

Statistical Analysis Plan

Intestinal Microbiota Transplant as a Strategy to Enhance the Resilience Capacity of the Elderly Aiming to Retain Muscular, Cognitive, and Metabolic Functions in a Stressful Environment.

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Purpose. This Statistical Analysis Plan (SAP) prespecifies the efficacy, safety, and exploratory analyses for the randomized, double-blind, placebo-controlled clinical trial evaluating intestinal microbiota transplantation (IMT) from young physically active donors in older adults. It defines the hierarchy of the registered primary outcome measures and the prespecified confirmatory primary endpoint for inferential analyses and documents the blinded pre-unblinding data review and data handling decisions undertaken while treatment allocation remained concealed.

1. Administrative information

This document prespecifies the statistical methods that will be used for the analysis of the randomized, double-blind, placebo-controlled trial of IMT versus placebo in older adults. It is intended to define the confirmatory and supportive analyses before database lock and before inspection of comparative outcome data.

This SAP is based on the approved protocol and subsequent amendments available as of the date listed on the cover page. Where the protocol contains broad objectives or multiple potential outcomes, this SAP establishes a formal hierarchy in order to preserve transparency, reduce analytical flexibility, and distinguish confirmatory analyses from exploratory analyses.

2. Study overview

- Study design: randomized, double-blind, placebo-controlled parallel-group clinical trial.
- Population: 80 older adults aged 65-84 years.
- Allocation: 1:1 to IMT from young physically active donors or matching placebo, using a block randomization method with concealed block sizes to ensure balanced allocation.
- Visits for repeated efficacy assessments: baseline, Week 4, Week 8, and Week 20 after IMT; cognition assessed at baseline, Week 8, and Week 20.
- Main scientific framework: muscular effects are prioritized, with cognitive and metabolic consequences evaluated as key downstream domains, and microbiome-related analyses used to explore biological mechanisms.

3. Analysis objectives

The primary objective is to evaluate whether IMT improves muscular function relative to placebo in older adults. Secondary objectives are to evaluate whether IMT influences frailty, cognition, metabolic/hepatic function, safety, and microbiome-related measures, and whether baseline perceived stress modifies treatment effects.

Additional analyses of biologically plausible associations may be conducted. Any analysis not explicitly listed as primary, key secondary, or secondary in this SAP will be considered exploratory and hypothesis-generating.

Outcome hierarchy

ClinicalTrials.gov lists isometric handgrip strength, the GDLAM Global Index, and safety as primary outcome measures. The prespecified inferential hierarchy defines isometric handgrip strength as the confirmatory primary endpoint, while GDLAM and safety are analysed as additional registered primary outcome domains. This hierarchy was established and documented while treatment allocation remained concealed and prior to the planned unblinding.

Prespecified inferential endpoint hierarchy

Tier	Endpoint	Primary timepoint / scale	Planned analysis
Primary	Handgrip / isometric dynamometry	Baseline to Week 20	MMRM
Registered supportive	GDLAM Global Index	Baseline to Week 20	Longitudinal mixed model
Secondary/ Supportive	Other muscular, frailty-related, cognitive, metabolic/hepatic, and safety outcomes	As specified	Domain-appropriate models
Exploratory	Microbiome and mechanistic outcomes	As specified	Exploratory analyses; FDR control where appropriate

4. Registered primary outcome measures

4.1 Isometric handgrip strength

Isometric handgrip strength is a registered primary outcome and constitutes the confirmatory primary endpoint for inferential analyses. Prior to unblinding, the participant-level outcome was defined as the highest value obtained across the two measurements from each hand. The confirmatory endpoint is the change in isometric handgrip strength from baseline to Week 20.

4.2 Functional autonomy (GDLAM Global Index)

Functional autonomy assessed using the GDLAM Global Index is a registered primary outcome. Lower GDLAM Global Index values indicate better functional autonomy. The Global Index was calculated according to the protocol-defined scoring formula.

$$GI = [[(W10 + SSP + SPP + PTS) \times 2] + SCMA]/4$$

W10: 10-meter walk test; SSP: Sit-to-stand test; SPP: Supine-to-stand test; PTS: Shirt test; SCMA: Agility test with cone circuit

A valid Global Index was derived only when all required test components were completed; otherwise, the outcome was classified as missing.

