Clinical trial results:
A multicenter, randomized, double-blind, active-controlled, 2 week treatment, parallel-group study to assess the efficacy and safety of indacaterol acetate delivered via the Concept1 inhalation device in children greater or equal to 6 and less than 12 years of age with asthma

Summary

EudraCT number	2016-002113-21
Trial protocol	DE SK BE HU HR
Global end of trial date	17 July 2019

Results information

Result version number	v1 (current)
This version publication date	01 February 2020
First version publication date	01 February 2020

Trial information

Trial identification

Sponsor protocol code	CQMF149G2202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02892019
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharmaceuticals
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharmaceuticals, 41 613241111, novartis.email@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	
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	17 July 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 July 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective for this trial was to evaluate indacaterol acetate 75 µg once daily and 150 µg once daily in terms of change from baseline in pre-dose trough Forced Expiratory Volume in 1 Second after 2 weeks of treatment

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	18 April 2017
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	Germany: 3
Country: Number of subjects enrolled	Colombia: 13
Country: Number of subjects enrolled	Guatemala: 8
Country: Number of subjects enrolled	Hungary: 8
Country: Number of subjects enrolled	Philippines: 4
Country: Number of subjects enrolled	Russian Federation: 9
Country: Number of subjects enrolled	Slovakia: 2
Country: Number of subjects enrolled	South Africa: 20
Country: Number of subjects enrolled	Turkey: 13
Worldwide total number of subjects	80
EEA total number of subjects	13

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)	80
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: -

Pre-assignment

Screening details:

randomized set : 80 participants (41 and 39) Full analysis set : 79 participants (41 and 38) safety set : 79 participants (41 and 38) per protocol set : 35 participants (35 and 34)

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	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Indacaterol acetate 150 µg o.d.

Arm description:

Indacaterol acetate 150 µg o.d. delivered via Concept1 inhaler

Arm type	Experimental
Investigational medicinal product name	QMF149
Investigational medicinal product code	
Other name	Indacaterol acetate
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

Indacaterol acetate 150 µg o.d. delivered via Concept 1 inhaler (in the morning)

Arm title	Indacaterol acetate 75 µg o.d.

Arm description:

Indacaterol acetate 75 µg o.d. delivered via Concept1 inhaler

Arm type	Experimental
Investigational medicinal product name	QMF149
Investigational medicinal product code	
Other name	Indacaterol acetate
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

Indacaterol acetate 75 µg o.d. delivered via Concept 1 inhaler (in the morning)

Number of subjects in period 1	Indacaterol acetate 150 µg o.d.	Indacaterol acetate 75 µg o.d.
Started	41	39
Completed	40	36
Not completed	1	3
randomized but not treated	-	1

Consent withdrawn by subject	-	1
Adverse event, non-fatal	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Indacaterol acetate 150 µg o.d.
Reporting group description:	
Indacaterol acetate 150 µg o.d. delivered via Concept1 inhaler	
Reporting group title	Indacaterol acetate 75 µg o.d.
Reporting group description:	
Indacaterol acetate 75 µg o.d. delivered via Concept1 inhaler	

Reporting group values	Indacaterol acetate 150 µg o.d.	Indacaterol acetate 75 µg o.d.	Total
Number of subjects	41	39	80
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)	41	39	80
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	9.3	9.1	
standard deviation	± 1.47	± 1.58	-
Sex: Female, Male Units:			
Female	13	15	28
Male	28	24	52
Race/Ethnicity, Customized Units: Subjects			
Caucasian	17	17	34
Black	3	3	6
Asian	1	3	4
Native American	3	3	6
Unknown	1	0	1
Other	16	13	29

End points

End points reporting groups

Reporting group title	Indacaterol acetate 150 µg o.d.
Reporting group description:	
Indacaterol acetate 150 µg o.d. delivered via Concept1 inhaler	
Reporting group title	Indacaterol acetate 75 µg o.d.
Reporting group description:	
Indacaterol acetate 75 µg o.d. delivered via Concept1 inhaler	

