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LIVE HEALTHIER LONGER

Biophytis: Assessing the reduction of GLP1-RA-induced muscle mass or function loss in patients with obesity using the drug candidate BIO101 (20E). LB 6

15th Edition

ICFSR 2025
International Conference on Frailty and Sarcopenia Research

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Toulouse • France

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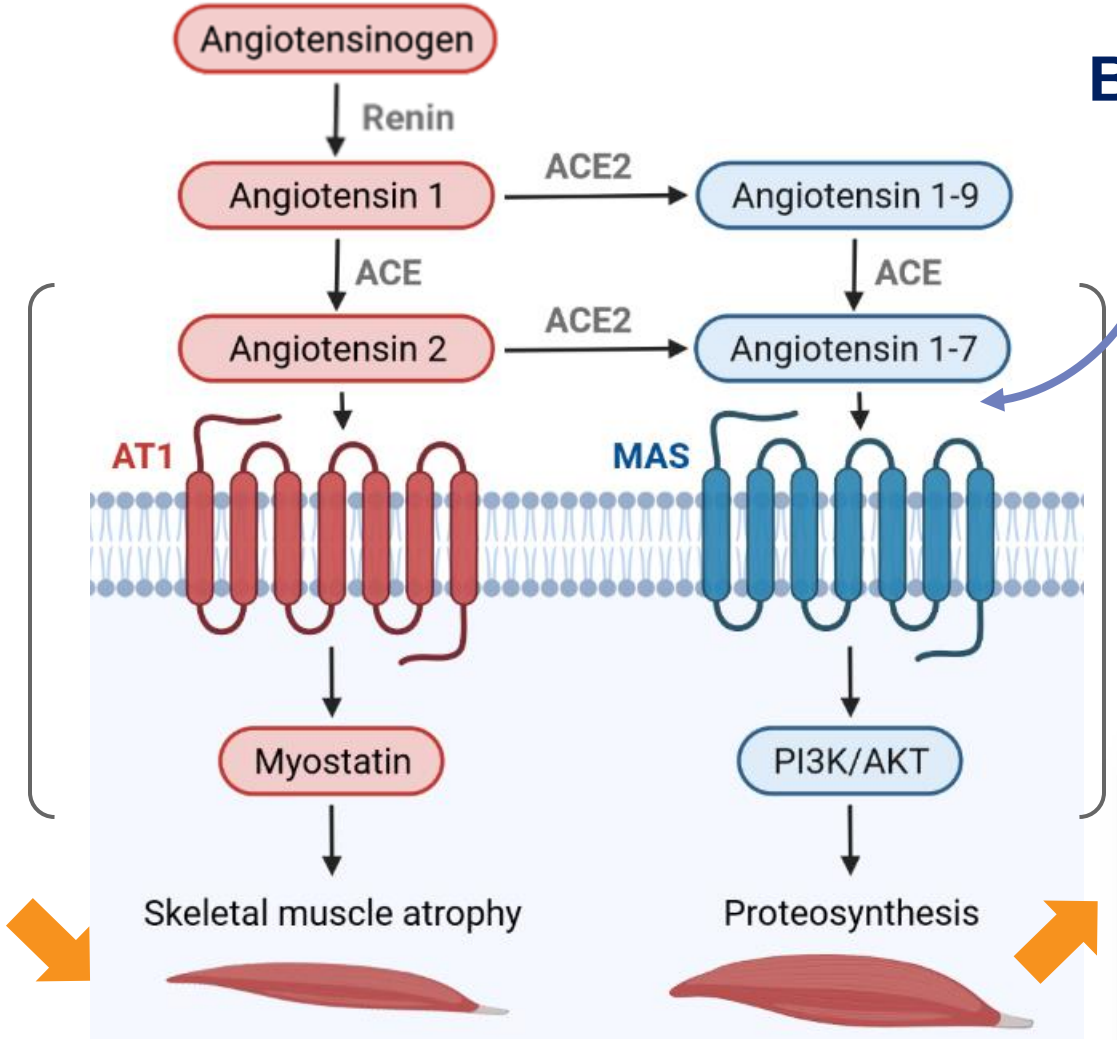
Chief Clinical Operations Officer

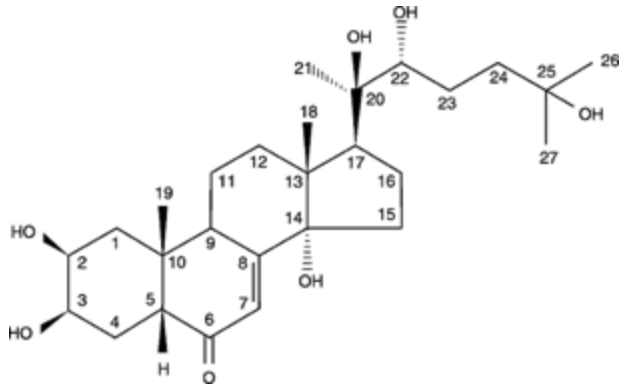
BIO101, a MAS receptor activator with beneficial effect on muscle



