Clinical trial results:
A Phase IIa, Multicenter, Randomized, Placebo-Controlled, Double-Blind Study to Evaluate the Efficacy, Safety, and Pharmacokinetics of MTPS9579A in Patients With Asthma Requiring Inhaled Corticosteroids and a Second Controller.

Summary

EudraCT number	2019-000795-41
Trial protocol	PL DE
Global end of trial date	19 May 2022

Results information

Result version number	v2 (current)
This version publication date	03 September 2023
First version publication date	27 May 2023
Version creation reason	• Correction of full data set Changes in the screening details and outcome measure section.

Trial information

Trial identification

Sponsor protocol code	GB41149

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04092582
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hoffmann-La Roche
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	Medical Communications, F. Hoffmann-La Roche AG, + 41 616878333, global.trial_information@roche.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	19 May 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 May 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the efficacy, safety, and pharmacokinetics of MTPS9579A compared with placebo in participants with uncontrolled asthma despite the use of inhaled corticosteroids (ICS) and a second controller.

Protection of trial subjects:

The study was conducted in full conformance with the ICH E6 guideline for Good Clinical Practice and the principles of the Declaration of Helsinki, or the laws and regulations of the country in which the research is conducted, whichever affords the greater protection to the subject. All subjects were required to sign an informed consent form before enrolling in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 October 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	Argentina: 12
Country: Number of subjects enrolled	Peru: 6
Country: Number of subjects enrolled	United States: 33
Country: Number of subjects enrolled	Germany: 25
Country: Number of subjects enrolled	Poland: 58
Worldwide total number of subjects	134
EEA total number of subjects	83

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)	102
From 65 to 84 years	32
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 26 investigative sites in 5 countries (Argentina, Germany, Peru, Poland, and the United States) from 31 October 2019 to 19 May 2022.

Pre-assignment

Screening details:

This study included a 2-week single-blind placebo run-in period. A total of 135 participants were randomized in double-blind treatment period. Of the 135 participants randomized, 134 participants received at least one dose of study drug and their intended treatment.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Carer, Subject, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	MTPS9579A, 1800 mg

Arm description:

Participants with uncontrolled moderate to severe asthma received Placebo, given as intravenous (IV) infusion, for 14 days in the Placebo run-in period. Participants then received MTPS9579A, 1800 mg, given as IV infusion at randomization (Week 2), Week 6, and every 4 weeks thereafter through Week 46.

Arm type	Experimental
Investigational medicinal product name	MTPS9579A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

MTPS9579A was administered as an IV Infusion at a dose of 1800 mg.

Arm title	Placebo

Arm description:

Participants with uncontrolled moderate to severe asthma received Placebo, given as IV infusion, for 14 days in the Placebo run-in period. Participants received MTPS9579A matching placebo, given as IV infusion at randomization (Week 2), Week 6, and every 4 weeks thereafter through Week 46.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

MTPS9579A-matching placebo was administered as an IV Infusion.

Number of subjects in period 1	MTPS9579A, 1800 mg	Placebo
Started	69	65
Safety Population	69	65
Completed	64	63
Not completed	5	2
Adverse event, serious fatal	1	1
Consent withdrawn by subject	4	1

Baseline characteristics

Reporting groups	
Reporting group title	MTPS9579A, 1800 mg
Reporting group description:	
Participants with uncontrolled moderate to severe asthma received Placebo, given as intravenous (IV) infusion, for 14 days in the Placebo run-in period. Participants then received MTPS9579A, 1800 mg, given as IV infusion at randomization (Week 2), Week 6, and every 4 weeks thereafter through Week 46.	
Reporting group title	Placebo
Reporting group description:	
Participants with uncontrolled moderate to severe asthma received Placebo, given as IV infusion, for 14 days in the Placebo run-in period. Participants received MTPS9579A matching placebo, given as IV infusion at randomization (Week 2), Week 6, and every 4 weeks thereafter through Week 46.	