Primary: Trough Forced Expiratoty Volume in 1 Second (FEV1)

End point title	Trough Forced Expiratoty Volume in 1 Second (FEV1)[1]
End point description:	
Change from baseline in pre-dose trough FEV1 after 2 weeks of treatment with indacaterol acetate 75 µg o.d and 150 µg o.d. The primary endpoint is change from baseline in pre-dose trough FEV1 (mL) after 2 weeks of treatment. The pre-dose trough FEV1 (mL) is defined as the mean of the two FEV1 (mL), values measured at -45 min and -15 min pre-dose.	
End point type	Primary
End point timeframe:	
2 weeks	

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 Analysis were performed

End point values	Indacaterol acetate 150 µg o.d.	Indacaterol acetate 75 µg o.d.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	38		
Units: Liter				
arithmetic mean (standard deviation)	0.171 (± 0.1664)	0.212 (± 0.2521)		

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 1 and Day 14 after inhalation of indacaterol acetate 75 µg and 150 µg.	
End point type	Secondary
End point timeframe:	
day 1, day 14	

End point values	Indacaterol acetate 150 µg o.d.	Indacaterol acetate 75 µg o.d.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	38		
Units: pg/mL				
arithmetic mean (standard deviation)				
Day 1 <=-2 hours	0.0 (± 0.0)	0.0 (± 0.0)		
Day 1, 15 minutes	204.1 (± 98.27)	73.7 (± 39.55)		
Day 1, 1 hour	125.8 (± 63.13)	43.9 (± 20.84)		
Day 14 <=-2 hours	80.9 (± 32.51)	46.7 (± 29.61)		
Day 14, 15 minutes	393.1 (± 182.11)	137.3 (± 47.43)		
Day 14, 1 hour	255.5 (± 117.67)	103.0 (± 37.88)		

Statistical analyses

No statistical analyses for this end point

Secondary: Asthma Control as assessed by pediatric interviewer-administered Asthma Control Questionnaire

End point title	Asthma Control as assessed by pediatric interviewer-administered Asthma Control Questionnaire

End point description:

Asthma Control as assessed by pediatric interviewer-administered Asthma Control Questionnaire (ACQ-IA) score at week 2 (mean change). A decrease in the score shows an improvement.
The scale ranges from 0 (no symptoms) to 6 (severe symptoms every day).
Results are given as a change as compared from baseline

End point type	Secondary

End point timeframe:

2 weeks

End point values	Indacaterol acetate 150 µg o.d.	Indacaterol acetate 75 µg o.d.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	38		
Units: score on a scale				
arithmetic mean (standard deviation)	-0.375 (± 0.3796)	-0.270 (± 0.6341)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-dose morning and evening Peak Expiratoty Flow (PEF)

End point title	Pre-dose morning and evening Peak Expiratoty Flow (PEF)

End point description:

Pre-dose morning and evening PEF over 2 weeks of treatment as determined by electronic peak flow meter data (mean change)

End point type	Secondary

End point timeframe:

2 weeks

End point values	Indacaterol acetate 150 µg o.d.	Indacaterol acetate 75 µg o.d.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	38		
Units: L/min				
arithmetic mean (standard deviation)				
Morning PEF	29.6 (± 26.41)	14.7 (± 29.38)		
Evening PEF	29.7 (± 25.57)	15.2 (± 28.58)		

Statistical analyses

No statistical analyses for this end point

Secondary: Rescue medication usage (mean daiily number of puffs)

End point title	Rescue medication usage (mean daiily number of puffs)

End point description:

Rescue medication usage over 2 weeks of treatment as determined by patient diary data for indacaterol acetate 75 µg and 150 µg o.d.Results given as mean change of puffs of rescue medication.

End point type	Secondary

End point timeframe:

2 weeks

End point values	Indacaterol acetate 150 µg o.d.	Indacaterol acetate 75 µg o.d.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	38		
Units: number of puffs				
arithmetic mean (standard deviation)	-0.19 (± 1.479)	-0.22 (± 0.930)		

Statistical analyses

No statistical analyses for this end point

Secondary: Rescue medication usage (percentage of rescue medication free days)

End point title	Rescue medication usage (percentage of rescue medication free days)

End point description:

Rescue medication usage over 2 weeks of treatment as determined by patient diary data for indacaterol acetate 75 µg and 150 µg o.d.

