SARA Clinical program for evaluating safety and efficacy of Sarconeos in a Phase 2b clinical trial

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Abstract

Introduction

Sarcopenia is a key underlying cause of physical frailty, a reversible condition in older subjects, which may lead to mobility disability and dependency. Sarcopenia is characterized by the loss of muscle mass and function. Biophyt has developed a drug candidate (Sarconeos (BIO101)) acting via McI, the Angiotensin-I receptor for treatment and prevention of Sarcopenia. McI receptor is one of the principal targets of the Remi-Angiotensin System.

Methods

SARCAROLS Clinical study design

Sarcopenia is defined according to the criteria of the Foundation of NIH (Studenski et al., 2014). The risk of mobility disability is operationalised using the Short Physical Performance Battery (SPPB; Guralnik et al., 1994) • Short 6/12
• Absolute ALM (% 19.75 in men and % 15.02 in women)
• ALM/BMI (% 19.75 in men and % 15.02 in women) measured by DXA.

Main objective

Characterise the target population in Europe and USA
• Estimate the prevalence of sarcopenia including sarcopenic obesity in a sample of older persons with poor physical function.

Secondary endpoints

Body composition: Gait speed; Grip strength; 6 minutes walk

End-Points exploratories

Absolute SPPB, ALM, ALM/BMI, SARA (Myostatin; PIINP; IL-6; HscCGRP; Aldosterone; Renin; Isolated PBMC, etc.)

Results

SARA- OBS Workflow

• 61% of the prescreened patients were not retained. Main reasons were disease of the exclusion criterion, the absence of mobility issues.
• Prescreening failure (Prescreened vs included) was rather high: only 49% of the prescreened patients were included.
• Screening failure was high: only 15% 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 SPPB=8 (61%); ALM/ BMI > 19.75 or < 15.02 kg/m2 (24%) and Other: 30%.

Baseline characteristics of SARA included patients

After an average period of 4 months post SIV, the following characteristics can be outlined:

Conclusions

Target population

Sarconeos 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 (Studenski et al., 2014)
• SPPB 6/12
• Absolute ALM (> 19.75 kg in men and ≤ 15.02 kg in women)
• and ALM/ BMI (≥ 19.75 in men, < 0.512 in women) measured by DXA

References

Primary objectives:

• To evaluate the impact of two daily doses of BIO101 versus placebo on gait speed at the 400m test.

Key secondary objectives

• To compare the change from baseline of the Patient Reported Outcome (PRO): The Physical Function Domain (PF-10) of the Short Form Health Survey (SF-36).
• To Rising from a chair

Other Secondary, Tertiary and Exploratory Objectives

Body composition; Muscle strength; stair climbing; SPPB; PRO (SF-36, SarQol, TSD-CC); Actimetry; Biomarkers (Myostatin; PIINP; IL-6; HscCGRP; Aldosterone; Renin; Isolated PBMC, etc.)

SARA-INT clinical study design

• SARA-INT is an EU and US double-blind, placebo controlled, randomized INterventional Clinical trial.
• SARA-INT aims to examine the safety and efficacy of Sarconeos (BIO101), the investigational drug orally administered for 6 months.
• SARA-INT is being performed in campaigns of 7 country regions, i.e. 21 sites.
• Most of the sites are currently recruiting in SARA-OBS, and Additional sites are currently being selected

SARA OBS included patients

After an average period of 4 months post SIV, the following characteristics can be outlined:

Conclusions

• Preliminary observations in SARA-OBS confirmed recruitment opportunities in some European countries (EWGSOP criteria: Studenski et al., 2014; ALM/BMI≤19.75 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 accepted the challenge to select low performers at SPPB<6 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-OBS will be eligible to be investigated in the drug candidate Sarconeos (BIO101) in the SARA-INT phase 2 interventional study.

• As seen in other large sarcopenia clinical trials, patients showed high BMI.
• 400 m gait speed was equivalent to the Life study (0.83 m/s at baseline Pahor et al., 2014).
• Mean SPPB is rather low (6.57/12), corresponding to patients at risk of mobility disability and comparable to other sarcopenia studies (The Life study with 7.4±1.6 in the physical activity group, Pahor et al., 2014).
• Gait speed SPPB is <0.8 m/s, fitting with the definition of sarcopenia from the EWGSGOP.
• ALM/ BMI in men was lower than the FINN threshold (0.66 vs. 0.79%) and similar in women (0.49 vs. 0.52).
• The 0.6mGD at 314.86 meters was expected for patients of the mean age (78.65 years) and BMI (30.78)

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