Reporting group values	MTPS9579A, 1800 mg	Placebo	Total
Number of subjects	69	65	134
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)	52	50	102
From 65-84 years	17	15	32
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	54.7	52.9	
standard deviation	± 12.0	± 13.2	-
Sex: Female, Male Units: participants			
Female	39	34	73
Male	30	31	61
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	3	0	3
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	3	3
White	62	59	121
More than one race	0	0	0
Unknown or Not Reported	4	3	7
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	10	12	22

Not Hispanic or Latino	59	53	112
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	MTPS9579A, 1800 mg

Reporting group description:

Participants with uncontrolled moderate to severe asthma received Placebo, given as intravenous (IV) infusion, for 14 days in the Placebo run-in period. Participants then received MTPS9579A, 1800 mg, given as IV infusion at randomization (Week 2), Week 6, and every 4 weeks thereafter through Week 46.

Reporting group title	Placebo

Reporting group description:

Participants with uncontrolled moderate to severe asthma received Placebo, given as IV infusion, for 14 days in the Placebo run-in period. Participants received MTPS9579A matching placebo, given as IV infusion at randomization (Week 2), Week 6, and every 4 weeks thereafter through Week 46.

Primary: Time to First Composite Asthma Exacerbations (CompEX) Event

End point title	Time to First Composite Asthma Exacerbations (CompEX) Event

End point description:

CompEX=time from randomisation to first asthma exacerbation/diary worsening during treatment.Asthma exacerbation=new/increased asthma symptoms in one/both: Hospitalisation/emergency department visit with administration of systemic corticosteroid treatment (SC);Treatment with SC for atleast 3 days,/a long-acting depot corticosteroid preparation with therapeutic effectiveness of atleast 3 days.Diaryworsening=occurrence of prespecified changes:morning peak expiratory flow rate (PEFR),evening PEFR,morning symptom score,evening symptom score,morning short-acting rescue therapy use,&evening short-acting rescue therapy use.999=Data for median upper limit (UL) of confidence interval (CI) was not estimable due to insufficient number of participants with events.9999=Data for UL of CI was not estimable due to insufficient number of participants with events.Hazard ratio was used for analysis.mITT population included all randomised participants who received at least one dose of study treatment.

End point type	Primary

End point timeframe:

Randomisation [Week 2] to end of treatment (EOT) [Week 50]

End point values	MTPS9579A, 1800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	65		
Units: weeks				
median (confidence interval 95%)	999 (31.3 to 9999)	45.4 (19.0 to 9999)		

Statistical analyses

Statistical analysis title	MTPS9579A (1800 mg) versus Placebo
Comparison groups	MTPS9579A, 1800 mg v Placebo

Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6835
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.47

Secondary: Rate of Asthma Exacerbations

End point title	Rate of Asthma Exacerbations

End point description:

The number of asthma exacerbations per year was reported for this outcome measure. Asthma exacerbation was defined as new or increased asthma symptoms (wheezing, coughing, dyspnea, chest tightness, and/or nighttime awakenings due to these symptoms) that resulted in one or both of the following: Hospitalization or emergency department visit with administration of systemic corticosteroid treatment; Treatment with systemic corticosteroids for at least 3 days, or a long-acting depot corticosteroid preparation with a therapeutic effectiveness of at least 3 days. Poisson regression was used for the analysis. mITT population included all randomised participants who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

Randomisation [Week 2] to Week 50

End point values	MTPS9579A, 1800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	65		
Units: Asthma exacerbations per patient-year				
number (not applicable)	0.4689	0.4267		

Statistical analyses

Statistical analysis title	MTPS9579A (1800 mg) versus Placebo
Comparison groups	MTPS9579A, 1800 mg v Placebo

Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7648
Method	Poisson regression
Parameter estimate	Rate Ratio
Point estimate	1.0989
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5925
upper limit	2.0381

Secondary: Absolute Change From Randomisation in Pre-Bronchodilator Forced Expiratory Volume in 1 Second (FEV1) at Week 50

End point title	Absolute Change From Randomisation in Pre-Bronchodilator Forced Expiratory Volume in 1 Second (FEV1) at Week 50