Analyses of the GDLAM Global Index will be reported as part of the registered primary outcome measures. Although prospectively registered as a primary outcome domain, it is not included in the confirmatory inferential testing hierarchy and will therefore be interpreted as a supportive analysis.

4.3 Safety

Safety is a registered primary outcome and will be evaluated in all participants included in the Safety Analysis Set. Safety endpoints include:

- Participants with at least one adverse event (AE).
- Participants with at least one serious adverse event (SAE).
- Withdrawals due to adverse events.
- Deaths.
- Treatment-related adverse events.

The safety analysis set comprised all randomized participants who received at least one dose of the blinded study intervention or placebo (n = 80). Causality assessments were performed by the study investigators while treatment allocation remained blinded and referred to the blinded study intervention rather than to the known randomized treatment assignment.

5. Inferential endpoints

5.1 Primary endpoint

The primary endpoint is the change in handgrip / isometric muscle strength measured by dynamometry from baseline to Week 20. The confirmatory estimand is the adjusted between-group difference in mean change over time, with emphasis on the contrast at Week 20.

5.1.1 Primary estimand

The primary estimand targets the effect of assignment to IMT versus placebo on isometric handgrip strength at Week 20 in all randomized participants, regardless of intervention adherence or discontinuation, consistent with a treatment-policy strategy. Handgrip measurements collected after intervention discontinuation will remain eligible for inclusion in the primary ITT analysis. Participants who withdraw consent for further data collection will contribute all data collected before withdrawal. Deaths and other intercurrent events preventing outcome collection will result in missing post-baseline measurements and will be addressed through the prespecified missing-data analyses.

5.2 Secondary and supportive endpoints

No key secondary endpoint is designated for confirmatory hypothesis testing. The GDLAM Global Index will be analysed as a registered supportive outcome. Other muscular, frailty-related, cognitive, psychosocial, metabolic, hepatic, and safety outcomes will be analysed as prespecified secondary or supportive outcomes. Results for these endpoints will be reported using effect estimates, 95% confidence intervals, and nominal p-values and will not affect the confirmatory interpretation of the primary handgrip endpoint.

5.3 Secondary muscular outcomes

- Frailty phenotype category (non-frail / pre-frail / frail).
- Lean mass and fat mass by DEXA.
- Rectus femoris thickness and pennation angle by muscle ultrasound.
- Physical activity and sleep metrics from actigraphy.
- Blood biomarkers relevant to muscular health and inflammation, including CK, skeletal muscle troponin T, IGF-1, C-reactive protein, vitamin D, TNF-alpha, IL-6, IL-1beta, and lactate.
- PBMC-based mitochondrial respiration and autophagy-related markers.

5.4 Secondary cognitive and psychosocial outcomes

- Mini-Mental State Examination (MMSE).
- Trail Making Test A and Trail Making Test B.
- Digit span forward and backward.
- Frontal Assessment Battery (FAB).
- Verbal fluency (FAS).
- Ryff psychological well-being score.
- Subjective happiness score.
- Life satisfaction score.

5.5 Secondary metabolic and hepatic outcomes

- Fasting glucose, insulin, total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, ALT, AST, and gamma-GT.
- Presence or grade of NAFLD assessed by ultrasound, if an ordinal or categorical classification is available.
- Serum MMP-9 and IL-6.
- Non-invasive hepatic fibrosis scores derived according to protocol definitions.

5.6 Safety outcomes

- Any adverse event.
- Treatment-related adverse events.
- Serious adverse events.
- Discontinuation due to adverse events.
- Solicited and unsolicited tolerability information collected during follow-up visits and scheduled contacts.

5.7 Microbiome and mechanistic outcomes

- Alpha-diversity indices and beta-diversity metrics derived from 16S or shotgun sequencing, depending on the final laboratory platform.
- Differential taxonomic and pathway abundance analyses.
- Short-chain fatty acid measurements in stool.
- Associations between microbiome-related measures and muscular, cognitive, metabolic, and stress-related outcomes.

