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Acceptability and tolerability of a new phe-free protein substitute for the dietary management of patients with phenylketonuria, aged ≥16 years

Submission date
09/07/2019

Recruitment status
Suspended

Registration date
10/07/2019

Overall study status
Completed

Last Edited
12/07/2022

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
This is a prospective 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 16 and over. 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 16+) is a phenylalanine (phe)-free protein substitute for the dietary management of children with PKU, aged 16 and over. 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 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.

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

What does the study involve?
Two visits are foreseen. At the first visit, all participants are asked to replace their protein substitute with the study product partially or totally (from 1 to 3 intakes/daily). 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 is at the end of the treatment period. During the 7-day treatment period at home, participants are asked to complete a daily diary by recording information on compliance (actual daily intake versus prescribed intake) and ease of use, and any gastrointestinal signs/symptoms. An Acceptability Questionnaire is also completed at Visit 2; it considers perceptions about visual appearance, smell, taste, after-taste, mouth feeling /palatability, overall liking of the product and the patient's potential interest at taking the new

product on a long-term basis. At both visits, participants are asked to undergo routine blood spot testing for phe, in fasting conditions, for measuring blood phe levels. In the study, the product prescription is specified on an individual basis by the metabolic Dietitian responsible for the participant's nutritional management and is dependent on age and bodyweight of the patient.

Where are the possible benefits and risks of participating?
A number of protein substitutes are already available, in various forms and presentations. However, patient compliance with taking protein substitutes continues to be a difficult issue and a source of growing concern in view of the fact that a low protein diet and the intake of protein substitutes are recommended for life. Poor adherence has been associated with high plasma phe levels and adverse events throughout the lifespan of PKU patients. 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 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 of the amino acids from the formulation and the consequent absorption of the amino acids in blood is prolonged over time, to mimic more closely the physiological absorption of amino acids from natural protein intake from food. These aspects, together with the opportunity to take this new protein substitute with cold/warm 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 patient's refusal to take the new protein substitute resulting in poor metabolic control (i.e. higher blood phenylalanine). However, this risk will be minimised as the patient will be monitored. If a patient refuses to take the product for 24 hours, he/she will return to the normal protein substitute (i.e. the one used before entering the study) to ensure no harm is done. Occasionally, protein substitutes may cause gastrointestinal adverse events, including abdominal pain, vomiting or diarrhoea particularly if these products are not taken with a sufficient volume of fluids. The onset of gastrointestinal signs and symptoms during the dietary management with PKU GOLIKE PLUS 16+ will be monitored during the study.

Where is the study run from?
National Hospital for Neurology & Neurosurgery, London (UK)

When is the study starting and how long is it expected to run for?
April 2019 to August 2020

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

Who is the main contact?
Nadia Giarratana
nadia.giarratana@apr.ch

Contact information

Type(s)
Scientific

Contact name

Ms Nadia Giarratana

Contact details
APR Applied Pharma Research s.a.
Via Corti 5
Balerna
Switzerland
6828
+41 (0)916957020
nadia.giarratana@apr.ch

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
265934

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
APR/MF/03/2019, IRAS 265934

Study information

Scientific Title
PKU GOLIKE PLUS 16+ – acceptability and tolerance market research study

Study objectives
Phenylketonuria (PKU) is an inherited error of metabolism caused by a deficiency in the enzyme phenylalanine hydroxylase. This enzyme converts the amino acid phenylalanine (phe) to tyrosine, another amino acid. When the enzyme is inactive or is less efficient, the concentration of phe and its metabolites in the body can build up to toxic levels which could result in mental retardation, organ damage, unusual posture, if not correctly diagnosed with neonatal screening and no suitable nutritional management is started. As phe is an essential AA, the goal of nutritional management of PKU patients is to maintain adequate plasma phe concentrations to support optimal 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.