End point description:

FEV1 is calculated as the volume of air forcibly exhaled in one second as measured by a spirometer. Estimates are based on a mixed model for repeated measures (MMRM) analysis with an unstructured covariance matrix. The model used the absolute change pre-bronchodilator FEV1 as the response variable and included terms for treatment arm, study visit, treatment arm by study visit interaction, baseline FEV1 as well as its interaction with study visit, in addition to the stratification factors: blood eosinophil level at visit 1 (<150, >=150 to <=300, >300 cells/microliter (uL)), number of asthma exacerbations requiring the use of systemic corticosteroids within the 12 months prior to the study entry (1 or >=2 events), and geographic region. Overall number of participants analysed are the number of participants available for analysis.mITT population included all randomised participants who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

Randomisation [Week 2] to Week 50

End point values	MTPS9579A, 1800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	61		
Units: liters				
arithmetic mean (standard error)	0.11 (± 0.034)	0.03 (± 0.034)		

Statistical analyses

Statistical analysis title	MTPS9579A (1800 mg) versus Placebo
Comparison groups	MTPS9579A, 1800 mg v Placebo

Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.125
Method	Mixed model for repeated measures (MMRM)

Secondary: Time to First Asthma Exacerbation

End point title	Time to First Asthma Exacerbation

End point description:

The time from randomisation to first asthma exacerbation was measured. Asthma exacerbation was defined as new or increased asthma symptoms (wheezing, coughing, dyspnea, chest tightness, and/or nighttime awakenings due to these symptoms) that resulted in one or both of the following: Hospitalization or emergency department visit with administration of systemic corticosteroid treatment; Treatment with systemic corticosteroids for at least 3 days, or a long-acting depot corticosteroid preparation with a therapeutic effectiveness of at least 3 days. 99999=The data for median, lower and upper limit of CI was not estimable due to insufficient number of participants with events. Cox regression was used for the analysis. mITT population included all randomised participants who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

Randomisation [Week 2] to Week 50

End point values	MTPS9579A, 1800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	65		
Units: weeks				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

Statistical analysis title	MTPS9579A (1800 mg) versus Placebo
Comparison groups	MTPS9579A, 1800 mg v Placebo
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5248
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	1.54

Secondary: Absolute Change From Randomisation in Fractional Exhaled Nitric Oxide (FeNO) at Week 50

End point title	Absolute Change From Randomisation in Fractional Exhaled Nitric Oxide (FeNO) at Week 50

End point description:

FeNO is a volatile marker of airway inflammation that decreases with inhaled corticosteroid treatment. The measurements recorded were according to standardized procedures by the American Thoracic Society. Estimates are based on a MMRM analysis with an unstructured covariance matrix. The model used the absolute change pre-bronchodilator FeNO as the response variable and included terms for treatment arm, study visit, treatment arm by study visit interaction, baseline FeNO as well as its interaction with study visit, in addition to the stratification factors: blood eosinophil level at visit 1 (<150, >=150 to <=300, >300 cells/uL), number of asthma exacerbations requiring the use of systemic corticosteroids within the 12 months prior to the study entry (1 or >=2 events), and geographic region. Overall number of participants analysed are the number of participants available for analysis.mITT population included all randomised participants who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

Randomisation [Week 2] to Week 50

End point values	MTPS9579A, 1800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	54		
Units: parts per billion (ppb)				
arithmetic mean (standard error)	-1.67 (± 2.722)	-1.52 (± 2.791)		

Statistical analyses

Statistical analysis title	MTPS9579A (1800 mg) versus Placebo
Comparison groups	MTPS9579A, 1800 mg v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9693
Method	Mixed model for repeated measures (MMRM)

Secondary: Relative Percent Change From Randomisation in Pre-Bronchodilator FEV1 at Week 50

End point title	Relative Percent Change From Randomisation in Pre-Bronchodilator FEV1 at Week 50

End point description:

