***PLEASE NOTE:*** *This study has been imported from ClinicalTrials.gov without additional data checks.*

## Trial Description

### Title

**A Multi-centre, Phase II, Double-blind, Randomised, Placebo-controlled, Parallel Group, Dose-ranging Study in Patients With Faecal Incontinence; to Evaluate the Efficacy, Safety and Tolerability of Locally Applied NRL001 Over an 8 Week Treatment Period**

### Trial Acronym

**[---]***

### URL of the trial

**[---]***

### Brief Summary in Lay Language

**The purpose of this study is to evaluate the safety, tolerability and efficacy of NRL001 in
the treatment of faecal incontinence, compared against placebo**

### Brief Summary in Scientific Language

**[---]***

## Organizational Data

- DRKS-ID: **DRKS00006394**
- Date of Registration in DRKS: **2014/08/28**
- Date of Registration in Partner Registry or other Primary Registry: **2012/08/01**
- Investigator Sponsored/Initiated Trial (IST/IIT): **no**
- Ethics Approval/Approval of the Ethics Committee: **[---]***
- (leading) Ethics Committee Nr.: **[---]***

## Secondary IDs

- Primary Registry-ID: **NCT01656720 (ClinicalTrials.gov)**
- Sponsor-ID: **NRL001-01/2011 (SEFI) (Norgine)**

Sponsor-ID: **NRL001-01/2011 (SEFI) (Norgine)**

## Health condition or Problem studied

- Free text: **Faecal Incontinence**
- ICD10: **R15 - Faecal incontinence**

## Interventions/Observational Groups

- Arm 1: **Drug: 1R, 2S-methoxamine hydrochloride**
- Arm 2: **Drug: Placebo**

## Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Randomized controlled trial**
- Blinding: **[---]***
- Who is blinded: **patient/subject, investigator/therapist**
- Control: **Placebo, Active control**
- Purpose: **Treatment**
- Assignment: **Parallel**
- Phase: **II**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **[---]***

### Primary Outcome

**- Evaluate the efficacy of NRL001 in faecal incontinence by assessing the improvement of the incontinence status after 4 weeks of treatment compared to baseline by means of the Wexner score; time frame: Up to 8 weeks**

### Secondary Outcome

**- To provide data on the efficacy of NRL001 in patients with faecal incontinence over an 8 week treatment period; time frame: 8 weeks**
**- To provide preliminary data on the safety and tolerability of NRL001 (5mg, 7.5mg and 10mg) over an 8 week treatment period compared to placebo; time frame: 8 weeks**
**- To evaluate the population pharmacokinetics and to establish any pharmacokinetic/pharmacodynamic relationship with adverse events; time frame: 8 weeks**

**- To evaluate the dose-response relationship in order to identify the appropriate dose(s) of NRL001 for future studies; time frame: 8 weeks**
**- To evaluate the effect of treatment according to the patient's Faecal Incontinence Quality of Life questionnaire at 4 and 8 weeks; time frame: 8 weeks**
**- To evaluate the effect of treatment according to the Vaizey score at 4 and 8 weeks; time frame: 8 weeks**

## Countries of recruitment

- CZ **Czech Republic**
- FR **France**
- DE **Germany**
- HU **Hungary**
- IT **Italy**
- PL **Poland**
- ES **Spain**
- SE **Sweden**
- UK **United Kingdom**

## Locations of Recruitment

- **Zentrum Fur Darm-Und Beckenchirurgie, Berlin**
- **Martin-Luther-Krankenhaus, Berlin**
- **Universitats-Frauenklink, Heidelberg**

## Recruitment

- Planned/Actual: **[---]***
- (Anticipated or Actual) Date of First Enrollment: **2012/02/27**
- Target Sample Size: **580**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **International**

### Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **no maximum age**

**Additional Inclusion Criteria**

**- An ultrasound assessment of the internal anal sphincter within the previous 12 months**
**confirming an intact circular internal sphincter with minimal scars (maximum 60**
**degrees scarring circumferentially).**

**- Diagnosis of faecal incontinence with a Wexner score of 8 - 20 inclusive at Visit 1 -**
**Screening Visit.**

**- Historical clinical evidence (past 6 months prior to Visit 1 - Screening Visit) of**
**faecal incontinence episodes (solids, liquid, gas or mucus).**

**- Greater than or equal to two faecal incontinence episodes (solids, liquid, gas or**
**mucus) per week during the 4 week historical period prior to Visit 1 - Screening**
**Visit.**

**- Able and willing to receive rectal examinations and treatments.**

**- Patients must be aged >18 without significant acute or uncontrolled chronic disease.**

**- Patients must understand the purpose and risks of the study and be able to provide**
**written informed consent and willing, able and competent to complete the entire study**
**and comply with study instructions as defined in the protocol.**

**- Female patients must be postmenopausal (for at least one year and confirmed by serum**
**FSH at screening), or surgically sterile, practicing true sexual abstinence, or using**
**Investigator-approved methods of contraception throughout the study until after the**
**post study physical examination and have a negative pregnancy test at screening.**