Classical arm

Protective arm

BIO101 / 20E



Ecdysteroides = 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 in Diet Induced Obese (DIO) mice (I)

C57BL6/J DIO, JanvierLabs
(male, 22 week-old, fed with specific diet* during 16 weeks)
n=48

*High fat (60%), D12492 from Research diet.

Treatment groups (n=12/group):
- Group 1: DIO, control, untreated
- Group 2: DIO, semaglutide 0.12mg/kg, s.c., 5 x/ week
- Group 3: DIO, semaglutide 0.12mg/kg, s.c. 5 x/ week + BIO101 50mg/kg (drinking water) : «COMBO»

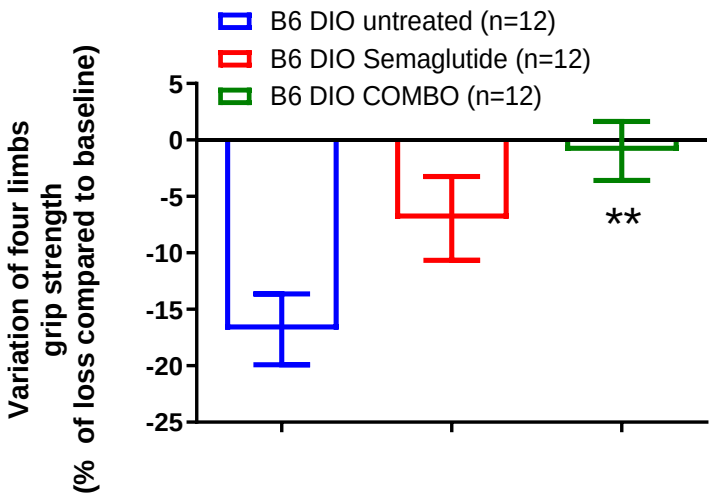
Treatment period (4 weeks)

- *In toto* tests: Grip test (strength)

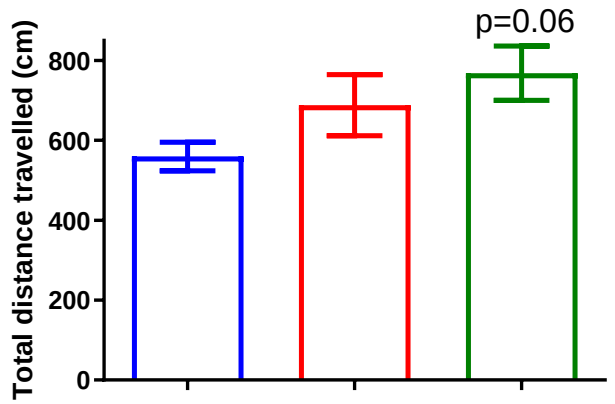
- *In toto* tests: Grip test (strength)
- Spontaneous activity: Actimeter
- Endurance test: treadmill

- *In situ* tests: EDL (contractility analysis)

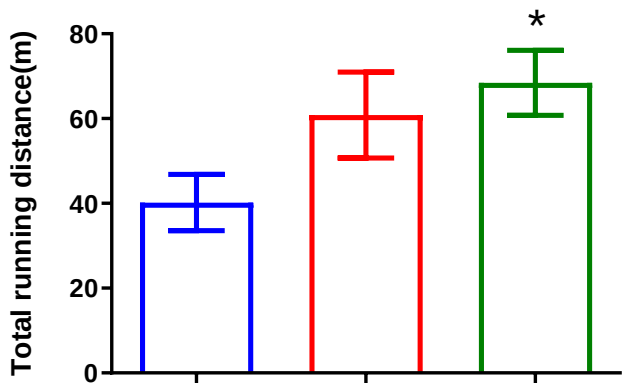
A Grip test (strength)



B Spontaneous activity



C Endurance test



➢ *Combination treatment (BIO101 + Semaglutide) significantly improve in toto tests compared to untreated mice*