FEV1 was the volume of air exhaled in the first second of a forced exhalation as measured by spirometer. Estimates are based on a MMRM analysis with an unstructured covariance matrix. The Model

used the relative change pre-bronchodilator FEV1 as response variable and included terms for treatment arm, study visit, treatment arm by study visit interaction, baseline FEV1 as well as its interaction with study visit, in addition to the stratification factors: blood eosinophil level at visit 1 (<150, >=150 to <=300, >300 cells/uL), number of asthma exacerbations requiring the use of systemic corticosteroids within 12 months prior to study entry (1 or >=2 events), and geographic region. Relative change (%) in FEV1 = (absolute change in FEV1 / baseline FEV1) x 100. Overall number of participants analysed are the number of participants available for analysis. mITT population included all randomised participants who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

Randomisation [Week 2] to Week 50

End point values	MTPS9579A, 1800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	61		
Units: percent change				
arithmetic mean (standard error)	6.44 (± 1.894)	3.15 (± 1.921)		

Statistical analyses

Statistical analysis title	MTPS9579A (1800 mg) versus Placebo
Comparison groups	MTPS9579A, 1800 mg v Placebo
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2249
Method	Mixed model for repeated measures (MMRM)

Secondary: Percentage of Participants with Adverse Events

End point title	Percentage of Participants with Adverse Events

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant or clinical investigation participant administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not considered related to the medicinal (investigational) product.The safety analysis population included all randomised participants who received at least one dose of study drug during the 48-week double-blind treatment period.

End point type	Secondary

End point timeframe:

Up to approximately Week 58

End point values	MTPS9579A, 1800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	65		
Units: percentage of participants				
number (not applicable)	79.7	86.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under Concentration-Time Curve for the First Dosing Interval (AUClast) of MTPS9579A

End point title	Area Under Concentration-Time Curve for the First Dosing Interval (AUClast) of MTPS9579A[1]

End point description:

PK-evaluable population includes all participants who had at least one evaluable PK sample.

End point type	Secondary

End point timeframe:

Randomization [Week 2] to Week 6

Notes:

[1] - 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: This endpoint measures pharmacokinetic parameter which is analysed only in the MTPS9579A group.

End point values	MTPS9579A, 1800 mg			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: day*ug/mL				
geometric mean (geometric coefficient of variation)	5263.14 (± 83.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Relative Percent Change From Randomisation in FeNO at Week 50

End point title	Relative Percent Change From Randomisation in FeNO at Week 50

End point description:

FeNO is a volatile marker of airway inflammation that decreases with inhaled corticosteroid treatment. Relative change (%) in FeNO = (absolute change in FeNO / baseline FeNO) x 100. Estimates are based on a MMRM analysis with an unstructured covariance matrix. Model used absolute change pre-bronchodilator FeNO as the response variable and included terms for treatment arm, study visit, treatment arm by study visit interaction, baseline FeNO as well as its interaction with study visit, in addition to the stratification factors: blood eosinophil level at visit 1 (<150, >=150 to <=300, >300 cells/uL), number of asthma exacerbations requiring the use of systemic corticosteroids within 12 months prior to study entry (1 or >=2 events), and geographic region. Overall number of participants analysed are the number of participants available for analysis. mITT population included all randomised participants who received at least one dose of study treatment.

End point type	Secondary
End point timeframe: Randomisation [Week 2] to Week 50	

End point values	MTPS9579A, 1800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	54		
Units: percent change				
arithmetic mean (standard error)	26.02 (± 10.223)	26.29 (± 10.482)		

Statistical analyses

Statistical analysis title	MTPS9579A (1800 mg) versus Placebo
Comparison groups	MTPS9579A, 1800 mg v Placebo
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9855
Method	Mixed model for repeated measures (MMRM)

Secondary: Maximum Serum Concentration (Cmax) for the First Dosing Interval of MTPS9579A

End point title	Maximum Serum Concentration (Cmax) for the First Dosing Interval of MTPS9579A[2]
End point description: PK-evaluable population includes all participants who had at least one evaluable PK sample.	
End point type	Secondary
End point timeframe: 2-hour post-dose on Week 2	

Notes:

[2] - 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: This endpoint measures pharmacokinetic parameter which is analysed only in the MTPS9579A group.