6. Analysis populations

Analysis set	Definition	Primary use
Intent-to-treat (ITT)	All randomized participants analyzed according to assigned group, irrespective of adherence.	Primary efficacy analyses
Per-protocol (PP)	Participants randomized and treated who had no major protocol deviations considered likely to affect the primary endpoint and who had at least one valid post-baseline handgrip assessment. Major protocol deviations and inclusion in the per-protocol population will be classified during a blinded review before database lock.	Sensitivity analyses
Safety set	All participants who receive study product or placebo.	Adverse event and tolerability analyses

7. General statistical principles

- All statistical tests will be two-sided unless otherwise stated.
- The nominal type I error rate for the primary endpoint will be 0.05.
- Continuous outcomes will be summarized using mean and standard deviation or median and interquartile range, depending on distribution; categorical outcomes will be summarized using counts and percentages.
- Effect estimates will be presented with 95% confidence intervals in addition to p-values.
- Baseline comparability will be described but not formally significance-tested for the purpose of evaluating randomization success.
- Analyses will be performed primarily in the ITT population, with PP analyses treated as sensitivity analyses.
- Statistical analyses will be conducted using validated software such as R, Stata, SAS, or equivalent validated statistical platforms.

8. Covariates and baseline adjustment

The main adjusted models will include treatment group, study visit, treatment-by-visit interaction, and the baseline value of the corresponding endpoint where appropriate. Prespecified covariates for adjusted efficacy analyses will include age and sex. Education will be added for cognitive models. Baseline perceived stress score (PSS-14) will be included as a prespecified effect-modification variable in dedicated interaction models and may also be included as a covariate in supportive adjusted analyses. Additional baseline covariates may be included if clearly justified by protocol-defined measurement structure or extreme imbalance, but any such departure from the core model will be identified as supportive rather than primary.

9. Primary efficacy analysis

The primary analysis of isometric handgrip strength will use a mixed model for repeated measures (MMRM). Post-baseline handgrip strength will be modelled as the dependent variable, with fixed effects

for treatment group, study visit, treatment-by-visit interaction, baseline handgrip strength, age, and sex. Within-participant correlations will initially be modelled using an unstructured covariance matrix.

If the unstructured covariance model fails to converge, the covariance structure will be simplified according to the following prespecified sequence: first-order autoregressive and then compound symmetry. The covariance structure ultimately used and the reason for any departure from the preferred structure will be documented in the final statistical report. The primary confirmatory contrast will be the adjusted between-group difference at Week 20. Contrasts at Week 4 and Week 8 will be reported as supportive longitudinal results.

10. Secondary efficacy analyses

10.1 Registered supportive analysis: GDLAM Global Index

The GDLAM Global Index will be analysed as a registered supportive outcome using a longitudinal mixed model analogous to the primary handgrip model. Post-baseline GDLAM Global Index values will be modelled as the dependent variable, with fixed effects for treatment group, study visit, treatment-by-visit interaction, baseline GDLAM Global Index, age, and sex. The principal supportive contrast will be the adjusted between-group difference at Week 20. Contrasts at Week 4 and Week 8 will also be reported. Because lower GDLAM values represent better functional autonomy, negative adjusted treatment effects will favour the IMT group.

10.2 Muscular secondary outcomes

- Continuous muscular outcomes (DEXA measures, ultrasound parameters, actigraphy-derived quantitative metrics, biomarkers, mitochondrial respiration metrics) will be analyzed with linear mixed-effects models or generalized linear mixed models as appropriate.
- Skewed biomarker distributions may be analyzed on the log scale; geometric mean ratios or back-transformed effects will be presented when relevant.
- The frailty phenotype category will be analyzed using ordinal logistic regression with repeated-measures extension when feasible; if proportional odds assumptions are not met, multinomial or binary category-collapsing approaches may be used as prespecified fallback strategies.

10.3 Cognitive and psychosocial outcomes

- Individual cognitive test scores will be analyzed as prespecified secondary outcomes using mixed-effects models, with transformation or non-Gaussian models when warranted by score distribution or ceiling/floor effects.
- Psychological well-being, subjective happiness, and life satisfaction will be analyzed using mixed-effects models on their original or transformed scales, depending on distributional properties.

