



Clinical trial results:

An open-label, two-period, single-sequence, crossover study to compare the systemic exposure of a single inhaled dose of mometasone furoate (MF) when administered alone via the MF Twisthaler® (TH) to a single inhaled dose of QMF149 indacaterol acetate/MF fixed dose combination when administered via the Concept 1 (C1) Breezhaler® device in 6 to < 12 year old asthma patients

Summary

EudraCT number	2020-002036-78
Trial protocol	HU
Global end of trial date	11 April 2022

Results information

Result version number	v1 (current)
This version publication date	29 September 2022
First version publication date	29 September 2022

Trial information

Trial identification

Sponsor protocol code	CQMF149G2203
-----------------------	--------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04589663
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharmaceuticals
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Study Director, Novartis Pharmaceuticals, 41 613241111, Novartis.email@Novartis.com
Scientific contact	Study Director, Novartis Pharmaceuticals, 41 613241111, Novartis.email@Novartis.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 April 2022
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	11 April 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the systemic exposure of MF resulting from single orally-inhaled doses of MF when administered as MF TH 100 µg versus QMF149 75/40 µg C1.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 June 2021
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	Hungary: 7
Country: Number of subjects enrolled	South Africa: 17
Worldwide total number of subjects	24
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)	24
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from 3 sites in 2 countries

Pre-assignment

Screening details:

Participants underwent a Screening period of up to 14 days

Period 1

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

Blinding implementation details:

Open label

Arms

Arm title	MF followed by QMF149
------------------	-----------------------

Arm description:

Single inhaled dose of mometasone furoate on Day 1 delivered via TH inhaler followed by 4-7 days of washout. On Day 6-9, single inhaled dose of QMF149 delivered via C1 inhaler.

Arm type	Experimental
Investigational medicinal product name	Mometasone furoate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Single inhaled dose of 100 µg mometasone furoate (MF) administered via Twisthaler® on Day 1

Investigational medicinal product name	Standard of Care (Soc)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Asthma therapy: budesonide and salbutamol being the most frequently used (excluding MF and indacaterol acetate)

Investigational medicinal product name	QMF149
Investigational medicinal product code	QMF149
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Single inhaled dose of QMF149 (75/40 µg indacaterol acetate/MF fixed dose combination) administered via Concept 1 device on Day 6-9

Number of subjects in period 1	MF followed by QMF149
Started	24
Completed	24

Baseline characteristics

Reporting groups

Reporting group title	MF followed by QMF149
-----------------------	-----------------------

Reporting group description:

Single inhaled dose of mometasone furoate on Day 1 delivered via TH inhaler followed by 4-7 days of washout. On Day 6-9, single inhaled dose of QMF149 delivered via C1 inhaler.

Reporting group values	MF followed by QMF149	Total	
Number of subjects	24	24	
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)	24	24	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous			
Units: Years			
arithmetic mean	9.0		
standard deviation	± 1.46	-	
Sex: Female, Male			
Units: Participants			
Female	6	6	
Male	18	18	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	1	1	
White	8	8	
More than one race	15	15	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	MF followed by QMF149
Reporting group description: Single inhaled dose of mometasone furoate on Day 1 delivered via TH inhaler followed by 4-7 days of washout. On Day 6-9, single inhaled dose of QMF149 delivered via C1 inhaler.	

Primary: Maximum observed Mometasone furoate plasma concentration (Cmax)

End point title	Maximum observed Mometasone furoate plasma concentration (Cmax) ^[1]
-----------------	--

End point description:

Mometasone furoate plasma concentrations were determined by a validated liquid chromatography with tandem mass spectrometry (LC-MS/MS) method. Cmax of mometasone furoate was determined with Phoenix WinNonlin (Version 8.0 or higher).

A correction factor was applied to MF pharmacokinetic parameters to consider the first-dose effect that is based on the fact that the participants in this study received a single dose from single unused (unprimed) C1 and TH devices. Unprimed devices are not coated with the formulation, and therefore may lead to lower fine particle mass (FPM) and delivered dose compared to later doses actuated from the device throughout its use time. The first-dose correction factor ($\text{FPM}_{\text{primed}}(\text{MF}) / \text{FPM}_{\text{unprimed}}(\text{MF})$) for MF delivered via TH was 1.26 and for MF delivered via C1 it was 1.62.