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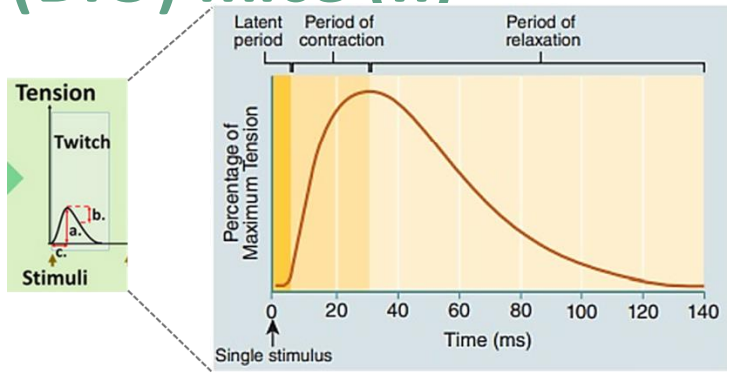
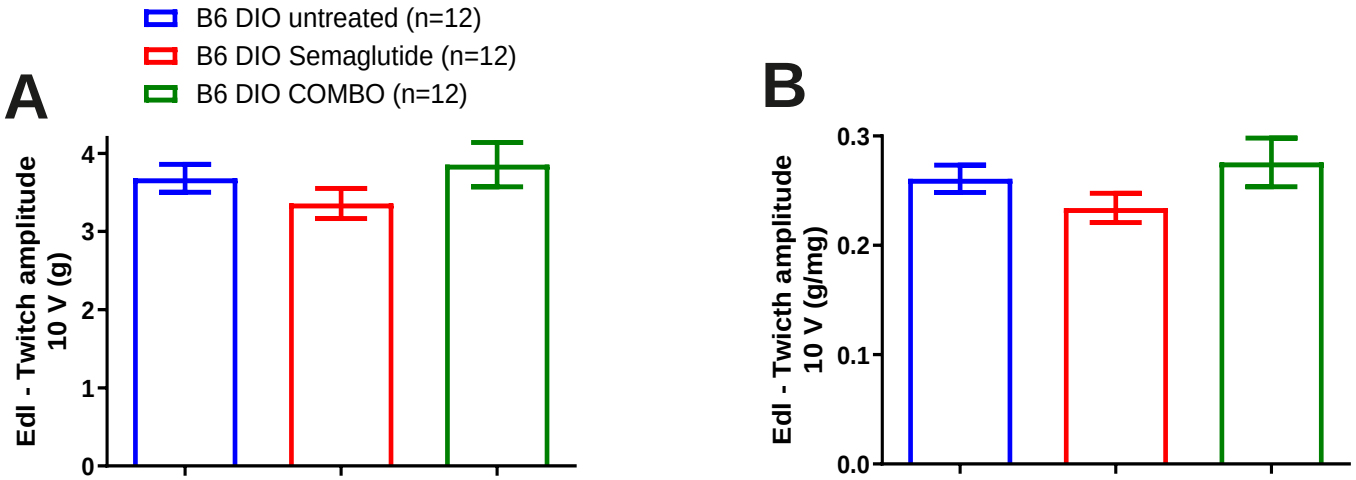
With *p<0.05 and **p<0.01 compared to B6 DIO untreated group

Preclinical BIO101 (20E) efficacy in Diet Induced Obese (DIO) mice (II)

Twitch test (end of study) – Extensor Digitorum Longus muscle (EDL)

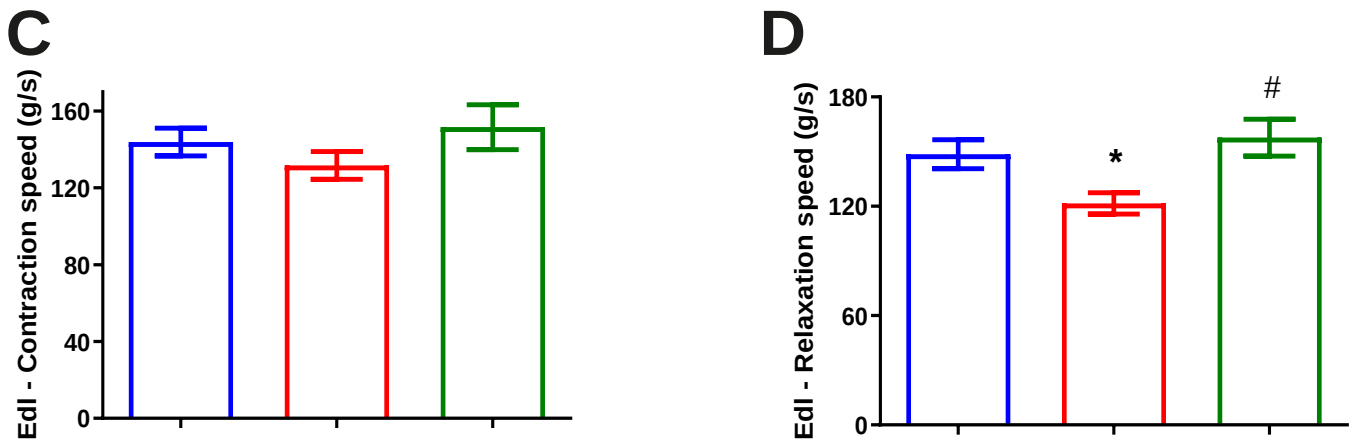


Twitch amplitude



- ***Combination treatment (BIO101+ Semaglutide) tends to revert contraction amplitude alterations due to Semaglutide alone.***