10.4 Metabolic and hepatic outcomes

- Continuous fasting metabolic variables and liver enzyme outcomes will be analyzed using mixed-effects models.
- Binary or ordinal ultrasound-derived NAFLD outcomes will be analyzed using generalized estimating equations or mixed-effects logistic / ordinal logistic models, depending on the final data structure.
- Derived fibrosis scores will be analyzed as continuous endpoints when validated as such; otherwise categorical risk classifications will be analyzed using ordinal or binary models.

10.5 Safety analyses

Safety analyses will be descriptive and comparative. The number and proportion of participants with any adverse event, treatment-related adverse events, serious adverse events, and discontinuations due to adverse events will be summarized by group. Group comparisons may use Fisher exact tests, chi-square tests, or generalized linear models with robust standard errors when estimation of risk ratios or risk differences is preferable. Safety analyses will be performed in the safety population.

11. Multiplicity control

The primary isometric handgrip strength endpoint will be tested at a two-sided alpha level of 0.05. No formal confirmatory testing hierarchy will be applied beyond the primary endpoint. The GDLAM Global Index and all other secondary outcomes will be interpreted as supportive and will be reported using effect estimates, 95% confidence intervals, and nominal p-values. Within families of related biomarkers or microbiome features, false discovery rate control using the Benjamini–Hochberg procedure will be applied where appropriate. Results from secondary and exploratory analyses will not alter the confirmatory interpretation of the primary endpoint.

12. Missing data

The primary analysis will use likelihood-based MMRM under a missing-at-random assumption. Missingness will be summarized by treatment group, study visit, and documented reason. If more than 10% of randomized participants lack the Week 20 primary outcome, a prespecified sensitivity analysis using multiple imputation by chained equations will be performed. The imputation model will include treatment assignment, baseline and available post-baseline handgrip measurements, age, sex, and variables associated with missingness. Estimates will be combined using Rubin's rules. A complete-case analysis will be presented only as a supportive sensitivity analysis and will not replace the primary ITT analysis.

13. Protocol deviations and sensitivity analyses

- A blinded protocol deviation review will classify major and minor deviations before database lock.
- A per-protocol analysis will be conducted for the primary endpoint as a sensitivity analysis.
- Additional sensitivity analyses may include alternative covariance structures, transformation of skewed outcomes, and models with additional clinically relevant baseline covariates.
- Major protocol deviations will include, at minimum: incorrect eligibility, failure to receive the assigned study intervention, major errors in intervention administration, unplanned unblinding, and violations considered likely to materially affect the primary endpoint. The final blinded classification will be completed before database lock.

14. Prespecified subgroup and effect-modification analyses

Baseline perceived stress is a prespecified effect modifier of interest. Rather than a purely post hoc subgroup analysis, the primary effect-modification analysis will incorporate baseline PSS-14 in interaction models. For the primary endpoint, a model including treatment, visit, baseline PSS-14, treatment-by-visit, treatment-by-PSS-14, visit-by-PSS-14, and treatment-by-visit-by-PSS-14 will be fit to evaluate whether the treatment effect differs according to baseline perceived stress.

A categorical supportive analysis may classify participants into lower versus medium/higher stress-anxiety groups using prespecified cut points or protocol-consistent definitions derived from PSS-14 and related scales. These subgroup analyses will be considered supportive because the trial is not powered primarily for interaction testing. Similar interaction analyses using baseline depression or anxiety scores may be performed as exploratory analyses.

15. Microbiome and mechanistic analyses

Microbiome analyses are prespecified as exploratory / mechanistic. Alpha-diversity metrics will be analyzed using mixed-effects models. Beta-diversity will be examined using appropriate distance-based approaches such as PERMANOVA with careful accounting for repeated measures where feasible. Differential abundance analyses of taxa or pathways will use methods suitable for sparse compositional microbiome data, such as ANCOM-BC, MaAsLin2, DESeq2, or other validated approaches chosen according to the final sequencing platform and preprocessing pipeline. The exact computational pipeline may depend on sequencing modality, but the inferential distinction remains fixed: these analyses are exploratory and intended to identify signatures associated with treatment response.

Associations between microbiome-derived features, short-chain fatty acids, and changes in muscular, cognitive, metabolic, or stress-related outcomes will be evaluated using correlation analyses and multivariable regression models. These association analyses are hypothesis-generating and will be clearly labeled as exploratory in any report or publication.

