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LIVE HEALTHIER LONGER

BIO101 + GLP-1RA to prevent potential muscle loss in patients with overweight and obesity: the OBA study

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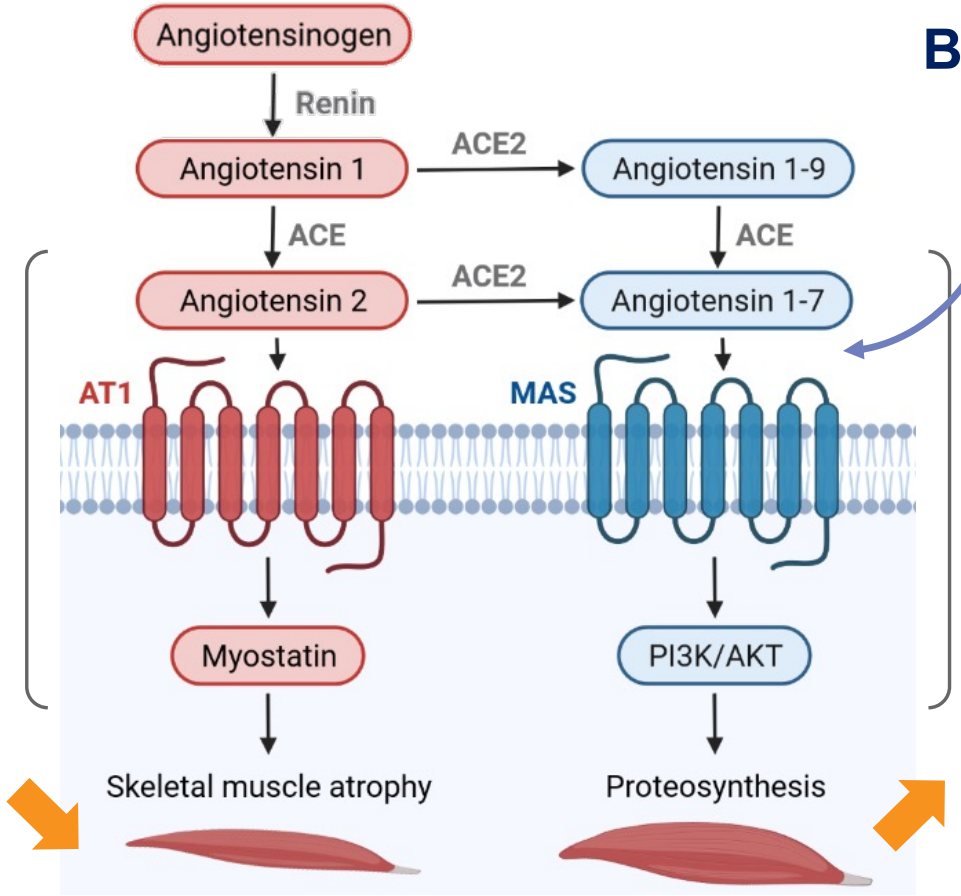
SCWD 2024, Washington DC, USA

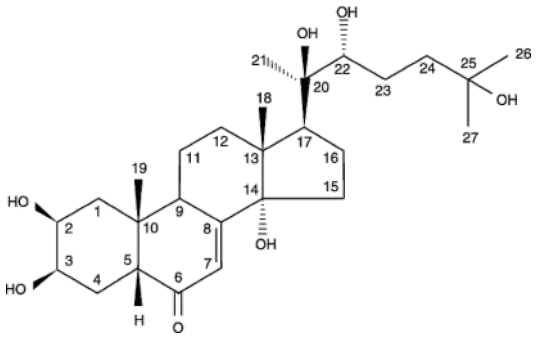
BIO101, a MAS receptor activator with beneficial effect on muscle



Classical arm

Protective arm

BIO101 / 20E



Ecdysteroids = class of steroid hormones

> J Mol Endocrinol. 2021 Dec 23;68(2):77-87. doi: 10.1530/JME-21-0033.