End point type	Primary
----------------	---------

End point timeframe:

pre-dose, 0.5, 1, 2, 3 and 6 hours post-dose on Day 1 and Day 6-9

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: Statistical analysis was not planned

Statistical analyses

No statistical analyses for this end point

Primary: Area under the plasma concentration-time curve from time zero to the last sampling time point 6h (AUC0-6h) of Mometasone Furoate

End point title	Area under the plasma concentration-time curve from time zero to the last sampling time point 6h (AUC0-6h) of Mometasone Furoate ^[2]
-----------------	---

End point description:

AUC0-6h of mometasone furoate was determined using non-compartment methods with Phoenix WinNonlin (Version 8.0 or higher). The linear trapezoidal rule was used for AUC0-6h calculation.

A correction factor was applied to MF pharmacokinetic parameters to consider the first-dose effect that is based on the fact that the participants in this study received a single dose from single unused (unprimed) C1 and TH devices. Unprimed devices are not coated with the formulation, and therefore may lead to lower fine particle mass (FPM) and delivered dose compared to later doses actuated from the device throughout its use time. The first-dose correction factor ($\text{FPM}_{\text{primed}}(\text{MF}) / \text{FPM}_{\text{unprimed}}(\text{MF})$)

(MF)) for MF delivered via TH was 1.26 and for MF delivered via C1 it was 1.62.

End point type	Primary
----------------	---------

End point timeframe:

pre-dose, 0.5, 1, 2, 3 and 6 hours post-dose on Day 1 and Day 6-9

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: Statistical analysis was not planned

Statistical analyses

No statistical analyses for this end point

Secondary: Systemic exposure to indacaterol in plasma

End point title	Systemic exposure to indacaterol in plasma
-----------------	--

End point description:

Systemic exposure to indacaterol in plasma following sparse pharmacokinetic (PK) sampling on Day 6-9 after inhalation of QMF149.

A correction factor was applied to indacaterol plasma concentrations to consider the first-dose effect that is based on the fact that the participants in this study received a single dose from single unused (unprimed) C1 and TH devices. Unprimed devices are not coated with the formulation, and therefore may lead to lower fine particle mass (FPM) and delivered dose compared to later doses actuated from the device throughout its use time. The first-dose correction factor (FPMprimed (indacaterol) / FPMunprimed (indacaterol)) for indacaterol delivered via C1 was 2.0.

End point type	Secondary
----------------	-----------

End point timeframe:

pre-dose, 0.25 and 1 hour post-dose on Day 6-9

End point values	MF followed by QMF149			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: pg/mL				
arithmetic mean (standard deviation)				
Pre-dose	0 (± 0)			
0.25 hours post-dose	102.0 (± 54.9)			
1 hours post-dose	62.3 (± 26.2)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from the start of treatment to 30 days after end of treatment, assessed up to maximum duration of 39 days.

Adverse event reporting additional description:

Any sign or symptom that occurs during the study treatment plus the 30 days post treatment

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	25.0
--------------------	------

Reporting groups

Reporting group title	MF 100 ug via Twisthaler
-----------------------	--------------------------

Reporting group description:

Single inhaled dose of mometasone furoate on Day 1 delivered via TH inhaler followed by 4-7 days of washout

Reporting group title	Total
-----------------------	-------

Reporting group description:

Total

Reporting group title	QMF149 75/40 ug via Concept 1
-----------------------	-------------------------------

Reporting group description:

Single inhaled dose of QMF149 delivered via C1 inhaler on Day 6-9

Serious adverse events	MF 100 ug via Twisthaler	Total	QMF149 75/40 ug via Concept 1
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	MF 100 ug via Twisthaler	Total	QMF149 75/40 ug via Concept 1
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 24 (12.50%)	3 / 24 (12.50%)	0 / 24 (0.00%)
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 24 (4.17%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	1	1	0
Product issues			

Device failure subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2	2 / 24 (8.33%) 2	0 / 24 (0.00%) 0
--	---------------------	---------------------	---------------------

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 March 2021	The protocol was amended to correct the details regarding laboratory assessments, blood sampling and to include the early termination visit assessment details.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported