Study Protocol with Statistical Analysis Plan and Informed Consent Form

Official Study Title:
Use of a Cysteine-Rich Whey Protein Isolate (Immunocal®) in Post COVID-19 Cognitive Impairment: A Controlled Clinical Trial

ClinicalTrials.gov Identifier (NCT Number):
NCT not yet assigned - Protocol Id 860013798-5

Principal Investigator:
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Study Location(s):
Cali, Colombia

Sponsor/Collaborators:
Immunotec, Inc.

Version/Date:
Protocol Version: 1.0
Date: September 16, 2025

Study Protocol with Statistical Analysis Plan

Study Design and Participants

This randomized, controlled, parallel-group trial will include subjects at least 18 years of age in Cali, Colombia, who recovered from COVID-19 infection and present with a mild-to-moderate cognitive impairment and no prior history of administration of Immunocal. Subjects with a history of cerebrovascular or cardiovascular disease and current or previous use of Immunocal will be excluded from selection. Ethical approval has been obtained from Universidad Libre's IRB, and informed consent will be secured.

Sampling and Protocol

A non-probabilistic consecutive sampling will be performed. For this study, a target sample of 120 subjects will be selected to achieve a 95% confidence level. A double-blind randomization process will be used to divide the subjects into three groups of 40 participants as follows: 1. CRWPI (Immunocal®) supplementation; 2. Structured neuropsychological rehabilitation (Neurorehabilitation), and no intervention (control).

A group of neuropsychologists with expertise on the application of cognitive tools and neuropsychological rehabilitation are responsible for the evaluation and management of the neuropsychological phase of the study. The neuropsychological rehabilitation consists of 45-minute face-to-face group sessions that will take place three times weekly for a period of 12 weeks. After 12-weeks, a neuropsychological evaluation will be completed on every subject.

The CRWPI Immunocal® (Immunotec ™) will be administered at a dose of 20 grams (2 sachets once daily) for 12 weeks consecutive months. The research team will personally deliver the Immunocal directly to subjects and will instruct them how to mix it and self-administer.

Pre-test cognitive functioning will be evaluated using the NEUROPSI attention and memory while only the NEUROPSI attention and memory will be used to assess the same cognitive domains at 12-weeks.

The main goal of the NEUROPSI Attention and Memory is to evaluate a wide spectrum of cognitive functions, including spatial, temporal and personal orientation; attention and concentration; working memory; verbal and visual memory, and executive and motor functions. The NEUROPSI Attention and Memory test considers age and schooling for the acquisition of both quantitative and qualitative data and classifies amnesic and attentional alterations in four different categories.

The 30-second sit-to-stand test (STST) is a widely used assessment designed to evaluate lower body strength and functional endurance. It measures how many full stands a person can complete from a seated position in 30 seconds, without using their arms for support. This test provides valuable insight into muscle strength and balance, making it a practical tool for monitoring physical performance and the effectiveness of interventions such as exercise programs or nutritional supplementation. The STST is often used to evaluate fatigue in lower limb and trunk muscles. This test will be performed to all available participants after the intervention period was completed.

Statistical Analysis

A data collection instrument will be designed using Excel to tabulate the information of the participants. Qualitative variables will be reported in their absolute and relative frequencies. After normality analysis, according to Kolmogorov-Smirnov procedure, quantitative variables will be expressed as median with interquartile range or as mean with standard deviation. The comparison of the two groups will be performed using the chi2 test or Fisher's exact test for qualitative variables and Student's t-test or Mann-Whitney U-test for quantitative variables. Multivariate logistic regression will be applied to evaluate the improvement in scores of the neuropsychological tests applied to compare the data between the two groups. A $p<0.05$ will be considered for statistical significance. Post hoc comparisons will be performed using Tukey's test. A p-value < 0.05 will be considered statistically significant. Randomization integrity and baseline equivalence will be checked for age and cognitive scores. Data will be analyzed using SPSS v25.

Informed Consent

Study Title:
Use of a Cysteine-Rich Whey Protein Isolate (Immunocal®) in Post COVID-19 Cognitive Impairment

Why is this study being done?
This study is being done to find out if a cysteine-rich whey protein isolate (Immunocal®) can improve memory, attention, and thinking problems in people who continue to have cognitive issues after COVID-19.

What will happen if I take part?

- You will be screened to see if you qualify for the study.
- If you join, you will be placed into one of three groups:
    1. Take Immunocal® daily for 12 weeks.
    2. Attend neuropsychological rehabilitation sessions.
    3. No intervention (observation only).
- You will have study visits at the beginning, and then at week 12.
- At each visit, your memory, attention, and physical function will be tested.

How long will I be in the study?
About 3 months.

What are the risks?

- Immunocal® may cause mild stomach upset (bloating, nausea, or diarrhea).
- You may feel tired or frustrated while completing memory or attention tests.
- There is a small risk of loss of confidentiality, but your data will be protected.

What are the benefits?

- You may notice improvements in your memory, attention, or quality of life.
- This research may help others with post COVID-19 cognitive impairment in the future.

Do I have to take part?
No. Taking part is your choice. You may leave the study at any time without penalty.

Will I be paid?
No payment is provided.

Who can I contact for questions?

- Questions about the study: Ingrid Mena – +573155414045

- Questions about your rights as a participant: Institutional Review Board – Romel Uribe +573004916435

Statement of Consent

By signing below, you are indicating that:

- You have read this consent form (or it has been read to you).
- Your questions have been answered.
- You agree to participate in this study.

Participant's Name: _____
Signature: _____ Date: _____

Person Obtaining Consent (Name & Title): _____
Signature: _____ Date: _____