**- Sexually active male patients must use condoms with their partners throughout the**
**study and for 90 days after completion of the study in addition to their partner's**
**normal mode of contraception.**

**- Male patients must not donate sperm during the study and for 90 days after the**
**completion of the study.**

**- Patients taking any continuous medication need to have been on a stable regimen for**
**at least 1 month prior to Visit 1 - Screening Visit.**

**Exclusion criteria**

**- External anal sphincter disruption related to faecal incontinence caused by trauma.**

**- Patients with complicating gastrointestinal (GI) disease including those with inflammatory bowel diseases, patients that have received radiotherapy or surgery for anal cancer, patients with rectal prolapse, transanal surgery.**

**- Relevant history of or presence of any significant or uncontrolled cardiovascular risk including:**

**1. Systolic > 160mmHg or Diastolic > 100mmHg. Patients on a stable regimen for > 3 months with controlled hypertension prior to Visit 1 - Screening Visit (Systolic < 140mmHg or Diastolic < 90mmHg) can be included.**

**2. Abnormal 24 hour Screening Holter: corrected QT interval (QTcf) prolongation with cut-off values of >460 ms for females and >430 ms for males, acute arrhythmia, nocturnal bradycardia with heart rate (HR) < 40bpm, atrial fibrillation, AV block Type II and III, Sick Sinus Syndrome, vasovagal syncope.**

**3. Fixed cardiac output states (severe aortic stenosis (AS), hypertrophic obstructive cardiomyopathy (HOCM).**

**4. Significant mitral regurgitation (MR).**

**5. Cardiac failure (New York Heart Association (NYHA) stage II-IV).**

**- Severe or uncontrolled asthma or chronic obstructive pulmonary disease determined by clinical history, physical examination, lung function tests or exercise tolerance**

**- Chronic liver disease (e.g. liver cirrhosis, chronic hepatitis, severe hepatic insufficiency).**

**- Vascular claudication after <50 metres walking distance.**

**- Severe renal impairment defined as glomerular filtration rate (GFR) ≤ 30 ml/min, uncontrolled and reno-vascular end stage renal disease.**

**- Patients with diabetic polyneuropathies.**

**- Any type of chronic diarrhoea or frequent diarrhoea (defined as >5 loose stools per day).**

**- Faecal impaction and overflow diarrhoea.**

**- Male patients with clinically diagnosed prostatic hyperplasia.**

**- Clinically significant electrolyte abnormalities, e.g. clinically significant low/high potassium and low sodium.**

**- Presence of clinical symptomatic haemorrhoids (grade III and IV), anal fissures or anorectal fistulas.**

**- Less than 2 episodes of faecal incontinence (solids, liquid, gas or mucus) per week during the 4 week historical period prior to Visit 1 - Screening Visit.**

**- Participation in a clinical drug study during the 90 days preceding the initial dose in this study.**

**- Known history of allergy to methoxamine or any other ingredients of the Investigational Medicinal Product.**

**- Patients who, in the opinion of the Investigator, are unsuitable for participation in the study due to any dependencies, general medical conditions or significant illness within two weeks prior to randomisation.**

**- Use of any disallowed concomitant medication or other medication that the Investigator believes may affect the study including over-the-counter (OTC) products within 30 days prior to the Investigational Medicinal Product administration.**

**- A personal or family history of QTcf prolongation or sudden death.**

**- Patients taking Loperamide (2mg) >8 tablets per day for faecal incontinence either alone or in combination with codeine phosphate and/or paracetamol (8/500mg).**

**- Patients using any device for the treatment of faecal incontinence.**

## Addresses

■ **Primary Sponsor**

**Norgine**

Telephone: **[---]***

**Primary Sponsor**

**Norgine**

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***
URL: **[---]***

- **Contact for Scientific Queries**

**Hopital Pontchaillou**
**Laurent Siproudhis, MD**

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***
URL: **[---]***

- **Contact for Public Queries**

**Deborah J Jones, BSc(Hons)**

Telephone: **+44189582**
Fax: **[---]***
E-mail: **djones3 at norgine.com**
URL: **[---]***

## Sources of Monetary or Material Support

- **[---]***

**Bitte wenden Sie sich an den Sponsor / Please refer to primary sponsor**

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***
URL: **[---]***

## Status

- Recruitment Status: **Recruiting ongoing**
- Study Closing (LPLV): **[---]***

## Trial Publications, Results and other documents

*The parameters in ClinicalTrials.gov and DRKS are not identical. Therefore the data import from ClinicalTrials.gov required adjustments. For full details please see the DRKS FAQs.*

*- Translation on version: 2*

*- Last processed date by ClinicalTrials.gov: 2014/11/27*

** This entry means the parameter is not applicable or has not been set.*

**** This entry means that data is not displayed due to insufficient data privacy clearing.*