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A clinical trial to investigate two products on supporting immune function in healthy adults

Submission date
19/07/2021

Recruitment status
No longer recruiting

Registration date
10/09/2021

Overall study status
Completed

Last Edited
15/05/2023

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
Acute respiratory tract infections like influenza infect nearly one billion people and cause up to 650,000 deaths each year worldwide. The impact of the flu during the flu season, which occurs in the fall and winter, causes over 45 million days of lost work and $40 billion USD a year. To combat this, vaccination against the flu has been adopted by many countries as the gold standard for prevention. In Canada, the national influenza vaccination coverage goal is 80% of those at risk of influenza-related complications or hospitalization.
The addition of adjuvant supplements or nutritional interventions have been investigated to improve the immune response to influenza and efficacy of the influenza vaccine. A vaccine model was used to examine if prophylactic supplementation of UP360 or UP446 modulates the immune response that is induced by the immunological challenges associated with vaccines.
The objective of this study was to investigate the efficacy of the investigational product (IP), UP360 and UP446 consisting of polysaccharides and polyphenols on supporting immune function in response to influenza vaccination studied in a vaccine model, in healthy adults.

Who can participate?
Healthy volunteers between 40 and 80 years of age, inclusive, who had not yet, but were willing, to receive the influenza vaccine.

What does the study involve?
Participants are randomly allocated to receive the flu vaccine plus capsules of either one of the investigational products or placebo. Two capsules are taken per day for 56 days.

What are the possible benefits and risks of participating?
While there may be no immediate benefit to you, the results of this study will provide some of the required scientific evidence for the study products in this clinical research study.
Your participation in this study provides the research that is required to ensure the science behind the study products.
It is possible that you could have problems or side effects from the study product that nobody knows about yet. There may be unknown risk with taking the investigational product. In rare cases, allergic reactions can happen when taking study products or the Flu Vaccine. The risk is increased for people with history of allergies and could be fatal.

Where is the study run from?
KGK Science Inc. (Canada)

When is the study starting and how long is it expected to run for?
November 2020 to July 2021

Who is funding the study?
Unigen, Inc. (USA)

Who is the main contact?
Lidia Alfaro Brownwell, lbrownell@unigen.net

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Protocol serial number
Protocol Number: 21UIHU

Study information

Scientific Title
A triple-blind placebo-controlled parallel study on healthy volunteers to evaluate the immune protection of 2 dietary supplements in a 56 day period pre and post flu vaccination at 28 days.

Study objectives
The objective of this study is to investigate the efficacy of two investigational products (IPs), UP360 and UP446, on supporting immune function in healthy adults.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 02/02/2021, Advarra IRB (373 Hollandview Trail, Suite 300, Aurara ONL4G OA5, Canada; +1 877-992-4724; adviser@advarra.com), ref: Pro00049388

Primary study design
Interventional

Study design
Randomized triple-blind placebo-controlled parallel study

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Prevention of flu and flu like symptoms

Interventions
This study will enroll 75 healthy participants. One gender will not exceed 65% and that one age category will not exceed 40%. Each participant must fulfill the inclusion criteria and not meet any of the exclusion criteria as described. Subjects will be assigned to products A, B or C .
Study duration 56 days, single-center study.

Study Arm Number of Participants
UP360 + Flu Vaccine N = 25
UP446 + Flu Vaccine N = 25
Placebo + Flu Vaccine N = 25
Total N = 75

Participants will be instructed to take two capsules per day, one in the morning and one in the evening around mealtimes with food and 4-6 ounces of water for 56 days. Clinic staff will instruct participants to save all unused and open packages and return them to KGK Science Inc. for a determination of compliance. If a dose is missed participants are instructed to take the next dose as soon as possible. Participants will be advised not to exceed the required 4 capsules daily.
A randomization schedule will be created and provided to the Qualified Investigator indicating the order of randomization. Each participant will be assigned a randomization code according to the order of the randomization list generated using www.randomization.com. Enrolled participants will be randomized to the different study arms at day 0. One gender will not exceed 65% and that one age category will not exceed 40%.

Blinding and Allocation Concealment
Concealment of the allocation of study arms will be employed through the use of opaque sealed envelopes, each labeled with a randomization number. Each envelope will contain information regarding the study arm associated with each randomization number. These envelopes will be readily available for the Qualified Investigator to open in the event that it becomes necessary to know which product a participant is taking for the sake of the participant's health care. Unblinding should not occur except in the case of emergency situations. In the event that a serious adverse event occurs, for which the identity of the investigational product administered is necessary to manage the participant’s condition, the study arm assigned to the participant will

be unblinded and the investigational product identified. The Sponsor must be notified of any unblinding within 24 hours. Details of participants who are unblinded during the study will be included in the Final Report.