20-Hydroxyecdysone activates the protective arm of the RAAS via the MAS receptor

René Lafont [1,2], Maria Serova [1], Blaise Didry-Barca [1], Sophie Raynal [1], Louis Guibout [1], Laurence Dinan [1], Stanislas Veillet [1], Mathilde Latil [1], Waly Dioh [1], Pierre J Dilda [1]

Affiliations + expand

PMID: 34825653 DOI: 10.1530/JME-21-0033

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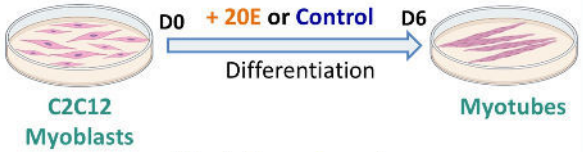
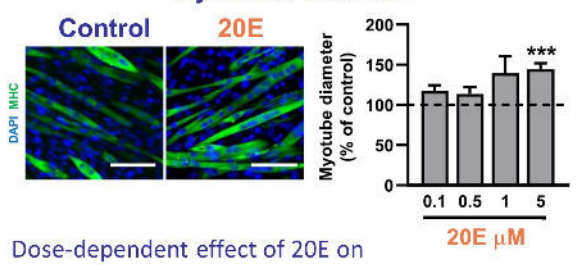
Preclinical 20E efficacy data in myocytes, old mice and HFD mice

20E effects on myocytes

In vitro 20E has pro-differentiating effects in murine and human myocytes, increasing myotubes diameter

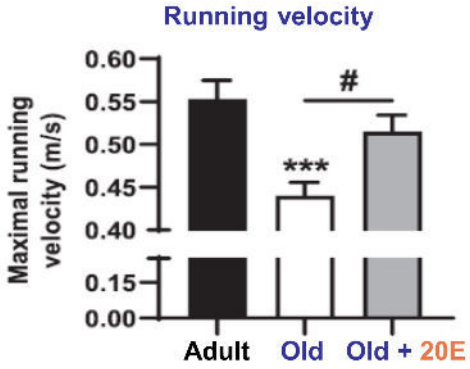




Dose-dependent effect of 20E on myoblast differentiation (fusion index, number of nuclei per myotube and myotube diameters)

20E on muscular activity in old mice

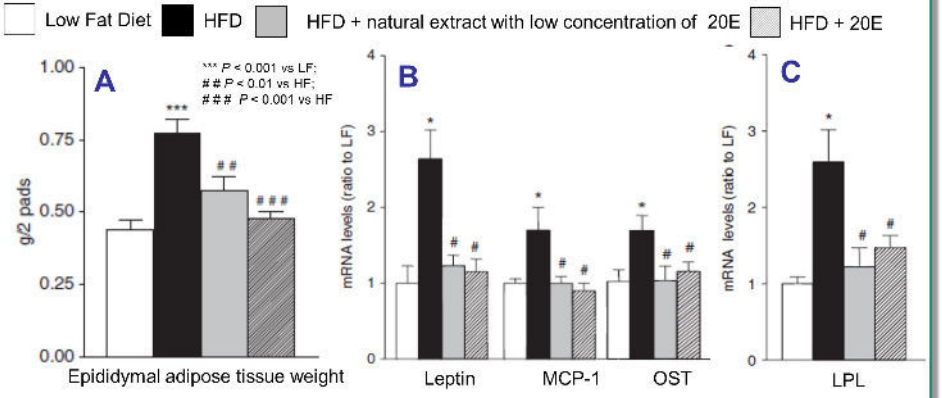
In vivo, 20E improved muscle function and physical capacity in old mice (Serova et al. 2024).