Twitch kinetic

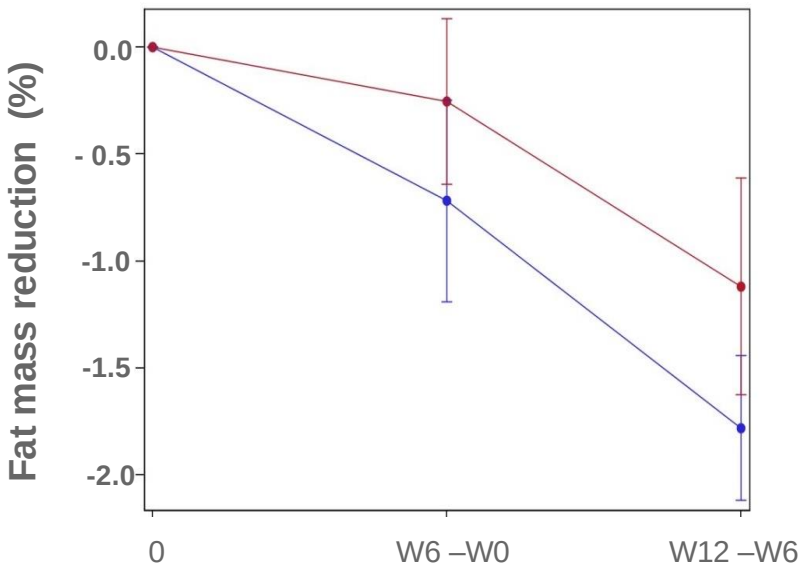


- ***Combination treatment (BIO101+ Semaglutide) reverts contraction kinetic alterations due to Semaglutide alone.***

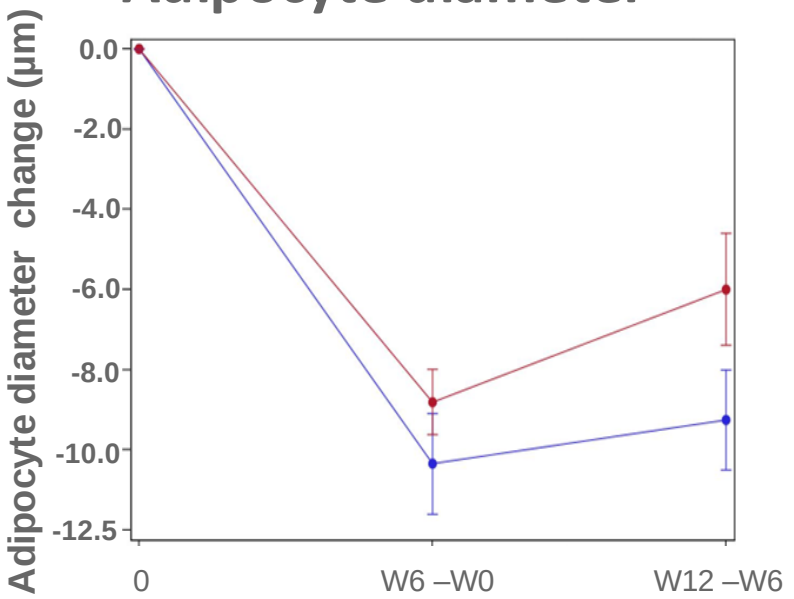
With *p<0.05 compared to B6 DIO untreated group
With #p<0.05 compared to B6 DIO Semaglutide group