End point type	Secondary

End point timeframe:

2 weeks

End point values	Indacaterol acetate 150 µg o.d.	Indacaterol acetate 75 µg o.d.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	38		
Units: percentage				
arithmetic mean (standard deviation)	7.4 (± 22.37)	3.1 (± 19.42)		

Statistical analyses

No statistical analyses for this end point

Secondary: Forced Expiratoty Volume in 1 Second (FEV1) and Forced Vital Capacity (FVC)

End point title	Forced Expiratoty Volume in 1 Second (FEV1) and Forced Vital Capacity (FVC)

End point description:

FEV1 and FVC at 30 minutes and 1-hour post dose at week 2 for indacaterol acetate 75 µg and 150 µg o.d.

End point type	Secondary

End point timeframe:

2 weeks

End point values	Indacaterol acetate 150 µg o.d.	Indacaterol acetate 75 µg o.d.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	38		
Units: Liter				
arithmetic mean (standard deviation)				
30 minutes	0.234 (± 0.1786)	0.224 (± 0.2459)		
1 hour	0.224 (± 0.1725)	0.258 (± 0.2451)		

Statistical analyses

No statistical analyses for this end point

Secondary: Symptoms as recorded by patient e-diary (mean total daily symptom score)

End point title	Symptoms as recorded by patient e-diary (mean total daily symptom score)

End point description:

Symptoms as recorded by patient e-diary for indacaterol acetate 75 µg and 150 µg o.d. (mean change) The scale rages from 0 (no problem) - 4 (very severe problems).

End point type	Secondary

End point timeframe:

2 weeks

End point values	Indacaterol acetate 150 µg o.d.	Indacaterol acetate 75 µg o.d.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	38		
Units: score on a scale				
arithmetic mean (standard deviation)	-0.18 (± 0.695)	0.08 (± 0.365)		

Statistical analyses

No statistical analyses for this end point

Secondary: Symptoms as recorded by patient e-diary (percentage of asthma symptoms free days)

End point title	Symptoms as recorded by patient e-diary (percentage of asthma symptoms free days)

End point description:

Symptoms as recorded by patient e-diary for indacaterol acetate 75 µg and 150 µg o.d. (mean change)

End point type	Secondary

End point timeframe:

2 weeks

End point values	Indacaterol acetate 150 µg o.d.	Indacaterol acetate 75 µg o.d.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	38		
Units: percentage				
arithmetic mean (standard deviation)	12.3 (± 21.25)	4.4 (± 26.60)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Timeframe for AE	
Adverse event reporting additional description:	
AE additional description	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	QAB149 150 ug OD
Reporting group description:	
QAB149 150 ug OD	
Reporting group title	QAB149 75 ug OD
Reporting group description:	
QAB149 75 ug OD	

Serious adverse events	QAB149 150 ug OD	QAB149 75 ug OD	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 41 (0.00%)	0 / 38 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	QAB149 150 ug OD	QAB149 75 ug OD	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 41 (7.32%)	13 / 38 (34.21%)	
Investigations			
Blood glucose increased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	
Peak expiratory flow rate decreased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			

Limb injury			
subjects affected / exposed	0 / 41 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	
Cardiac disorders			
Defect conduction intraventricular			
subjects affected / exposed	0 / 41 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 41 (2.44%)	0 / 38 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 41 (2.44%)	1 / 38 (2.63%)	
occurrences (all)	1	1	
Vomiting			
subjects affected / exposed	0 / 41 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 41 (2.44%)	2 / 38 (5.26%)	
occurrences (all)	1	2	
Dysphonia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	0 / 41 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	2	
Rhinitis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	
Upper respiratory tract infection			

subjects affected / exposed occurrences (all)	0 / 41 (0.00%) 0	3 / 38 (7.89%) 3	

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