20E improves the in toto physical activity of old animals

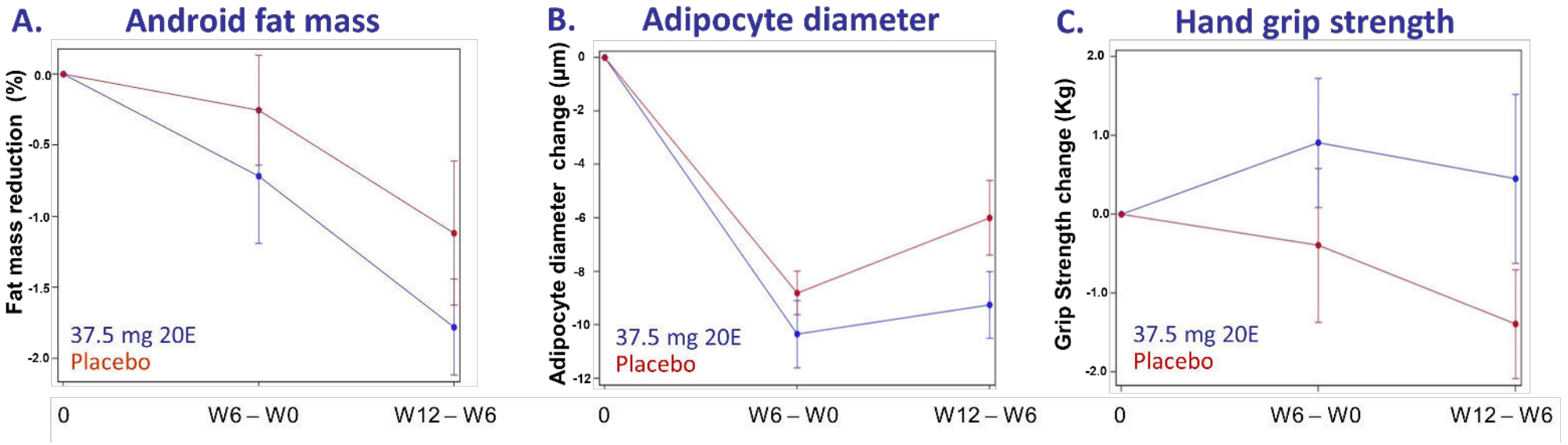
20E activity on adipocytes in high fat diet (HFD) fed mice

In HFD mice, 20E limited epididymal adipose tissue weight (**A**), reduced expression of leptin, MCP-1, and of osteopontin (OST) involved in insulin resistance (**B**) and lipoprotein lipase involved in lipid storage (**C**)



Source: Serova et al. 2024
Foucault et al. 2012

Randomized placebo-controlled study with 37.5 mg 20E in 58 subjects with obesity and overweight



Statistically significant decrease of android fat mass **(p=0.039)**

Statistically significant decrease in adipocyte diameter **(p=0.032)**

Trend for handgrip strength maintenance **in subjects who lost > 5% of their initial weight** during the weight loss phase **(p=0.097)**

W6 – W0: change in week 6 vs week 0
W12 – W6: change in week 12 vs week 6

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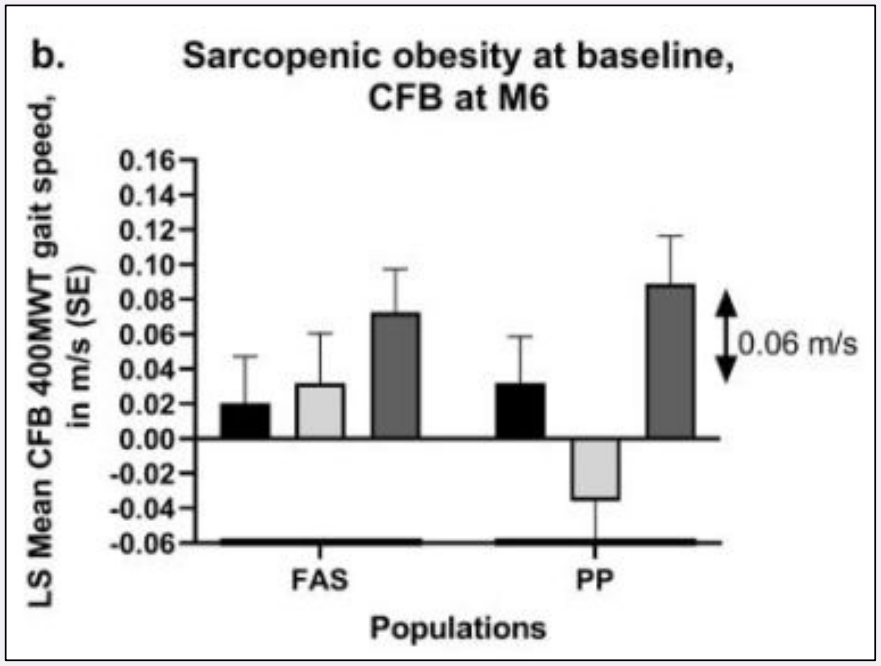
Data on file, Biophytis