End point values	MTPS9579A, 1800 mg			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: ug/mL				
geometric mean (geometric coefficient of variation)	419 (± 51.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Steady State Cmax of MTPS9579A

End point title	Steady State Cmax of MTPS9579A[3]

End point description:

PK-evaluable population includes all participants who had at least one evaluable PK sample.

End point type	Secondary

End point timeframe:

2-hour post-dose on Week 14

Notes:

[3] - 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: This endpoint measures pharmacokinetic parameter which is analysed only in the MTPS9579A group.

End point values	MTPS9579A, 1800 mg			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: ug/mL				
geometric mean (geometric coefficient of variation)	735 (± 31)			

Statistical analyses

No statistical analyses for this end point

Secondary: Steady State Ctrough of MTPS9579A

End point title	Steady State Ctrough of MTPS9579A[4]

End point description:

PK-evaluable population includes all participants who had at least one evaluable PK sample.

End point type	Secondary

End point timeframe:

Pre-dose on Week 14

Notes:

[4] - 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: This endpoint measures pharmacokinetic parameter which is analysed only in the MTPS9579A group.

End point values	MTPS9579A, 1800 mg			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: ug/mL				
geometric mean (geometric coefficient of variation)	226 (± 45.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Serum Concentration (Ctrough) Accumulation Ratio of MTPS9579A

End point title	Trough Serum Concentration (Ctrough) Accumulation Ratio of MTPS9579A[5]

End point description:

The accumulation ratio is calculated by taking the individual ratio of the Ctrough at Week 14 to the Ctrough at Week 6. PK-evaluable population includes all participants who had at least one evaluable PK sample.

End point type	Secondary

End point timeframe:

Predose on Weeks 6 and 14

Notes:

[5] - 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: This endpoint measures pharmacokinetic parameter which is analysed only in the MTPS9579A group.

End point values	MTPS9579A, 1800 mg			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: ratio				
geometric mean (geometric coefficient of variation)	1.92 (± 28.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Anti-Drug Antibodies (ADA) to MTPS9579A

End point title	Percentage of Participants With Anti-Drug Antibodies (ADA) to MTPS9579A

End point description:

Treatment Emergent ADA is (a) negative or missing baseline ADA result(s) and at least one positive post-baseline ADA result, OR (b) positive ADA result at baseline and one or more post-baseline titer results that are at least 0.60 titer unit (t.u.) greater than the baseline titer result. The immunogenicity analysis population included all participants with at least one ADA assessment.

End point type	Secondary

End point timeframe:

Pre-dose Week 54

End point values	MTPS9579A, 1800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	65		
Units: percentage of participants				
number (not applicable)	5.9	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Time to Serum Concentration (Tmax) of MTPS9579A

End point title	Maximum Time to Serum Concentration (Tmax) of

End point description:

PK-evaluable population includes all participants who had at least one evaluable PK sample.

End point type	Secondary

End point timeframe:

Pre-dose and 2-hour post-dose on Weeks 2, 6, 10, 14, 22, 30, 38; and pre-dose on Weeks 3, 50, and Week 54 or ET visit

Notes:

[6] - 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: This endpoint measures pharmacokinetic parameter which is analysed only in the MTPS9579A group.

End point values	MTPS9579A, 1800 mg			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: day				
median (standard deviation)	0.12 (± 3.14)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to approximately Week 58

Adverse event reporting additional description:

Safety analysis population included all randomized participants who received at least one dose of study drug during the 48-week double-blind treatment period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	MTPS9579A, 1800 mg

Reporting group description:

Participants with uncontrolled moderate to severe asthma received Placebo, given as IV infusion, for 14 days in the Placebo run-in period. Participants then received MTPS9579A, 1800 mg, given as IV infusion at randomization (Week 2), Week 6, and every 4 weeks thereafter through Week 46.

