



Clinical trial results:

A randomised, open, controlled pilot study to investigate the potential of Buparid/PARI SINUS versus Budes® Nasal Spray to avoid or postpone sinus surgery in adult patients with Chronic Rhinosinusitis (CRS)

Summary

EudraCT number	2013-002421-30
Trial protocol	DE
Global end of trial date	29 July 2021

Results information

Result version number	v1 (current)
This version publication date	11 September 2021
First version publication date	11 September 2021
Summary attachment (see zip file)	Study Synopsis (Synopsis_12082.102_Buparid_final_210729_wo

Trial information

Trial identification

Sponsor protocol code	12082.102
-----------------------	-----------

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 Trial Manager, PARI Pharma GmbH, 49 8974284676, friedrich.gruber@pari.com
Scientific contact	Clinical Trial Manager, 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	29 July 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 analyse whether Buparid/PARI SINUS has a higher potential to avoid or postpone sinus surgery in adult patients with CRS than Standard of Care therapy with Budes® Nasal Spray. The results of this study are expected to provide estimates for a proper sample size calculation to conduct a pivotal study.

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	02 April 2014
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: 19
Worldwide total number of subjects	19
EEA total number of subjects	19

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)	19
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Enrolment period 33 months

3 clinical centres in Germany participated in the trial

Pre-assignment

Screening details:

Diagnosis and main criteria for inclusion:

Patient with confirmed diagnosis of chronic rhinosinusitis (CRS), i.e. inflammation of nasal mucosa and paranasal sinus. 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)

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 suspension
Routes of administration	Intranasal use

Dosage and administration details:

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

Arm title	Budes® Nasal Spray 50 µg/pump (Hexal AG)
------------------	--

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 will be administered with 2 pumps per nostril twice daily (in the morning and the evening).

Number of subjects in period 1	Buparid 1 mg/2 ml nebuliser solution (PARI Pharma GmbH)	Budes® Nasal Spray 50 µg/pump (Hexal AG)
Started	10	9
Completed	10	9

Baseline characteristics

End points

End points reporting groups

Reporting group title	Buparid 1 mg/2 ml nebuliser solution (PARI Pharma GmbH)
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)
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)	Budes® Nasal Spray 50 µg/pump (Hexal AG)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: change from baseline				
number (confidence interval 95%)	461.5 (320 to 602)	551.5 (408 to 694)		

Statistical analyses

Statistical analysis title	Rhinomanometry
Comparison groups	Buparid 1 mg/2 ml nebuliser solution (PARI Pharma GmbH) v Budes® Nasal Spray 50 µg/pump (Hexal AG)
Number of subjects included in analysis	19
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)	Budes® Nasal Spray 50 µg/pump (Hexal AG)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: change from baseline				
arithmetic mean (confidence interval 95%)	17.1 (5.5 to 28.7)	22.9 (10.5 to 35.3)		

Statistical analyses

Statistical analysis title	SNOT-20
Comparison groups	Buparid 1 mg/2 ml nebuliser solution (PARI Pharma GmbH) v Budes® Nasal Spray 50 µg/pump (Hexal AG)
Number of subjects included in analysis	19
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	1 / 10 (10.00%)	0 / 9 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Aneurysm			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
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: 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 / 10 (50.00%)	6 / 9 (66.67%)	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			

Cough subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 9 (0.00%) 0	
Nasal dryness subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 9 (11.11%) 1	
Epistaxis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	2 / 9 (22.22%) 2	
Psychiatric disorders Depression subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 9 (0.00%) 0	
Infections and infestations Rhinitis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	1 / 9 (11.11%) 1	
Sinusitis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	1 / 9 (11.11%) 1	
Tonsillitis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 9 (0.00%) 0	
Cystitis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 9 (11.11%) 1	
Influenza subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 1	1 / 9 (11.11%) 1	
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 9 (11.11%) 1	

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