This is a prospective 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 ≥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 22/10/2019, London - Camden & Kings Cross Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, UK; Tel: +44 (0) 20 7104 8222; Email: nrescommittee.london-camdenandkingscross@nhs.net), REC ref: 19/LO /1610

Study design
Prospective single-arm clinical study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format; please, use contact details to request a participant information sheet.

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

Interventions
The study product (PKU GOLIKE PLUS 16+) is a phe-free protein substitute for the dietary management of patients with PKU, aged ≥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 this 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 bodyweight of the patient. The new protein substitute can replace the amount of previous products patients were taking partially or totally (from 1 to 3 intakes/daily).

Two visits are foreseen. At the baseline visit (Visit 1), all subjects will be asked to replace totally or partially their protein substitute/s with the study product (PKU GOLIKE PLUS 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 (Visit 2) will be performed at the end of the treatment period.

During the 7-day period at home, patients will be asked to complete a daily diary by recording information on compliance (actual daily intake versus prescribed intake) and ease of use, and any gastrointestinal signs/symptoms. An Acceptability Questionnaire will also be completed at Visit 2; it will consider perceptions about visual appearance, smell, taste, after-taste, mouth feeling /palatability, overall liking of the product and patient's potential interested at taking the new product on a long-term basis. At both visits, subjects will be asked to undergo routine biochemical blood spot testing for phe, in fasting conditions, for measuring blood phe levels.

Intervention Type
Supplement

Primary outcome measure
1. Product acceptability (perceptions about visual appearance, smell, taste, after-taste and mouth feeling/palatability; overall liking of the study product and patient's potential interest at taking it on a long-term basis), assessed using an Acceptability Questionnaire at the end of the 7-day treatment
2. Gastrointestinal tolerance, assessed by collecting data about gastro-intestinal signs and symptoms (including abdominal discomfort/pain, diarrhoea, constipation, bloating or abdominal distension, nausea, vomiting, flatulence, regurgitation, burping) by means of a daily diary during the 7-day treatment

Secondary outcome measures
1. Compliance with the study product assessed by means of a diary 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 phe levels by routine biochemical blood spot testing for phe at the beginning and at the end of the trial

Overall study start date
01/04/2019

Completion date
30/08/2020

Eligibility

Key inclusion criteria
1. Male and female patients with a diagnosis of phenylketonuria, aged ≥16 years
2. Subjects who are already taking a protein substitute for PKU and are willing to replace at least part of their prescription with the new study product for 7 days
3. Willing and able to give a written informed consent

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
15

Key exclusion criteria
1. Presence of serious concurrent illness
2. Presence of current illnesses that could interfere with the study (for instance, inflammatory status, etc)
3. Status of pregnancy or lactation, for females
4. Likelihood that the patient will not be compliant with the protocol requirements, in the judgement of the Lead Dietitian
5. Participation in any other studies involving investigational or marketed products concomitantly or within two weeks prior to entry into the study
6. Use of antibiotics in the week prior to study entry
7. Use of sapropterin
8. Patients aged less than 16 years

Date of first enrolment
15/02/2020

Date of final enrolment
30/06/2020

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Charles Dent Metabolic Unit, National Hospital for Neurology & Neurosurgery
(University College London Hospitals NHS Foundation Trust, UCLH)
Queen Square
London
United Kingdom
WC1N 3BG

Sponsor information

Organisation
Applied Pharma Research (Switzerland)

Sponsor details
c/o Nadia Giarratana
APR Applied Pharma Research s.a.

via Corti 5
Balerna
Switzerland
6828
+41 (0)916957020
nadia.giarratana@apr.ch

Sponsor type
Industry

Website
http://www.apr.ch/

ROR
https://ror.org/05c2q0q08

Funder(s)

Funder type
Industry

Funder Name
Applied Pharma Research

Results and Publications

Publication and dissemination plan
Data of the clinical study could be published in a journal as soon as the final study report is finalized. Data could be disseminated as abstract/poster or oral presentation in international scientific congresses.

Intention to publish date
30/03/2021

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 a 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?

HRA research summary	28/06/2023	No	No