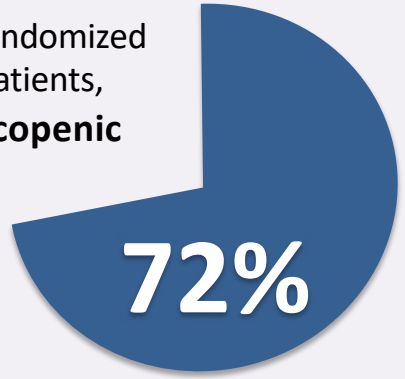
Phase 2 SARA-INT : gait speed from 400MWT in population with sarcopenic obesity

Gait speed in patients with sarcopenic obesity (% of body fat mass of >25% in men and >35% in women)



Placebo
BIO101 175 mg BID
BIO101 350 mg BID

Of the 233 randomized sarcopenia patients, 72% had **sarcopenic obesity**



⇒ **treatment was a nominally statistically significant factor in the MMRM analysis (p=0.0037) in the PP population**

MMRM: mixed effect model repeat measurement
Source : CSR SARA INT 14.2.1.13.3.1-2

BA

A Phase 2, double-blind, randomized, placebo-controlled multicenter study in 164 patients to evaluate the efficacy and safety of 20-Hydroxyecdysone (20E) in reducing the muscle strength loss from GLP1 agonists in combination with dieting in adult patients with obesity

