min post-dose on Day 1, Day 2, Day 3, Day 4

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: hour				
arithmetic mean (standard deviation)	7.10 (± 3.72)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent clearance (CL/F) - etripamil plasma

End point title	Apparent clearance (CL/F) - etripamil plasma

End point description:

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1.5, 3. 5, 7, 10, 15, 25, 50, 90, 240, 360, 720 min post-dose on Day 1, Day 2, Day 3, Day 4

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: L/h				
arithmetic mean (standard deviation)	1070 (± 553)			

Statistical analyses

No statistical analyses for this end point

Secondary: volume of distribution (Vz/F) - etripamil plasma

End point title	volume of distribution (Vz/F) - etripamil plasma

End point description:

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1.5, 3. 5, 7, 10, 15, 25, 50, 90, 240, 360, 720 min post-dose on Day 1, Day 2, Day 3, Day 4

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: liter				
arithmetic mean (standard deviation)	3500 (± 1090)			

Statistical analyses

No statistical analyses for this end point

Secondary: Amount excreted unchanged in urine (Aeu) - Etripamil

End point title	Amount excreted unchanged in urine (Aeu) - Etripamil

End point description:

End point type	Secondary

End point timeframe:

Pre-dose and 0-120, 120-240, 240-360, 360-720, 720-1440 minutes post-dose, Day 2, Day 3, Day 4

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: mg				
arithmetic mean (standard deviation)	0.00873 (± 0.00804)			

Statistical analyses

No statistical analyses for this end point

Secondary: Fraction of dose excreted in urine (etripamil only) (fe)

End point title	Fraction of dose excreted in urine (etripamil only) (fe)

End point description:

End point type	Secondary

End point timeframe:

Pre-dose and 0-120, 120-240, 240-360, 360-720, 720-1440 minutes post-dose, Day 2, Day 3, Day 4

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: percent				
arithmetic mean (standard deviation)	0.0124 (± 0.0115)			

Statistical analyses

No statistical analyses for this end point

Secondary: Renal clearance, calculated as Aeu,0-t/AUC0-t (CLr)

End point title	Renal clearance, calculated as Aeu,0-t/AUC0-t (CLr)

End point description:

End point type	Secondary

End point timeframe:

Pre-dose and 0-120, 120-240, 240-360, 360-720, 720-1440 minutes post-dose, Day 2, Day 3, Day 4

End point values	Pharmacokinetics set			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: L/h				
arithmetic mean (standard deviation)	0.173 (± 0.228)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: All AEs occurring after the consent form is signed and up to the end-of-study (EOS) are reported. Adverse events must be followed until resolution, or to a maximum of 28 days after the EOS.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups	
Reporting group title	Overall study
Reporting group description: Only 1 arm for this study	

Serious adverse events	Overall study		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Overall study		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)		
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 7 (85.71%)		
occurrences (all)	9		
Burning sensation mucosal			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
General disorders and administration site conditions			

Discomfort subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Eye disorders Lacrimation increased subjects affected / exposed occurrences (all)	3 / 7 (42.86%) 3		
Gastrointestinal disorders Toothache subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2 1 / 7 (14.29%) 1		
Respiratory, thoracic and mediastinal disorders Nasal congestion subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all) Nasal dryness subjects affected / exposed occurrences (all) Dry throat subjects affected / exposed occurrences (all) Nasal discomfort subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all) Throat irritation subjects affected / exposed occurrences (all)	7 / 7 (100.00%) 8 5 / 7 (71.43%) 7 4 / 7 (57.14%) 5 2 / 7 (28.57%) 2 2 / 7 (28.57%) 2 2 / 7 (28.57%) 2 2 / 7 (28.57%) 2		

Dyspnoea subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1 1 / 7 (14.29%) 1		
Renal and urinary disorders Pollakiuria subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 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