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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)

Clinical Study Report

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2 SYNOPSIS

Name of Sponsor/Company: PARI Pharma GmbH	Individual Study Table Referring to Part of the Dossier	*(For National Authority Use only)*
Name of Finished Product: Buparid/PARI SINUS	Volume:	
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Title of Study:

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)

Investigators:

Principal Investigator: Prof. Dr. med. Martin Canis

Study centres:

Ludwig-Maximilians-University Munich, Germany

Georg-August-University, Göttingen, Germany

Johannes Gutenberg-University, Mainz, Germany

Publication (reference):

None

Studied period (years):		Phase of development:
Study initiation date (first patient in):	27 October 2015	Pilot Study
Study completion date (date of last follow-up):	27 September 2018	

Objectives:

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.

Methodology:

This is a randomised, open, controlled pilot study in the therapy of CSR in adult patients.

Number of patients planned:

20 patients are planned for this study.

Diagnosis and main criteria for inclusion:

1. 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,

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running nose, postnasal drip, facial pain and hyposmia with a duration of > 3 months (according to EPOS3) and on MRT-imaging (Lund-Mackey Score [Score: 0-24])

2. Patient without alternative other than sinus surgery
3. Patient's written informed consent obtained prior to any screening or study-specific procedure
4. Male or female, ≥ 18 years of age
5. Patient is able to undergo nasal therapy without restrictions
6. Capable to correctly use the PARI SINUS device (closing of the soft palate) in accordance with the package insert
7. Capable of understanding the purpose and risk of the clinical trial
8. Female patients with childbearing potential must have a negative urine pregnancy test prior to first IMP administration. Both women and men must agree to use a medically acceptable method of contraception throughout the IMP treatment period and for 3 months after IMP discontinuation.
9. Patient is able to participate in the study according to Investigator's opinion

Test drug:

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

Mode of admimistration:

A) 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.

Reference drug:

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

Mode of administration:

B) 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).

Criteria for evaluation:

Following screening and consenting, all participants regardless of treatment allocation will receive Budes Nasal Spray 50 µg (2 pumps/nostril BID) in a 1-week Wash-in Phase before starting the IMP-treatment to prevent a bias of study results due to former individualised therapies.

After passing the Wash-in Phase patients will be randomly assigned to one of the following treatments:

Treatment arm A (Buparid/PARI SINUS, BuPS):

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Buparid 1 mg/2 ml once daily for 8 weeks (2 months), resulting in a daily delivered dose of 280 µg Buparid.

Treatment arm B (Budes Nasal Spray, BuNS):

Budes Nasal Spray (50 µg/pump) 2 pumps per nostril twice daily for 8 weeks (2 months), resulting in a daily delivered dose of 400 µg.

Efficacy:

- Health-related quality of life
- Nasal obstruction
- Inflammation of nasal mucosa and paranasal sinus
- Clinical parameters
- Symptoms of rhinosinusitis
- Loss of taste/Loss of smell
- Avoidance or postponing of sinus surgery
- Customer satisfation regarding the PARI SINUS device, if applicable

Safety:

- Treatment-emergent adverse events (AEs)

Statistical methods:

An exploratory statistical analysis was performed. The treatment groups were characterized using methods of descriptive data analysis. Treatment group comparisons were based mainly on 95% confidence intervals for differences between mean values or rates.

Summary – Conclusions:

All patients (10 BuPS-group, 9 BuNS-group) entered the trial with an indication for sinunasal surgery, but the majority of the subjects in both groups no longer had an acute indication for surgery at end of treatment (BuPS 60.0%; BuNS 55.6%). It therefore appears that both treatments may have had a clinically meaningful effect in postponing surgery.

Patients experienced an improved quality-of-life after the 8-week treatment-course (median: BuPS -6.5/-14.8%; BuNS -3.0/-11.1%). After treatment, reduction of rhinorrhoea was achieved in the BuPS-group (-2.5/-22.6%) with no or lower changes in the BuNS-group (+3.0/+7.1%) comparable to sinusitis-related impairment (BuPS -34.5/-47.1%; BuNS -3.0/-10.0%).

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With regard to the objective of this study to identify clinically relevant and change-sensitive endpoints to further investigate the efficacy of Buparid/SINUS in CRS without polyposis nasi the assessments of subjective measures (disease-related quality of life by SNOT-20, symptoms of rhinosinusitis by means of visual analogue scales) seem most suitable.		
Safety Results: About half of the patients in both groups reported adverse events (AE) under treatment, most of them with mild to moderate intensity. Comparable in both groups the frequency of AEs was very low (overall majority of cases in: System Organ Class (SOC) infections: 3 patients, SOC vascular disorders: 3 patients, SOC gastrointestinal disorders: 3 patients). Epistaxis occurred in only two patients of the BuNS-group.		
Conclusion: Pulsating airflow for aerolized delivery of budesonide is effective to avoid or postpone sinus surgery for CRSsNP. In comparison to nasal spray a potentially stronger and prolonged treatment-effect may be achieved that needs to be investigated in a pivotal study. Health-related quality of life (assessed by SNOT 20 questionaire) and symptoms of rhinosinusitis (assessed by visual analoque scale) may be suitable endpoints for a pivotal study.		
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