The safety and gastro-intestinal tolerance of recombinant human lactoferrin (rhLF) in apparently healthy human volunteers

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To study the safety and digestive tolerance of recombinant human Lactoferrin (rhLF) as expressed in milk of transgenic cattle.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal motility and defaecation conditions
Study type	Interventional

Summary

ID

NL-OMON34362

Source
ToetsingOnline

Brief title
Safety and gastro-intestinal tolerance of rhLF

Condition

- Gastrointestinal motility and defaecation conditions

Synonym
gastro-intestinal tolerance, gut health

Research involving
Human

Sponsors and support

Primary sponsor: Pharming Group
Source(s) of monetary or material Support: Pharming Technologies B.V.

Intervention

Keyword: gastro-intestinal tolerance, lactoferrin, safety

Outcome measures

Primary outcome

Main study parameters are clinical laboratory and gastro-intestinal tolerance

as measured by questionnaires.

Secondary outcome

Secondary parameters are human lactoferrin (hLF) in faeces and blood, and

anti-hLF antibodies in blood

Study description

Background summary

Lactoferrin is a natural human protein which was first isolated from human milk in 1960. Lactoferrin is a major iron-binding protein, and it is synthesized by glandular epithelial cells. Lactoferrin is secreted not only into milk, but also in tears, saliva, mucous, nasal fluids, pancreatic-, bronchial-, gastrointestinal-, and reproductive tissue secretions(6) as well as in the secondary granules of neutrophils.

The properties of lactoferrin have been extensively studied, both in vitro and in vivo, demonstrating the involvement of lactoferrin in the innate host defense against infection and severe inflammation, most notably at mucosal surfaces such as those of the gastro-intestinal tract. The diverse functions not only relate to its binding of iron, but also binding to a variety of ligands and interactions with specific receptors. Lactoferrin has been proposed as potential treatment for a vast array of indications, among others, related to its antimicrobial and iron-scavenging properties.

At the moment no human lactoferrin is commercially available. Therefore substitutes have been developed in the market. In the 1990-ies, dairy companies have been purifying and developing bovine lactoferrin as a functional food ingredient. Only breast fed infants have availability of human lactoferrin of natural origin. Pharming has developed a recombinant hLF (rhLF), which is

expressed in milk from transgenic cattle.

Study objective

To study the safety and digestive tolerance of recombinant human Lactoferrin (rhLF) as expressed in milk of transgenic cattle.

Study design

The study is designed as a randomized, placebo-controlled, multiple dose, double-blind, cross-over study. Twenty-four apparently healthy male and female volunteers will participate in the study.

Group screen 2-week Period 1 2-week Period 2 2-week Period 3 ca. 4 week

Follow-up
A (n=4) Placebo 300 mg 1000 mg
B (n=4) 300 mg 1000 mg Placebo
C (n=4) 1000 mg Placebo 300 mg
D (n=4) 1000 mg 300 mg Placebo
E (n=4) Placebo 1000 mg 300 mg
F (n=4) 300 mg Placebo 1000 mg

Intervention

Intervention 1: 300 mg recombinant humaan lactoferrine with skimmed milkpowder
Intervention 2: 1000 mg recombinant humaan lactoferrine with skimmed milkpowder
Intervention 3: placebo = skimmed milkpowder

Study burden and risks

A healthy volunteer will not experience any benefits from participating in this study. However, by participating in this study, knowledge is acquired on the safety of rhLF in humans.

We ask the subjects to consume a milk drink (ca.100 ml) for 6 weeks. This is in accordance with dietary habits of the Dutch population, therefore the burden of consuming this milk drink for the subjects is considered to be very small. The in-study actions (blood sampling, collecting faeces, filling in questionnaires) are not unusual and financial compensation is tuned to these actions.

No risks are known to us by participating to this study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Healthy as assessed by the
- TNO health and lifestyle questionnaire, (P8896 F02; in Dutch)
- results of the pre-study safety laboratory tests
2. Volunteers aged > 25 and < 50 years at Day 01 of the study (gender distribution ideally 50%-50%, must not exceed 40%-60%)
3. Body Mass Index (BMI) 18-28 kg/m2
4. Regular and normal Dutch eating habits as assessed by P8896 F02
5. Voluntary participation
6. Having given written informed consent
7. Willing to comply with the study procedures
8. Willing to accept use of all encoded data, including publication, and the confidential use and storage of all data for at least 15 years

9. Willing to accept the disclosure of the financial benefit of participation in the study to the authorities concerned.

Exclusion criteria

1. Participation in any clinical trial including blood sampling and/or administration of substances up to 90 days before Day 01 of this study
2. Participation in any non-invasive clinical trial up to 30 days before Day 01 of this study, including no blood sampling and/or oral, intravenous, inhalatory administration of substances
3. Having a history of medical or surgical events that may significantly affect the study outcome
4. Frequent and/or intense sports practice (more than 10 hours/week)
5. Smoking
6. Alcohol consumption > 21 units/week for males and > 14 units/week for females.
7. Any history of any allergy, sensitivity or anaphylaxis, especially if related (but not limited) to food products (e.g. chocolate, wheat, dairy products, or milk-derived products, egg, nuts, etc.) and seasonal allergy (e.g. hay fever)
8. Current or intermittent gastro-intestinal complaints (stomach upsets, diarrhoea, constipation, flatulence, abdominal colic, etc.), or any known gastro-intestinal disorder (e.g. ulcerative colitis, Crohn*s disease)
9. Reported unexplained weight loss or gain of > 2 kg in the month prior to the pre-study screening
10. Use of antibiotics or laxatives within 1 month before day 01 of the study
11. Reported slimming or medically prescribed diet
12. Reported vegan, vegetarian or macrobiotic
13. Pregnant or lactating female or wishing to become pregnant in the period of the study
14. Females not using acceptable contraception
15. Recent blood donation (<1 month prior to the start of the study)
16. Not willing to give up blood donation during the study.
17. Personnel of TNO Quality of Life location Zeist, their partner and their first and second degree relatives
18. Not having a general practitioner
19. Not willing to accept information-transfer concerning participation in the study, or information regarding his/her health, like laboratory results, findings at anamnesis or physical examination and eventual adverse events to and from his general practitioner.

Study design

Design

Study type: Interventional

Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-10-2011
Enrollment:	24
Type:	Actual

Ethics review

Approved WMO

Date:	22-04-2010
Application type:	First submission
Review commission:	METC Brabant (Tilburg)

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
CCMO	NL32013.028.10