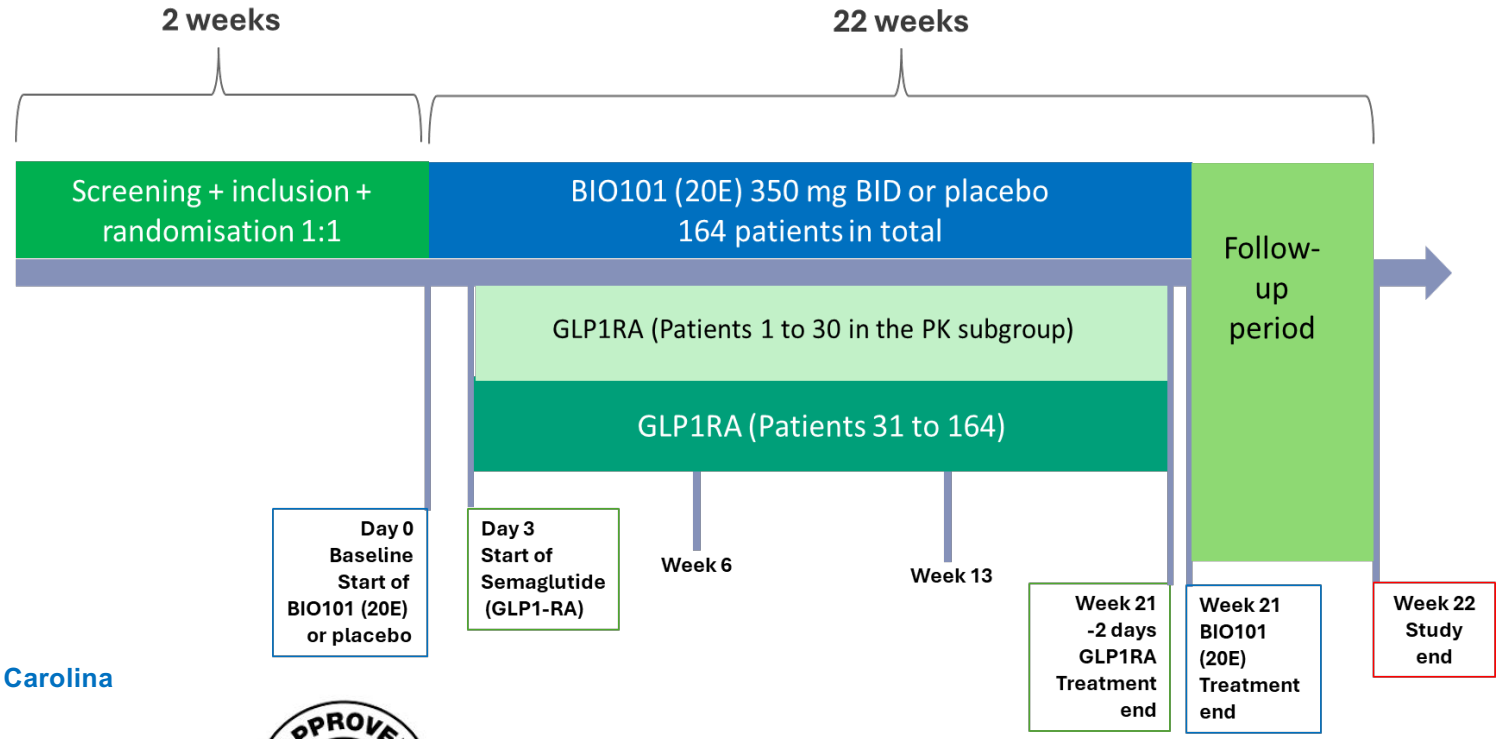
Sample size : 164 patients

Target population:

Patients with obesity (BMI ≥30) or overweight (BMI ≥27) with one or more weight-related sequalae (e.g. hypertension) who will start treatment with semaglutide a GLP-1 agonist.

Site Location :

PI: Marc-Andre Cornier
Medical University of South Carolina



APPROVED FDA APPROVED

IND approved
"Study may proceed" letter

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A Phase 2, double-blind, randomized, placebo-controlled multicenter study in 164 patients to evaluate the efficacy and safety of 20-Hydroxyecdysone (20E) in reducing the muscle strength loss from GLP1 agonists in combination with dieting in adult patients with obesity

Key inclusion criteria:

- Age: 18 and older
- BMI ≥30 or BMI ≥27 with one or more weight-associated co-morbidities (e.g. hypertension, dyslipidemia, obstructive sleep apnea or cardiovascular disease)
- Start of treatment with semaglutide for weight loss at the start of the study
- Willing to maintain a diet with an average intake of at least 1 gr/kg body weight protein daily
- Willing to maintain sufficient exercise, i.e. at least 150 minutes per week moderate-vigorous exercise
- Body weight stable (within a 5 kg range) in the 3 months prior to enrolment

Key exclusion criteria:

- Presence of contra-indications to semaglutide
- Current diabetes (both insulin dependent and T2DM)
- BMI >40
- Previous or planned surgical obesity treatment
- Use of anti-obesity (weight-loss) medication or use of any GLP-1 RA for diabetes within 90 days before enrolment
- Clinically significant liver disease, ALT/AST >5x ULN, or total bilirubin > 2x ULN
- Patients with obesity due to other endocrinologic disorders (e.g., hyper- or hypothyroidism, Cushing Syndrome, Prader Willi Syndrome).
- Neuromuscular or Autoimmune/inflammatory disorders that may cause muscle wasting

A Phase 2, double-blind, randomized, placebo-controlled multicenter study in 164 patients to evaluate the efficacy and safety of 20-Hydroxyecdysone (20E) in reducing the muscle strength loss from GLP1 agonists in combination with dieting in adult patients with obesity

Primary Objective

To assess the efficacy of 20E on muscle strength

Primary Endpoint :

knee extension strength evaluated by isokinetic dynamometry

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Secondary and exploratory Objectives

Secondary and exploratory Objectives	Endpoints
To explore the efficacy of 20E on another measure of muscle strength	• Knee extension strength at intermediate timepoints • Knee flexion strength evaluated by Isokinetic Dynamometry. • Hand Grip Strength (HGS)
To explore the efficacy of 20E on performance and mobility	• 6MWD • 5XSST • Stair climb
To explore 20E effect on body composition	DXA: appendicular and total lean body mass and fat mass (central reading)
To explore 20E effect on health related QoL	• SF-36 • WQoL- Lite CT Physical Function score and total score
To explore 20E effect on body weight and anthropometry	BMI, Body weight, waist circumference
To explore 20E effect on Insuline sensitivity, glucose control, blood pressure	HOMA, (fasted insulin + glucose) + Hba1c, LDL, HDL, triglycerides Blood pressure: SBP+DBP

Questions and discussion

Contact: rob.vanmaanen@biophytis.com