16. Derived variables and scoring rules

Frailty, cognitive, metabolic, and hepatic outcomes will primarily be analysed using their individual prespecified measures and original validated scoring systems. No post hoc composite score will be used for confirmatory inference. Any additional composite score developed for exploratory purposes will be fully documented, clearly identified as exploratory, and will not alter the prespecified interpretation of the primary endpoint.

Derived hepatic fibrosis scores and any binary or ordinal disease classifications will follow published formulae or protocol-defined cutoffs.

17. Interim analyses and blinding

No formal interim efficacy analysis is planned in this SAP unless explicitly mandated by an independent oversight body. Statistical programming, derivation of endpoints, and protocol deviation review should be finalized while treatment groups remain masked whenever feasible. Any unblinding prior to database lock will be documented and justified.

18. Tables, figures, and data presentation

- Participant flow will be summarized in a CONSORT-style diagram.
- Baseline characteristics will be displayed by randomized group.
- For longitudinal endpoints, plots of adjusted means with 95% confidence intervals over time will be presented.
- For microbiome analyses, diversity plots, ordinations, and differential-feature summaries will be clearly labeled as exploratory.
- All deviations from the SAP, if any, will be identified and justified in the final report.

19. Interpretation framework

The isometric handgrip strength endpoint constitutes the confirmatory inferential endpoint of this trial. The GDLAM Global Index and all other secondary outcomes will provide supportive evidence across functional, muscular, cognitive, metabolic, hepatic, and safety domains. Exploratory analyses may identify additional biological associations or treatment-responsive features, but these findings will not supersede the prespecified interpretation of the primary endpoint.

20. Pre-unblinding Data Review and Data Handling Decisions

This section documents all data review procedures, data handling decisions, and source verification activities completed while treatment allocation remained blinded and before the planned unblinding. No inferential analyses or comparisons between randomized treatment groups were performed during this review.

20.1 Data and blinding status

- Data cut-off date: 21 July 2026, 18:24 CLT
- Dataset extraction date: 22 July 2026, 11:19 CLT
- Database status: Frozen. Editing permissions in REDCap were removed before the blinded data review to preserve the integrity of the analytical dataset.

Treatment allocation remained concealed throughout the review. All descriptive summaries, graphical inspections, and data verification procedures were performed using pooled blinded data without access to treatment assignment. The randomization code remained concealed throughout the preparation, review, and approval of this Statistical Analysis Plan (Version 1.3). Following finalization and approval of this SAP, the analytical dataset will be formally locked. Treatment allocation will subsequently be unblinded, and no unblinded comparative analyses will be conducted before completion of these procedures.

20.2 Blinded descriptive review of registered primary outcome measures

Blinded descriptive summaries of the registered primary outcome measures were generated using pooled data to evaluate data completeness, potential outliers, and internal consistency while treatment allocation remained concealed and prior to the planned unblinding.

20.2.1 Primary Outcome 1 – Isometric handgrip Strength

Descriptive statistics and completeness of isometric handgrip strength measurements were reviewed across all study visits using pooled blinded data. Source verification was undertaken for observations requiring clarification before completion of the blinded review.

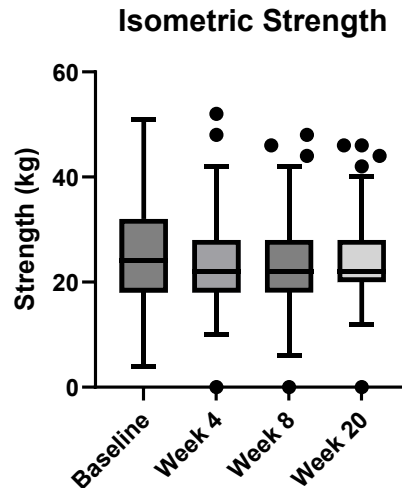
Initial data review

Descriptive statistics and boxplots were generated for all study visits.

