ISRCTN12387189 https://doi.org/10.1186/ISRCTN12387189

Acceptability and tolerability of a new phe-free protein substitute for the dietary management of patients with phenylketonuria

Submission date
20/03/2019

Recruitment status
No longer recruiting

Registration date
22/03/2019

Overall study status
Completed

Last Edited
21/01/2021

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Phenylketonuria (PKU) is an inherited disorder where the body can't break down the amino acid phenylalanine (phe), which then builds up in the blood and brain. This can lead to brain damage, organ damage and unusual posture, if not correctly diagnosed and no suitable nutritional management is started. As phe is an essential amino acid, the goal of nutritional management of PKU patients is to maintain adequate phe levels to support growth, normal brain development and mental functioning while providing a nutritionally complete diet and preventing neurological and psychological changes. Thus, patients with PKU require lifelong adherence to a low-phe diet that is restricted in natural foods, in order to limit the intake of natural protein and, at the same time, to provide adequate amounts of phe, in addition to the intake of phe-free protein substitutes to meet their protein needs. The aim of this study is to assess the acceptability and tolerability of a new protein substitute for the nutritional management of patients with phenylketonuria, aged 3-16 years. The outcome of this assessment will be used in a submission to regulatory authorities to get the study product reimbursable on prescription in the UK. The study product (PKU GOLIKE PLUS 3-16) is a phe-free protein substitute for the dietary management of children with PKU, aged 3-16 years. Specifically, the study product is an amino acid mixture engineered with a modified-release technology (Physiomimic technology), containing 17 amino acids, vitamins, minerals, other nutrients and two food additives forming a coating layer. The coating can mask the typical taste and odour of the amino acids. This coating is also able to provide a gradual release (prolonged release over time) of the amino acids from the formulation, in order to mimic more closely the absorption of amino acids from natural protein intake from food.

Who can participate?
Male and female patients with PKU, aged 3-16, who are already taking a protein substitute in addition to appropriate nutritional management.

What does the study involve?
At the first visit, participants are asked to replace their protein substitute with the study product (PKU GOLIKE PLUS 3-16). The treatment with the study product lasts for 7 days. As the study

product contains vitamins and minerals, no supplementation is required. The last visit takes place at the end of the treatment period (day 7). During this time, caregivers are asked to complete a daily questionnaire recording information on patient's compliance and any issues with administration and any gastro-intestinal side-effects. Additional questions are completed at the end of the study that consider perceptions about taste, appearance, smell, presentation and packaging of the product, ease of administration, and how it is taken. At both visits, participants are asked to undergo routine biochemical blood spot testing for phenylalanine and tyrosine in fasting conditions, for measuring blood phenylalanine levels. In the study, the product prescription is specified on an individual basis by the metabolic dietitian responsible for the patients' nutritional management and is dependent on age and weight of the patient, but wholly replaces their currently prescribed protein substitute.

Where are the possible benefits and risks of participating?
A lot of protein substitutes are already available. However, compliance with taking protein substitutes continues to be a challenge. As a low protein diet is recommended for life, long-term compliance is a growing concern. As a result, improving the choice in terms of product type may aid compliance.
For PKU patients, this phe-free amino acid mixture engineered with a modified-release technology (Physiomimic technology), PKU GOLIKE PLUS 3-16, can represent a new option for the dietary management of this metabolic disease. Due to the coating covering the amino acids, the typical taste and odour of the amino acids are masked, and the release and consequent absorption of the amino acids is prolonged over time, to mimic more closely the absorption of amino acids from natural protein intake from food. These aspects, together with the opportunity to take this new protein substitute with non-hot beverages and foods with a creamy consistency as well, without modifying the taste of natural food, could improve patients' compliance and adherence to diet and the whole nutritional management of PKU patients.
Potential risks of the study may include refusal to take the product resulting in higher levels of phenylalanine (phe) in their blood. However, this risk will be minimised as the patient will be monitored clinically. If participants refuse to take the product for 24 hours, they will return to their normal protein substitute (i.e. the one used before entering the study) to ensure no harm is done to the child. Occasionally, different protein substitutes may cause abdominal pain, vomiting or diarrhoea, particularly if not taken with sufficient fluid. If there are any problems with tolerance children can stop the market research at any time on request of parents /caregivers or health care professionals or at the Lead Dietitian's discretion.

