



## Clinical trial results:

**A comparative study to assess a fixed-dose combination of Budesonide-Salmeterol versus Serevent® Diskus® 50 g + Pulmicort® Turbuhaler® 100 µg co-administrated in asthmatic children: single dose, cross-over, randomized, 3-treatment**

### Summary

EudraCT number	2020-003404-14
Trial protocol	BG
Global end of trial date	26 April 2021

### Results information

Result version number	v1 (current)
This version publication date	31 October 2021
First version publication date	31 October 2021

### Trial information

#### Trial identification

Sponsor protocol code	BUSAL-SD201
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#### Additional study identifiers

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

Notes:

### Sponsors

Sponsor organisation name	Laboratoires SMB S.A.
Sponsor organisation address	26-28 rue de la pastorale, Brussels, Belgium,
Public contact	Clinical Trial Information, Laboratoires SMB S.A., 32 2411 48 28, DptClinique@smb.be
Scientific contact	Clinical Trial Information, Laboratoires SMB S.A., 32 2411 48 28, DptClinique@smb.be

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	01 July 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 April 2021
Global end of trial reached?	Yes
Global end of trial date	26 April 2021
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The primary objective is to assess and compare the systemic exposure of budesonide and salmeterol after administration of the study products (two dosages of Budesonide-Salmeterol fixed dose combination versus Serevent® Diskus® 50 µg + Pulmicort® Turbuhaler® 100 µg co-administration) using C<sub>max</sub>, AUC<sub>∞</sub>, AUC<sub>0-30min</sub>, AUC<sub>0-2h</sub>, t<sub>max</sub> and t<sub>1/2</sub>.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki "Ethical principles for medical research involving human volunteer", reviewed during the 64th WMA General Assembly, Fortaleza, 2013, in compliance with the approved protocol, Good Clinical Practices (GCP) and applicable regulatory requirements

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 March 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	Bulgaria: 14
Worldwide total number of subjects	14
EEA total number of subjects	14

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)	14
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:

The screening period was maximum 21 days, the volunteers were randomised according to the inclusion/exclusion criteria, blood and urine analysis, physical test and medical history.

### Period 1

Period 1 title	Cross over phase (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

This pharmacokinetic study was a partially blinded study as blindness was maintained only between the both dosages of Budesonide/salmeterol combination.

### Arms

Are arms mutually exclusive?	No
<b>Arm title</b>	Pulmicort 100µg + Serevent 50µg

Arm description:

Serevent Diskus 50 µg + Pulmicort Turbuhaler 100 µg co-administration, one dose taken by inhalation via the inhalers, containing 50 µg of salmeterol and 100 µg of budesonide respectively

Arm type	Active comparator
Investigational medicinal product name	Budesonide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

One dose taken by inhalation via the inhaler containing 100 µg of budesonide

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

Dosage and administration details:

One dose taken by inhalation via the inhaler containing 50 µg of salmeterol

<b>Arm title</b>	BUSAL 75/25µg
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Arm description:

Budesonide-Salmeterol 75-25 µg (DPI), one capsule taken by inhalation via the Vertical-Haler®, containing 75 µg of budesonide and 25 µg of salmeterol xinafoate

Arm type	Experimental
Investigational medicinal product name	budesonide/salmeterol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

one capsule taken by inhalation via the Vertical-Haler®, containing 75 µg of budesonide and 25 µg of salmeterol xinafoate

<b>Arm title</b>	BUSAL 66/22µg
Arm description: Budesonide-Salmeterol 66/22 µg (DPI), one capsule taken by inhalation via the Vertical-Haler®, containing 66 µg of budesonide and 22 µg of salmeterol xinafoate	
Arm type	Experimental
Investigational medicinal product name	budesonide/salmeterol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

one capsule taken by inhalation via the Vertical-Haler containing 66 µg of budesonide and 22 µg of salmeterol xinafoate

<b>Number of subjects in period 1</b>	Pulmicort 100µg + Serevent 50µg	BUSAL 75/25µg	BUSAL 66/22µg
Started	14	14	14
Completed	14	14	14

## Baseline characteristics

### Reporting groups

Reporting group title	Cross over phase
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Reporting group description:

After being screened, 14 subjects were randomised in this study and 14 subjects completed the study. The safety and demographic data were analysed with 14 subjects and the pharmacokinetic endpoints were analysed with 14 subjects according to the SAP.

Reporting group values	Cross over phase	Total	
Number of subjects	14	14	
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)	14	14	
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	9.29		
standard deviation	± 1.68	-	
Gender categorical			
Units: Subjects			
Female	9	9	
Male	5	5	

## End points

### End points reporting groups

Reporting group title	Pulmicort 100µg + Serevent 50µg
Reporting group description:	Serevent Diskus 50 µg + Pulmicort Turbuhaler 100 µg co-administration, one dose taken by inhalation via the inhalers, containing 50 µg of salmeterol and 100 µg of budesonide respectively
Reporting group title	BUSAL 75/25µg
Reporting group description:	Budesonide-Salmeterol 75-25 µg (DPI), one capsule taken by inhalation via the Vertical-Haler®, containing 75 µg of budesonide and 25 µg of salmeterol xinafoate
Reporting group title	BUSAL 66/22µg
Reporting group description:	Budesonide-Salmeterol 66/22 µg (DPI), one capsule taken by inhalation via the Vertical-Haler®, containing 66 µg of budesonide and 22 µg of salmeterol xinafoate

### Primary: Budesonide Cmax

End point title	Budesonide Cmax
End point description:	
End point type	Primary
End point timeframe:	Period I, period II and Perido III

