Clinical trial results:
A randomised, open, controlled pilot study to investigate the efficacy and safety of Buparid/PARI SINUS versus Budes® Nasal Spray in the therapy of Chronic Rhinosinusitis (CRS) with polyposis nasi in adult patients

Summary

EudraCT number	2013-002414-12
Trial protocol	DE
Global end of trial date	21 June 2021

Results information

Result version number	v2 (current)
This version publication date	11 September 2021
First version publication date	30 July 2021
Version creation reason	• Correction of full data set Correction of data on 26. Aug 2021
Summary attachment (see zip file)	Study Synopsis (12082.101 Synopsis wo signature pages.pdf)

Trial information

Trial identification

Sponsor protocol code	12082.101

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	PARI Pharma GmbH
Sponsor organisation address	Lochhamer Schlag 21, Gräfelfing, Germany, 82166
Public contact	Clinical Development Department, PARI Pharma GmbH, +49 8974284676, friedrich.gruber@pari.com
Scientific contact	Clinical Development Department, PARI Pharma GmbH, +49 8974284676, friedrich.gruber@pari.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	03 February 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 June 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study is to create data for the selection of a clinically relevant primary endpoint to assess the efficacy and safety of Buparid/PARI SINUS as compared to Budes Nasal Spray in the therapy of chronic rhinosinusitis (CRS) with polyposis nasi in adult patients. Ideally, the selected parameter should allow a correlation between an objective methodology and the clinical outcome of the study patients.

Protection of trial subjects:

Special caution is necessary in patients with active or quiescent pulmonary tuberculosis and in patients with fungal or viral infections in the airways.
During transfer from oral therapy to Buparid, a generally lower systemic corticosteroid action will be experienced, which may result in the appearance of allergic or arthritic symptoms such as rhinitis, eczema and muscle and joint pain. Specific treatment should be initiated for these conditions. A general insufficient glucocorticosteroid effect should be suspected if, in rare cases, symptoms such as tiredness, headache, nausea and vomiting should occur. In these cases a temporary increase in the dose of oral glucocorticosteroids is sometimes necessary.
Patients, who have required high dose emergency corticosteroid therapy or prolonged treatment at the highest recommended dose of inhaled corticosteroids, may also be at risk of impaired adrenal function. These patients may exhibit signs and symptoms of adrenal insufficiency when exposed to severe stress. Additional systemic corticosteroid treatment should be considered during periods of stress or elective surgery.
Systemic effects may occur with any inhaled corticosteroids, particularly at high doses prescribed for long periods. These effects are much less likely to occur with inhalation treatment than with oral corticosteroids. Possible systemic effects include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract, glaucoma and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children).
Oral candidiasis may occur during the therapy with inhaled corticosteroids. This infection may require treatment with appropriate antifungal therapy and in some patients discontinuation of treatment may be necessary.

Background therapy: -
Evidence for comparator: -

Actual start date of recruitment	28 August 2013
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: 18
Worldwide total number of subjects	18
EEA total number of subjects	18

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)	18
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Enrolment period: 18 months;
3 clinical centres in Germany participating in the trial

Pre-assignment

Screening details:

Diagnosis and main criteria for inclusion: Patient with confirmed diagnosis of CRS, i.e. inflammation of nasal mucosa and paranasal sinus, with polyposis nasi grade I-III. Diagnosis is based on history of symptoms (nasal obstruction, running nose, postnasal drip, facial pain and hyposmia with a duration of > 3 months and on MRT-imaging)

Period 1

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

Blinding implementation details:

n.a.

Arms

Are arms mutually exclusive?	Yes
Arm title	Buparid 1 mg/2 ml nebuliser solution (PARI Pharma GmbH); API:

Arm description:

Buparid 1 mg/2 ml nebuliser solution (PARI Pharma GmbH); API: Budesonide

Arm type	Experimental
Investigational medicinal product name	Buparid 1 mg/2 ml nebuliser solution (PARI Pharma GmbH); API: Budesonide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser solution
Routes of administration	Intranasal use

Dosage and administration details:

In patients allocated to receive Buparid, the drug was administered by a once daily inhalation (in the evening) using the PARI SINUS nebuliser. At every study visit, one inhalation cycle was monitored by the clinical trial centre personnel.

