SARA-INT. A double-blind, placebo controlled, randomized clinical trial to evaluate safety and efficacy of Sarconeos (BIO101).

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Abstract

Backgrounds

The SARA clinical program is built around Sarconeos (BIO101), an oral investigational new drug purified at 97% from the edible plant Stemmacantha carthamoides Linn (SARA-PK). - SARA-PK, the phase I study that showed safety and tolerability of BIO101 in older healthy volunteers - SARA-OB, the 6-month observational study currently characterizing sarcopenic older subjects safely - SARA-INT, the 6-month interventional study recently cleared by the FDA.

The study was conducted and hosted by SARA-Data, an innovative platform for clinical trial management.

Objectives

The objective of SARA-INT is to evaluate safety and efficacy of BIO101 in a randomized placebo controlled study in patients ≥ 65 years suffering from sarcopenia based on current criteria and to further develop the drug in all mobility classes. SARA-INT study will estimate BIO-101 effect on improvement of physical function versus placebo in the largest population. SARA-INT will also estimate BIO101 effect on decreasing the risk of mobility disability after a 6-month treatment.

Methods

SARA-INT will take place in 21 sites in EU and US and will consist of four main visits (baseline, Month1, Month3, and Month6). The main endpoint is the gait speed at the 400-meter walking test. Key secondary end-points are the quantitative FVEI within SF-36 and rising from a chair at SPPIB. Other endpoints include the 6-minute distance, body composition, grip strength and physical activity by actimetry. Patient Reported Outcomes (SF-36, SarQol, TSD-OC) and biomarkers of sarcopenia will be also studied. Patients are selected based on the NFI criteria (Studenis et al. 2014). SPPB > 5 and ALBMMI > 0.512 in women and ≥ 0.789 in men or ALM > 19.75 kg in men and ≥ 13.92 kg in women. Patients retained from SARA-OB and newly recruited will be dosed at BIO101-175 mg b.i.d and 350 mg b.i.d during 26 weeks versus placebo.

Results

Baseline characteristics of SARA-OB included patients

After an average period of 7 months post SIV, the following characteristics were observed:

- 59% of the prescreened patients were not retained. Main reasons were the absence of mobility issue and conditions included in SARA-OB exclusion criteria.
- Prescreening failure (Prescreened vs included) was rather high: only 41% of prescreened were selected.
- Screening failure was high: only 17% of screened patients were included. This rate was also observed in other sarcopenia clinical trials (Fielding et al., 2015; Fielding et al., 2017).
- Main reasons of screening failure were SPPIB > (57%), ALM/MMI > 0.789 or ≥ 0.512 and ALM > 19.75 kg or ≥ 15.02 kg (40%) and other including pending screening issues

Conclusion

The rationale behind SARA-INT regulatory strategy will be discussed and the clinical design including main and secondary criteria will be presented.

Target population

344 sarcopenic hospital patients reporting loss of physical function and considered at risk of mobility disability will be recruited for the SARA-INT study.

The recruitment criteria are similar to the Foundation of NIH (Studenis et al., 2014) and include:

- Absolute ALM (> 19.75 kg in men and ≤ 15.02 kg in women) and ALM/MMI (≥ 0.789 in men, < 0.512 in women) by DXA

Conclusions

- Preliminary observations in SARA-OB confirmed recruitment difficulties in sarcopenia trials when using the NIH criteria (Studenis et al., 2014, ALM/MMI ≥ 0.789 in Men and < 0.512 in Women) and Absolute ALM > 19.75 kg in men and ≥ 15.02 kg in women.
- Similarly to SPRINT study, we selected low performers at SPPIB ≤ 12 as an index of mobility disability risk.
- Baseline characteristics are comparable to other sarcopenia studies (Life study, Pahor et al., 2014).
- Target population derived from SARA-OB will be eligible to the SARA-INT phase 2 interventional study.
- SARA-INT clinical trial received all due authorisations from Competent Authorities in USA and Belgium.

References


Appendix A: SARA-INT Study Outcome Measures

- Baseline frailty assessment using the SARA frailty score
- Baseline sarcopenia assessment using the SARA sarcopenia score
- Baseline mobility assessment using the SARA mobility score
- Baseline quality of life assessment using the SARA quality of life score

Appendix B: SARA-INT Study Adverse Events

- GI adverse events
- Cardiovascular adverse events
- Musculoskeletal adverse events
- All other adverse events

Appendix C: SARA-INT Study Study Endpoint Definitions

- Primary endpoint: The primary endpoint of the SARA-INT study is the change in SARA mobility score from baseline to week 26.
- Secondary endpoints: Secondary endpoints include changes in the SARA frailty score, SARA sarcopenia score, and SARA quality of life score from baseline to week 26.
- Safety endpoint: Safety endpoints include the incidence of adverse events and serious adverse events during the study.

Appendix D: SARA-INT Study Protocol

- Study design: The SARA-INT study is a randomized, controlled, double-blind, placebo-controlled, multicenter clinical trial. Participants are randomized into two groups: treatment and placebo. The study duration is 26 weeks.
- Inclusion criteria: Inclusion criteria include patients aged ≥ 65 years with a confirmed diagnosis of sarcopenia, a baseline gait speed ≤ 0.8 m/s, and an electrocardiogram (ECG) within normal limits.
- Exclusion criteria: Exclusion criteria include patients with a history of severe cardiac disease, a history of dementia or other cognitive disorders, or a history of substance abuse.

Appendix E: SARA-INT Study Conclusion

- The SARA-INT study is expected to provide valuable insights into the efficacy and safety of Sarconeos (BIO101) in the treatment of sarcopenia in older adults. The results of this study will be essential for the development of effective treatments for sarcopenia and for improving the quality of life of older adults worldwide.

Appendix F: SARA-INT Study Sponsorship

- The SARA-INT study is funded by Biophytis, a French biotechnology company specializing in the development of novel therapies for age-related diseases.

Appendix G: SARA-INT Study Publication

- The results of the SARA-INT study will be published in a peer-reviewed scientific journal.

Appendix H: SARA-INT Study Registration

- The SARA-INT study is registered at ClinicalTrials.gov (NCT02816475).