Intervention Type
Supplement

Primary outcome(s)
The difference in the increase in immune parameters as assessed by lymphocyte populations (CD3+, CD4+, CD8+,CD25+) and immunoglobulins (IgG, IgM, and IgA) in blood between UP360, UP446 and placebo at Day 28 and 56

Key secondary outcome(s)
1. The difference between UP360, UP446 and placebo at Day 28 and 56 in:
1.1. Number of confirmed COVID-19 infections
1.2. Impact of COVID-19 on quality of life assessed by the COVID-19 Impact on QoL Questionnaire
2. The difference between UP360, UP446 and placebo at Day 56 in:
2.1. Number of hospitalizations due to COVID-19
3. The difference in change between UP360, UP446 and placebo at Day 28 and 56 in:
3.1. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)
3.2. Hematology parameters: white blood cell (WBC) count with differential (neutrophils, lymphocytes, monocytes, eosinophils, basophils), reticulocyte count, red blood cell (RBC) count, hemoglobin, hematocrit, platelet count, RBC indices (mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and red cell distribution width (RDW)
3.3. Complement C3 and C4 proteins
3.4. Mean global severity index, as measured by area under the curve (AUC) for the Modified Wisconsin Upper Respiratory Symptom Survey (WURSS)-24 daily symptom scores
3.5. Mean symptom severity scores, as measured by AUC for the WURSS-24 daily severity symptom scores
3.6. Number of well days (defined as days scored as 0 (not sick) for the question, “How sick do you feel today?”) as assessed by the Modified WURSS-24 Questionnaire
3.7. Number of sick days (defined as days scored as any number from 1 through 7 (sick) for the question, “How sick do you feel today?”) as assessed by the Modified WURSS-24 Questionnaire
3.8. Frequency of common upper respiratory tract infection (UTRI) symptoms as assessed by the Modified WURSS-24 Questionnaire
3.9. Duration of common UTRI symptoms as assessed by the Modified WURSS-24 Questionnaire
3.10. Severity of common UTRI symptoms as assessed by the Modified WURSS-24 Questionnaire
3.11. Vitality and quality of life as assessed by the Vitality and Quality of Life (QoL) Questionnaire

Completion date
30/07/2021

Eligibility

Key inclusion criteria
1. Males and females between 40 and 80 years of age, inclusive
2. Female participant is not of child-bearing potential, defined as females who have undergone a sterilization procedure (e.g. hysterectomy, bilateral oophorectomy, bilateral tubal ligation, complete endometrial ablation) or have been post-menopausal for at least 1 year prior to

screening, or,
Females of child-bearing potential must have a negative baseline urine pregnancy test and agree to use a medically approved method of birth control for the duration of the study. All hormonal birth control must have been in use for a minimum of three months. Acceptable methods of birth control include:
• Hormonal contraceptives including oral contraceptives, hormone birth control patch (Ortho Evra), vaginal contraceptive ring (NuvaRing), injectable contraceptives (Depo-Provera, Lunelle), or hormone implant (Norplant System)
• Double-barrier method
• Intrauterine devices
• Non-heterosexual lifestyle or agrees to use contraception if planning on changing to heterosexual partner(s)
• Vasectomy of partner at least 6 months prior to screening
3. Participants who have not yet but willing to receive the influenza vaccine
4. Agrees to provide a verbal history of flu vaccination
5. Agrees to maintain current lifestyle habits as much as possible throughout the study depending on your ability to maintain the following: diet, medications, supplements, exercise, and sleep and avoid taking new supplements
6. Healthy as determined by medical history and laboratory results as assessed by Qualified Investigator (QI)
7. Willingness to complete questionnaires and diaries associated with the study and to complete all clinic visits
8. Provided voluntary, written, informed consent to participate in the study

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Women who are pregnant, breast feeding, or planning to become pregnant during the study
2. Participant has a known allergy to the active or inactive ingredients in UP360, UP446, placebo, or QIV
3. Self-reported diagnosis of COVID-19 prior to baseline
4. Unvaccinated participants with self-reported flu prior to baseline
5. Current use of prescribed immunomodulators (including corticosteroids) such as immunosuppressants or immunostimulants within 4 weeks of baseline
6. Current use of dietary supplement or herbal medicines associated with boosting or modulating the immune system.
7. Current use of specific prescribed cardiac medication or over-the-counter medication or supplements that may aggravate electrolyte imbalance as assessed by QI
8. Participation in other clinical research studies 30 days prior to enrollment will be assessed on a case-by-case basis by the QI
9. Individuals who are unable to give informed consent

10. Any other condition or lifestyle factor, that, in the opinion of the QI, may adversely affect the participant's ability to complete the study or its measures or pose significant risk to the participant

Date of first enrolment
16/02/2021

Date of final enrolment
03/05/2021

Locations

Countries of recruitment
Canada

Study participating centre
KGK Science Inc.
Suite 1440 & 1680, One London Place
255 Queens Ave
London
Canada
N6A 5R8

Sponsor information

Organisation
Unigen Inc.

Funder(s)

Funder type
Industry

Funder Name
Unigen Inc.

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request. lbrownell@unigen.net

IPD sharing plan summary

Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	24/04/2023	15/05/2023	Yes	No
Protocol file	version 4	10/02/2021	16/08/2022	No	No