Table 1. Descriptive statistics (raw dataset)

Variable	Baseline	Week 4	Week 8	Week 20
n	80	80	79	79
Mean $\pm$ SD	24.86 $\pm$ 8.951	24.10 $\pm$ 9.079	23.94 $\pm$ 9.062	23.87 $\pm$ 8.524
Median	24.00	22.00	22.00	22.00
Min–Max	4.0 – 51.0	0.0 – 52.0	0.0 – 48.0	0.0 – 46.0

Figure 1: Isometric handgrip strength boxplot of the raw data



Source Data verification

Values of 0 kg were not recoded solely on the basis of their numerical value. Each observation was reviewed against the original source documentation and was recoded as missing only when source verification confirmed that it represented an operational placeholder indicating that the participant was unable to complete the assessment. The original values and all subsequent changes were retained in the data audit trail.

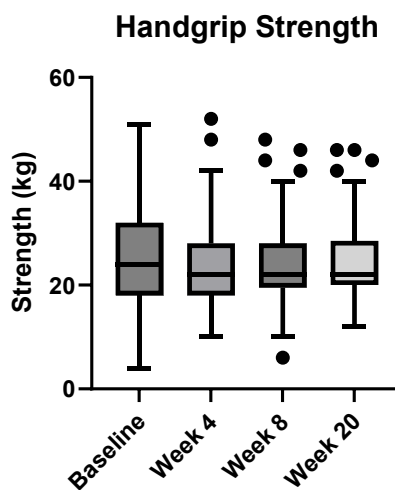
Dataset after source verification

Following source data verification, descriptive statistics and graphical inspection were repeated.

Table 2. Descriptive statistics (verified dataset)

Variable	Baseline	Week 4	Week 8	Week 20
n	80	79	78	78
Mean $\pm$ SD	24.9 $\pm$ 8.9	24.4 $\pm$ 8.7	24.2 $\pm$ 8.7	24.2 $\pm$ 8.1
Median	24.0	22.0	22.0	22.0
Min–Max	4.0 – 51.0	10.0 – 52.0	6.0 – 48.0	12.0 – 46.0

Figure 2: Isometric handgrip strength boxplot after data verification



20.2.2 Primary Outcome 2 – Global GDLAM Index

Descriptive summaries of the GDLAM Global Index were reviewed to assess completeness and consistency of the derived index. Source verification was performed for observations requiring clarification, including review of placeholder values.

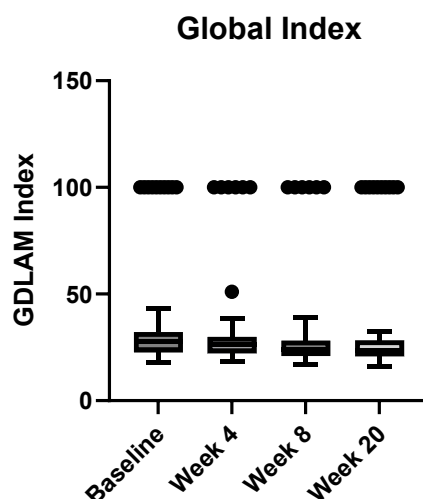
Initial data review

Descriptive statistics and boxplots were generated for all study visits.

Table 3. Descriptive statistics (raw dataset)

Variable	Baseline	Week 4	Week 8	Week 20
n	80	80	79	80
Mean $\pm$ SD	35.8 $\pm$ 24.9	31.7 $\pm$ 20.3	30.1 $\pm$ 20.7	33.1 $\pm$ 25.7
Median	28.0	26.4	24.2	23.5
Min–Max	17.7 – 100.0	18.3 – 100.0	17.0 – 100.0	15.9 – 100.0

Figure 3: Global Index boxplot of the raw data



Source Data verification

Values of 100 were not recoded solely on the basis of their numerical value. Each observation was reviewed against the original source documentation and was recoded as missing only when source verification confirmed that it represented an operational placeholder indicating that the participant was unable to complete the assessment. The original values and all subsequent changes were retained in the data audit trail

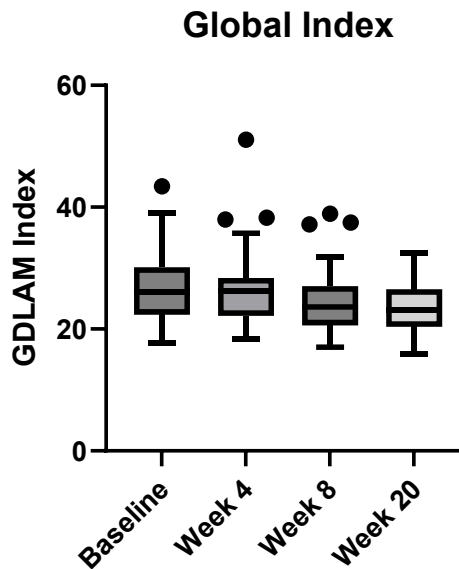
Dataset after source verification

Following source data verification, descriptive statistics and graphical inspection were repeated.