Arm title	Budes® Nasal Spray 50 µg/pump (Hexal AG); API: Budesonide

Arm description:

Budes® Nasal Spray 50 µg/pump (Hexal AG); API: Budesonide

Arm type	Active comparator
Investigational medicinal product name	Budes® Nasal Spray 50 µg/pump (Hexal AG); API: Budesonide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Intranasal use

Dosage and administration details:

In patients allocated to receive Budes Nasal Spray, the drug was administered with 2 pumps per nostril twice daily (in the morning and the evening).

Number of subjects in period 1[1]	Buparid 1 mg/2 ml nebuliser solution (PARI Pharma GmbH); API:	Budes® Nasal Spray 50 µg/pump (Hexal AG); API: Budesonide
Started	8	6
Completed	8	6

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 4 patients enrolled but not randomised

Baseline characteristics

Reporting groups	
Reporting group title	Buparid 1 mg/2 ml nebuliser solution (PARI Pharma GmbH); API:
Reporting group description:	
Buparid 1 mg/2 ml nebuliser solution (PARI Pharma GmbH); API: Budesonide	
Reporting group title	Budes® Nasal Spray 50 µg/pump (Hexal AG); API: Budesonide
Reporting group description:	
Budes® Nasal Spray 50 µg/pump (Hexal AG); API: Budesonide	

Reporting group values	Buparid 1 mg/2 ml nebuliser solution (PARI Pharma GmbH); API:	Budes® Nasal Spray 50 µg/pump (Hexal AG); API: Budesonide	Total
Number of subjects	8	6	14
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Age (mean +/- SD)			
Units: years			
arithmetic mean	49.0	59.5	
standard deviation	± 11.2	± 12.2	-
Gender categorical			
Units: Subjects			
Female	3	3	6
Male	5	3	8

End points

End points reporting groups	
Reporting group title	Buparid 1 mg/2 ml nebuliser solution (PARI Pharma GmbH); API:
Reporting group description: Buparid 1 mg/2 ml nebuliser solution (PARI Pharma GmbH); API: Budesonide	
Reporting group title	Budes® Nasal Spray 50 µg/pump (Hexal AG); API: Budesonide
Reporting group description: Budes® Nasal Spray 50 µg/pump (Hexal AG); API: Budesonide	

Primary: Nasal obstruction	
End point title	Nasal obstruction
End point description:	
End point type	Primary
End point timeframe: visits 1 to 4	

End point values	Buparid 1 mg/2 ml nebuliser solution (PARI Pharma GmbH); API:	Budes® Nasal Spray 50 µg/pump (Hexal AG); API: Budesonide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	6		
Units: Change from baseline				
median (confidence interval 95%)	755 (644 to 867)	646 (526 to 765)		

Statistical analyses

Statistical analysis title	Rhinomanometry
Comparison groups	Buparid 1 mg/2 ml nebuliser solution (PARI Pharma GmbH); API: v Budes® Nasal Spray 50 µg/pump (Hexal AG); API: Budesonide
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.95
Method	MMRM

Primary: Health-specific quality of life

End point title	Health-specific quality of life

End point description:

End point type	Primary

End point timeframe:

Visits 1 to 6

End point values	Buparid 1 mg/2 ml nebuliser solution (PARI Pharma GmbH); API:	Budes® Nasal Spray 50 µg/pump (Hexal AG); API: Budesonide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	6		
Units: change to baseline				
arithmetic mean (confidence interval 95%)	23.6 (19.7 to 27.6)	14.4 (9.8 to 18.9)		

Statistical analyses

Statistical analysis title	SNOT-22
Comparison groups	Buparid 1 mg/2 ml nebuliser solution (PARI Pharma GmbH); API: v Budes® Nasal Spray 50 µg/pump (Hexal AG); API: Budesonide
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	MMRM

Adverse events

Adverse events information	
Timeframe for reporting adverse events: from FPI until LPO	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	17
Reporting groups	
Reporting group title	Arm 1 Buparid SINUS
Reporting group description: -	
Reporting group title	Arm 2 Budes Nasal Spray
Reporting group description: -	

Serious adverse events	Arm 1 Buparid SINUS	Arm 2 Budes Nasal Spray	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (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: 0 %

Non-serious adverse events	Arm 1 Buparid SINUS	Arm 2 Budes Nasal Spray	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 8 (62.50%)	4 / 6 (66.67%)	
Nervous system disorders			
Parosmia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Sputum Increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	

Nasal Dryness			
subjects affected / exposed	1 / 8 (12.50%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Cough			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Epistaxis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Sensitive skin			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Infections and infestations			
Otitis media			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Nasopharyngitis			
subjects affected / exposed	1 / 8 (12.50%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Sinusitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	
occurrences (all)	1	0	

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