Reporting group title	Placebo

Reporting group description:

Participants with uncontrolled moderate to severe asthma received Placebo, given as IV infusion, for 14 days in the Placebo run-in period. Participants received MTPS9579A matching placebo, given as IV infusion at randomization (Week 2), Week 6, and every 4 weeks thereafter through Week 46.

Serious adverse events	MTPS9579A, 1800 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 69 (7.25%)	4 / 65 (6.15%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Tendon injury			
subjects affected / exposed	0 / 69 (0.00%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			
subjects affected / exposed	1 / 69 (1.45%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			

subjects affected / exposed	1 / 69 (1.45%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Accidental death			
subjects affected / exposed	1 / 69 (1.45%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	1 / 69 (1.45%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	0 / 69 (0.00%)	3 / 65 (4.62%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
COVID-19			
subjects affected / exposed	1 / 69 (1.45%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	MTPS9579A, 1800 mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 69 (46.38%)	38 / 65 (58.46%)	
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 69 (7.25%)	3 / 65 (4.62%)	
occurrences (all)	6	3	
Respiratory, thoracic and mediastinal disorders			

Rhinitis allergic			
subjects affected / exposed	0 / 69 (0.00%)	4 / 65 (6.15%)	
occurrences (all)	0	5	
Asthma			
subjects affected / exposed	19 / 69 (27.54%)	24 / 65 (36.92%)	
occurrences (all)	31	33	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 69 (4.35%)	4 / 65 (6.15%)	
occurrences (all)	3	4	
Back pain			
subjects affected / exposed	1 / 69 (1.45%)	4 / 65 (6.15%)	
occurrences (all)	1	4	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 69 (5.80%)	5 / 65 (7.69%)	
occurrences (all)	5	5	
COVID-19			
subjects affected / exposed	6 / 69 (8.70%)	6 / 65 (9.23%)	
occurrences (all)	6	6	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 August 2019	Inclusion criteria modified to remove requirement for FEV1/FVC < 70%. Safety follow-up reporting period now includes a safety follow-up telephone call at Week (Wk) 58. Requirement for gram staining of urine specimens, if clinically indicated, has been removed. Additional details on prospective monitoring for anaphylaxis have been provided. For participants who discontinue study drug but remain on study, it has been clarified that adverse event reporting should continue through end of the study (not only 84 days after the final dose of study drug). More detail has been provided for efficacy analyses calculations to clarify baseline calculation for the primary efficacy analysis and secondary efficacy analyses calculations.
22 November 2019	The requirement of documented history of asthma exacerbation within 12 months prior to screening has been increased from ≥1 to ≥2. Participants must be on daily maintenance ICS during prior exacerbations, but requirement that this ICS dose be at the same/higher dose as at screening has been removed. The in-person safety follow-up visit has been moved from 6 weeks to 8 weeks after the final dose of study drug. Language has been modified to better explain that within a single screening period, participants who did not meet the requirement of pre-bronchodilator FEV1 of 40%−80% or post-bronchodilator reversibility of FEV1 (liters) of ≥12% and ≥ 200 mL are allowed up to two additional attempts to meet these two eligibility criteria, but only if their prebronchodilator FEV1 was between 35% and 85%. The requirement that pre bronchodilator testing must be performed in morning has been removed. Smoking exclusion criterion has been clarified to include e-cigarettes or vaping use. To allow for ECGs to be collected 3 hours or more from participant's' last meal, the requirement that ECGs be obtained prior to other assessments has been removed.
18 September 2021	Text regarding the interim analyses (planned and optional) has been updated to reflect that enrollment may be permanently halted. Participants already enrolled continued to be treated and monitored per protocol. To accommodate the interim analyses, text regarding the requirements for the database to be frozen and cleaned has been removed. It has been clarified that urine biomarkers are to be collected pre-dose and that post-dose PK samples are to be collected 2 hours±30 minutes after the end of the dose.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
08 April 2020	Enrollment was initially halted on 08 April 2020 in response to the emerging pandemic and concerns regarding data integrity (e.g., missed study doses and visits).	22 June 2020

Notes:

Limitations and caveats

None reported