Table 4. Descriptive statistics (verified dataset)

Variable	Baseline	Week 4	Week 8	Week 20
n	70	74	73	70
Mean $\pm$ SD	26.7 $\pm$ 5.3	26.2 $\pm$ 5.5	24.3 $\pm$ 4.6	23.5 $\pm$ 4.1
Median	26.1	26.3	23.7	23.1
Min–Max	17.7 – 43.4	18.3 – 51.1	17.0 – 38.9	15.9 – 32.5

Figure 4. Global index boxplot after data verification



20.2.3 Primary Outcome 3 – Safety

Safety data were reviewed descriptively using pooled blinded data. The review included the number of participants with at least one adverse event (AE), serious adverse events (SAEs), withdrawals due to adverse events, and deaths. Causality assessments remained blinded throughout the review.

Initial data review

Descriptive summaries of all safety outcomes were generated using pooled blinded data. The review included the frequency and characteristics of adverse events, serious adverse events, withdrawals due to adverse events, and deaths.

Source data verification

Prior to unblinding, the safety database underwent a comprehensive quality review to verify:

- Participant identification
- Event description
- Date of onset
- Date of resolution (if applicable)
- Severity classification
- Seriousness classification
- Causality assessment
- Outcome status
- Consistency with the original source documentation

All reported adverse events were cross-checked against the original source documents to confirm the accuracy and completeness of the safety database.

Verified safety database

Table 5. Overall safety summary prior to unblinding

Variable	Value
Individuals screened/consented	80
Participants randomized	80
Participants receiving at least one dose	80
Participants included in the safety analysis set	80
Participants with ≥ 1 AE	60/80, 75.0%
Participants with ≥ 1 SAE	2/80, 2.5%
Participants who discontinued study intervention due to an AE	0/80
Participants withdrawn due to an adverse event	0/80
Deaths	0/80

Table 6. Relationship of adverse events to study intervention

Relationship	Number of events
Probably related	18
Possibly related	11
Not related	67

The safety analysis set comprised all randomized participants who received at least one dose of the blinded study intervention or placebo (n=80).

Causality assessments were performed by the study investigators while treatment allocation remained blinded and referred to the blinded study intervention rather than to a known randomized assignment. The causality assessment performed by the study investigators determined that none of the serious adverse events were related to the study intervention.

No changes affecting adverse event classification, seriousness, severity, causality, or outcome were made following source data verification.

20.3 Data handling decisions

Table 7 summarizes all placeholder values identified during the blinded data review and the corresponding recoding decisions following source data verification. No values were recoded solely on the basis of their numerical value. Each observation was individually reviewed against the original source documentation before any recoding decision was made.

Table 7: Summary of data recoding following source data verification

Outcome	Visit	Raw non-missing n	Placeholder values recoded	Verified non-missing n
Isometric handgrip	Baseline	80	0	80
Isometric handgrip	Week 4	80	1	79
Isometric handgrip	Week 8	79	1	78
Isometric handgrip	Week 20	79	1	78
GDLAM	Baseline	80	10	70
GDLAM	Week 4	80	6	74
GDLAM	Week 8	79	6	73
GDLAM	Week 20	80	10	70

21. Deviations from the SAP

No deviations from the prespecified SAP were introduced as a result of the blinded data review.

22. Signatures and document control

This Statistical Analysis Plan was finalized and approved before database lock and before any unblinded comparative analyses were undertaken. Following approval, the analytical dataset will be formally locked and treatment allocation will subsequently be unblinded. The final document will be archived and publicly disclosed as applicable.

Role	Name	Date
Prepared by	Camila Astudillo-Guerrero, PhD CINUT & INTA-Universidad de Chile	26.07.2026
Approved by	Gonzalo Jorquera Olave, PhD CINUT & INTA-Universidad de Chile	27.07.2026