Where is the study run from?
Birmingham Women's and Children NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
September 2018 to September 2019

Who is funding the study?
APR Applied Pharma Research sa, Balerna (Switzerland)

Who is the main contact?
Anna Barassi
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Contact information

Type(s)

Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
APR/MF/02/2018

Study information

Scientific Title
PKU GOLIKE PLUS 3-16 – Acceptability and Tolerance Market Research Study

Study objectives
This is a prospective, observational market research study that aims at evaluating the acceptability and tolerability of a new protein substitute for the nutritional management of patients with phenylketonuria, aged 3-16 years.
The outcome of this assessment will be used in a submission to regulatory authorities to get the study product reimbursable on prescription in the UK.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 25/06/2019, West Midlands - Solihull Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; Tel: +44 (0)207 1048191; Email: NRESCommittee.WestMidlands-Solihull@nhs.net), REC ref: 19/WM/0151

Study design
Prospective single-arm observational study

Primary study design
Observational

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Phenylketonuria

Interventions
The study product (PKU GOLIKE PLUS 3-16) is a phenylalanine-free protein substitute for the dietary management of patients with PKU, aged 3-16 years. Specifically, it is an amino acid mixture engineered with a modified-release technology (Physiomimic technology), containing 17 AAs, vitamins, minerals, other nutrients and two food additives forming a coating layer that modifies the organoleptic features of the product. The coating can indeed mask the typical taste and odour of the amino acids. This coating is also able to provide a gradual release (prolonged release over time) of the amino acids from the formulation, in order to mimic more closely the physiological absorption of amino acids from natural protein intake from food. In the study, the product prescription will be specified on an individual basis by the metabolic Dietitian responsible for the patients' nutritional management and will be dependent on age and body weight of the patient, but will wholly replace their currently prescribed protein substitute.

The study involves 8-10 patients with phenylketonuria, aged 3-16 years, who are already taking a protein substitute in addition to appropriate nutritional management.
Two visits are foreseen. At the first visit, all subjects will be asked to replace their protein substitute with the study product (PKU GOLIKE PLUS 3-16). The treatment with the study product will last for 7 days. As the study product contains vitamins and minerals, no supplementation is required. The last visit will be performed at the end of the treatment period (day 7).

During this time, caregivers will be asked to complete a daily questionnaire recording information on patient's compliance, any issues with administration, and any gastro-intestinal side-effects. Additional questions will also be completed at the end of the study that will consider perceptions about taste, appearance, smell, presentation and packaging of the product; ease of administration; and how it is taken. At both visits, subjects will be asked to undergo routine biochemical blood spot testing for phenylalanine and tyrosine, in fasting conditions, for measuring blood phenylalanine levels.

Intervention Type
Other

Primary outcome(s)
1. Product acceptability (ease of use and palatability, i.e. perceptions about taste, appearance, smell) assessed using a questionnaire at day 7, at the end of the treatment
2. Product tolerability assessed using a questionnaire collecting data about gastro-intestinal side effects (i.e. diarrhoea, constipation, nausea, vomiting, abdominal pain) on a daily basis during the 7-day treatment

Key secondary outcome(s))
1. Compliance with the study product assessed using standardized questionnaires where the actual number of intakes versus prescribed intakes are recorded on a daily basis during the 7-day treatment

2. Metabolic control evaluated by measuring fasting blood phenylalanine levels by routine biochemical blood spot testing for phenylalanine and tyrosine at the beginning and at the end of the trial

Completion date
30/09/2019

Eligibility

Key inclusion criteria
1. Male and female patients with a diagnosis of phenylketonuria, aged 3-16 years
2. Subjects who are already taking a protein substitute for PKU and are willing to try the study product for 7 days
3. Written informed consent obtained from parental caregiver

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
3 years

Upper age limit
16 years

Sex
All

Total final enrolment
13

Key exclusion criteria
1. Presence of serious concurrent illness
2. Lead Dietitian's uncertainty about the willingness or ability of the patient to comply with the protocol requirements
3. Participation in any other studies involving investigational or marketed products concomitantly or within two weeks prior to entry into the study
4. Any children having taken antibiotics over the previous 2 weeks leading up to the study
5. Children aged less than 3 years

Date of first enrolment
15/06/2019

Date of final enrolment
30/08/2019

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Birmingham Women's and Children NHS Foundation Trust
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Sponsor information

Organisation
APR Applied Pharma Research SA

ROR
https://ror.org/05c2q0q08

Funder(s)

Funder type
Industry

Funder Name
APR Applied Pharma Research SA

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available. They will be included as appendices to the Clinical Study Report (CSR) and will be submitted to the Research Committee and to ACBS. They will be available in case an inspection from an Health Authority is foreseen.

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	03/09/2020	20/01/2021	Yes	No
HRA research summary			28/06/2023	No	No