End point values	Pulmicort 100µg + Serevent 50µg	BUSAL 75/25µg	BUSAL 66/22µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	14	14	
Units: ng/ml				
arithmetic mean (standard deviation)	95.02 (± 77.94)	190.92 (± 78.34)	135.02 (± 67.10)	

### Statistical analyses

Statistical analysis title	T1 vs T2
Comparison groups	Pulmicort 100µg + Serevent 50µg v BUSAL 75/25µg
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Geometric mean ratio
Point estimate	243

Confidence interval	
level	90 %
sides	2-sided
lower limit	167.23
upper limit	353.14

<b>Statistical analysis title</b>	T1vsT3
Comparison groups	Pulmicort 100µg + Serevent 50µg v BUSAL 66/22µg
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Geometric mean ratio
Point estimate	173.23
Confidence interval	
level	90 %
sides	2-sided
lower limit	109.43
upper limit	274.21

### Primary: Budesonide AUCt

End point title	Budesonide AUCt
End point description:	
End point type	Primary
End point timeframe:	
Period I, period II and period III	

End point values	Pulmicort 100µg + Serevent 50µg	BUSAL 75/25µg	BUSAL 66/22µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	14	14	
Units: ng/ml*min				
arithmetic mean (standard deviation)	199.51 (± 179.33)	398.60 (± 139.10)	321.09 (± 112.63)	

### Statistical analyses

<b>Statistical analysis title</b>	T1 vs T2
Comparison groups	Pulmicort 100µg + Serevent 50µg v BUSAL 75/25µg

Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	GMR
Point estimate	279.96
Confidence interval	
level	90 %
sides	2-sided
lower limit	164.7
upper limit	475.89

<b>Statistical analysis title</b>	T1 vs T3
Comparison groups	Pulmicort 100µg + Serevent 50µg v BUSAL 66/22µg
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	GMR
Point estimate	235.82
Confidence interval	
level	90 %
sides	2-sided
lower limit	134.92
upper limit	412.17

### Primary: Salmeterol Cmax

End point title	Salmeterol Cmax
End point description:	
End point type	Primary
End point timeframe:	
PI, PII and PIII	

<b>End point values</b>	Pulmicort 100µg + Serevent 50µg	BUSAL 75/25µg	BUSAL 66/22µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	14	14	
Units: ng/ml				
arithmetic mean (standard deviation)	109.37 (± 61.00)	141.74 (± 58.68)	115.89 (± 55.61)	

## Statistical analyses

<b>Statistical analysis title</b>	T1 vs T2
Comparison groups	Pulmicort 100µg + Serevent 50µg v BUSAL 75/25µg
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	GMR
Point estimate	137.98
Confidence interval	
level	90 %
sides	2-sided
lower limit	111.14
upper limit	171.3

<b>Statistical analysis title</b>	T1 vs T3
Comparison groups	Pulmicort 100µg + Serevent 50µg v BUSAL 66/22µg
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	GMR
Point estimate	110.95
Confidence interval	
level	90 %
sides	2-sided
lower limit	88.78
upper limit	138.66

## Primary: Salmeterol AUCt

End point title	Salmeterol AUCt
End point description:	
End point type	Primary
End point timeframe:	
PI, PII and PIII	

<b>End point values</b>	Pulmicort 100µg + Serevent 50µg	BUSAL 75/25µg	BUSAL 66/22µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	14	14	
Units: ng/ml*h				
arithmetic mean (standard deviation)	174.83 (± 68.58)	158.10 (± 51.97)	132.19 (± 55.66)	

## Statistical analyses

<b>Statistical analysis title</b>	T1 vs T2
Comparison groups	Pulmicort 100µg + Serevent 50µg v BUSAL 75/25µg
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	GMR
Point estimate	92.37
Confidence interval	
level	90 %
sides	2-sided
lower limit	76.73
upper limit	111.19

<b>Statistical analysis title</b>	T1 vs T3
Comparison groups	Pulmicort 100µg + Serevent 50µg v BUSAL 66/22µg
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	GMR
Point estimate	75.36
Confidence interval	
level	90 %
sides	2-sided
lower limit	64.59
upper limit	87.91

## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

Screening, period I, period II, period III and end of study

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	24
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### Reporting groups

Reporting group title	Pulmicort 100µg + Serevent 50µg
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Reporting group description:

Serevent Diskus 50 mg + Pulmicort Turbuhaler 100 µg co-administration, one dose taken by inhalation via the inhalers, containing 50 µg of salmeterol and 100 µg of budesonide respectively

Reporting group title	BUSAL 75/25µg
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Reporting group description:

Budesonide-Salmeterol 75-25 mg (DPI), one capsule taken by inhalation via the Vertical-Haler®, containing 75 µg of budesonide and 25 µg of salmeterol xinafoate

Reporting group title	BUSAL 66/22
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Reporting group description:

Budesonide-Salmeterol 66/22 mg (DPI), one capsule taken by inhalation via the Vertical-Haler®, containing 66 µg of budesonide and 22 µg of salmeterol xinafoate

<b>Serious adverse events</b>	Pulmicort 100µg + Serevent 50µg	BUSAL 75/25µg	BUSAL 66/22
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 14 (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: 5 %

<b>Non-serious adverse events</b>	Pulmicort 100µg + Serevent 50µg	BUSAL 75/25µg	BUSAL 66/22
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 14 (0.00%)

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No adverse event were reported in the BUSALSD201 study

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported