Proof of concept clinical trial of safety and biological activity of Bifidobacterium Longum NCC 2705 in gluten sensitivity

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The primary objective is to evaluate in the two targeted populations (i.e. CD and self-reported NCGS subjects):1) the safety profile of BL NCC 2705 2) the gastro-intestinal (GI) tolerability of BL NCC 2705

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Food intolerance syndromes
Study type	Interventional

Summary

ID

NL-OMON46135

Source
ToetsingOnline

Brief title
Probiotic BL NCC 2705 and gluten sensitivity

Condition

- Food intolerance syndromes

Synonym
celiac disease, gluten sensitivity

Research involving
Human

Sponsors and support

Primary sponsor: Nestec
Source(s) of monetary or material Support: Bedrijf (Nestec)

Intervention

Keyword: celiac disease, gluten sensitivity, probiotics, safety

Outcome measures

Primary outcome

1) Adverse Events (AE) incidence, type, severity and causal relationship to the investigational product

2) GI scores from a Visual Analogue Scale (VAS) over both treatment periods at home (i.e. from day 1 to day 3) for each symptom of interest (i.e. 1) nausea, 2) vomiting, 3) diarrhea, 4) audible bowel sounds, 5) flatulence, 6) abdominal cramping)

Secondary outcome

1) Concentration of serpin in duodenal aspirates

2) Concentration of BL NCC 2705 in duodenal aspirates

3) Inhibition of the elastase activity in duodenal aspirates

4) Concentration immunogenic (33-mer) gluten-derived peptides in duodenal aspirates following a 3g gluten containing meal

5) Inhibition of glutenasic activity in duodenal aspirates

6) Urinary excretion of immunogenic (33-mer) gluten-peptides following the gluten-containing meal

Study description

Background summary

The rationale of the present clinical study is to generate proof of concept for the development of BL NCC 2705 as a complementary treatment to gluten-free diet

(GFD) in subjects with gluten-related disorders still experiencing symptoms due to accidental intake of hidden gluten.
BL NCC 2705 is expected to counteract the negative effects of hidden gluten by a dual mechanism of action, consisting of a) anti-inflammatory properties deriving from the inhibition of duodenal elastase activity and b) reduced production of immunogenic and toxic gluten peptides deriving from the inhibition of the glutenasic activity of the intestinal proteases by probiotic produced serpin.

Study objective

The primary objective is to evaluate in the two targeted populations (i.e. CD and self-reported NCGS subjects):

1) the safety profile of BL NCC 2705
2) the gastro-intestinal (GI) tolerability of BL NCC 2705

Study design

This trial is a multicenter, double blind, randomized, placebo controlled, 2 by 2 cross-over design. Recruitment of participants takes play by Maastricht University, and the study will also be conducted by Maastricht University. VieCuri Medisch Centrum performs one procedure (catheter placement) and is involved in sample analyses.

Intervention

The active product is a food supplement for human consumption. It contains 1.0x10^10 cfu of the probiotic strain Bifidobacterium longum NCC 2705 (BL NCC2705) premixed with a carrier which is maltodextrin. The placebo product contains only maltodextrin.
The products will be given to participants for a period of 4 consecutive days. Participants will have to ingest test products twice daily.

Study burden and risks

As this is a proof of concept study foreseeing a short-lasting administration of BL NCC 2705 to gluten sensitive subjects in symptomatic remission, participants will not receive any direct clinical benefit. However, the study targets an important unmet medical need * i.e. the persistence of symptoms in gluten sensitive subjects following a gluten-free diet * and is based on a rigorous and methodologically robust experimental approach that is expected to provide solid evidence on the mechanism of action of the product. This will be instrumental to the optimization of the subsequent phases of the clinical development plan.

Based on the nature of BL NCC 2705 (healthy infant-derived probiotic) and on the conclusion of the internal Nestlé Research Center safety evaluation (see Investigators* Brochure), no significant safety concern is expected from a short-term exposure to the investigational product (2 cycles of 3 and * days per subject of, respectively, active product or placebo in a cross-over design).
During the entire duration of the study all the adverse events will be thoroughly collected and reported. In addition, gastrointestinal tolerability will be explored through a self-assessment tool constituted by visual analogue scales measuring the intensity of possible gastrointestinal symptoms.
As part of the experimental model, two single administrations of gluten (one per treatment cycle) are foreseen to the purpose of assessing the effects of the investigational product on gluten digestion. This acute exposure to gluten is not expected to be harmful to the subjects because a) a low dose will be used (i.e. 3g, which is within the amount conventionally considered as gluten-contamination and b) the two administrations will be made with a minimum of 18 days apart. It has been shown that many days or weeks of continuous intake of even higher doses are needed to re-activate the clinical, histological and serological manifestations of gluten intolerance.
The experimental technique foresees the positioning of a naso-duodenal catheter that will stay in place for 7 to 8 hours. Each subject will undergo this procedure twice. The catheter position can be controlled under direct endoscopic view or by fluoroscopic assessment following the procedure. Both options will be proposed and discussed with the subjects. Endoscopy is a routine and well standardized medical procedure that can cause some discomfort but is devoid of any relevant complications.

Although there's no direct benefit for the participants, the benefit/risk assessment is judged as overall favorable in light of the low likelihood of relevant safety issues, the robustness of the experimental design and the relevance of the evidence that the study is expected to generate in terms of potential contribution to addressing an important unmet medical need.

Contacts

Public
Nestec

Avenue Nestle 55
Vevey CH-1800
CH
Scientific
Nestec

Avenue Nestle 55
Vevey CH-1800
CH

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Willing and able to sign written informed consent prior to trial entry
2. Male or female adults at a minimum age of 18
3. For NCGS: self-reported gluten sensitivity on gluten free diet for at least 6 weeks with self-reported significant symptomatic improvement
4. For CD: confirmed serologic and histologic diagnosis of CD and on GFD for at least 12 months with self-reported significant symptomatic improvement
5. Body Mass Index (BMI) within the range 18 * 30 kg/m2
6. Willing and able to comply with study procedures and restrictions
7. In good health as determined by a medical history and medical examination

Exclusion criteria

1) Documented IgE-mediated food allergy
2) Subjects following an overly imbalanced or restrictive diet as per nutritional advice
3) Concurrent systemic disease and/or laboratory abnormalities considered by investigators to be detrimental for the participants safety or potentially interfering with the study procedures and/or study outcomes
4) Concurrent organic GI pathology other than benign polyps, diverticulosis, hemorrhoids, lipomas and melanosis coli
5) Previous abdominal surgery with the exception of hernia repair, appendectomy, caesarian section, tubal ligation, hysterectomy, hemorrhoidectomy
6) Patients who received antibiotics in the previous 2 weeks
7) women of childbearing potential not willing to use an effective contraception method

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-11-2018
Enrollment:	32
Type:	Actual

Ethics review

Approved WMO Date:	26-10-2018
Application type:	First submission
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	08-11-2018
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	19-03-2019
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCTnrzalbinnen2wekenwordentoegewezen
CCMO	NL65701.072.18

Study results

Date completed:	19-08-2019
Actual enrolment:	38