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

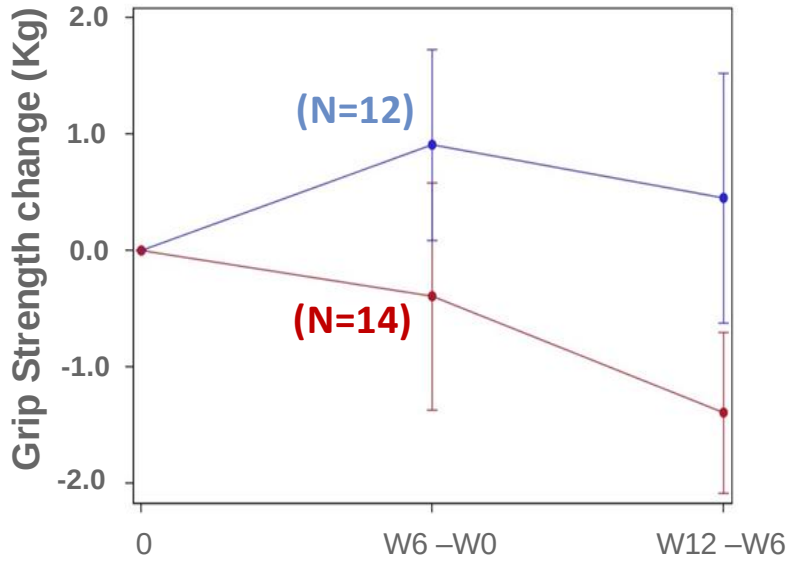
Android Fat mass



Adipocyte diameter



Hand grip strength



37.5 mg 20E ■ Placebo ■

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

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

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

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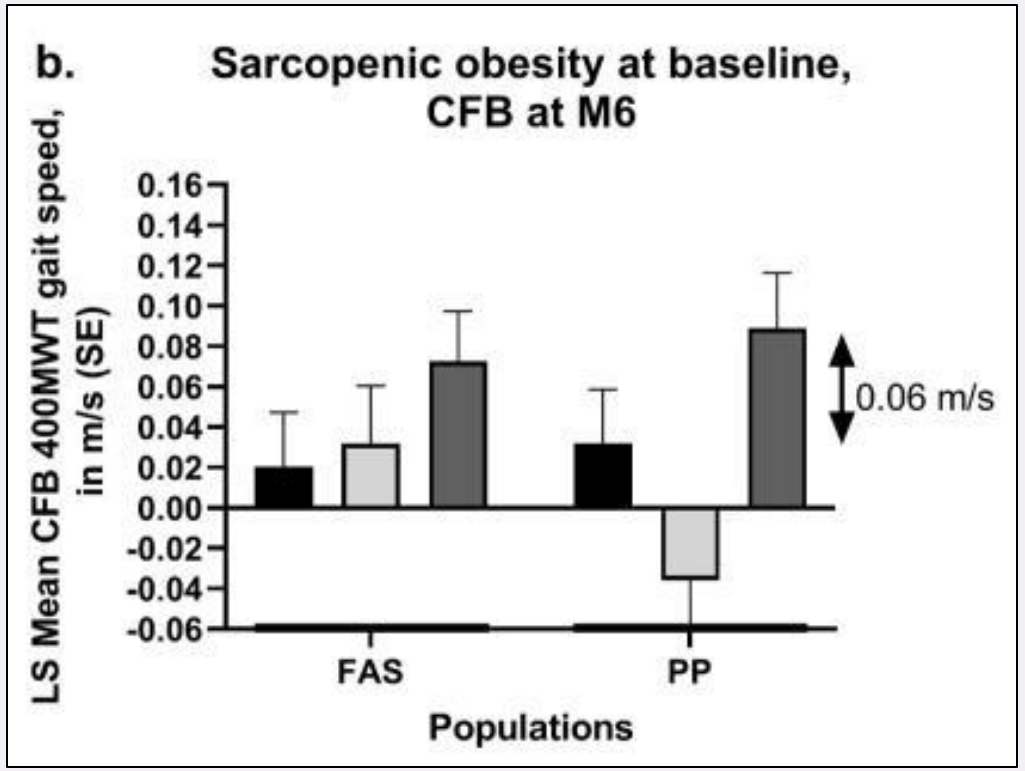
Data on file, Biophytis

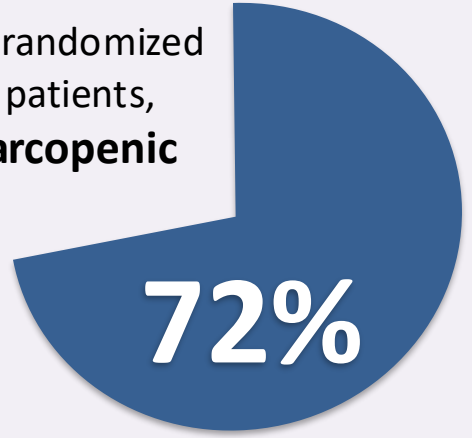
Phase 2 SARA-INT : gait speed from 400MWT in sub-population with sarcopenic obesity

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



Placebo
175 mg BID
350 mg BID

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



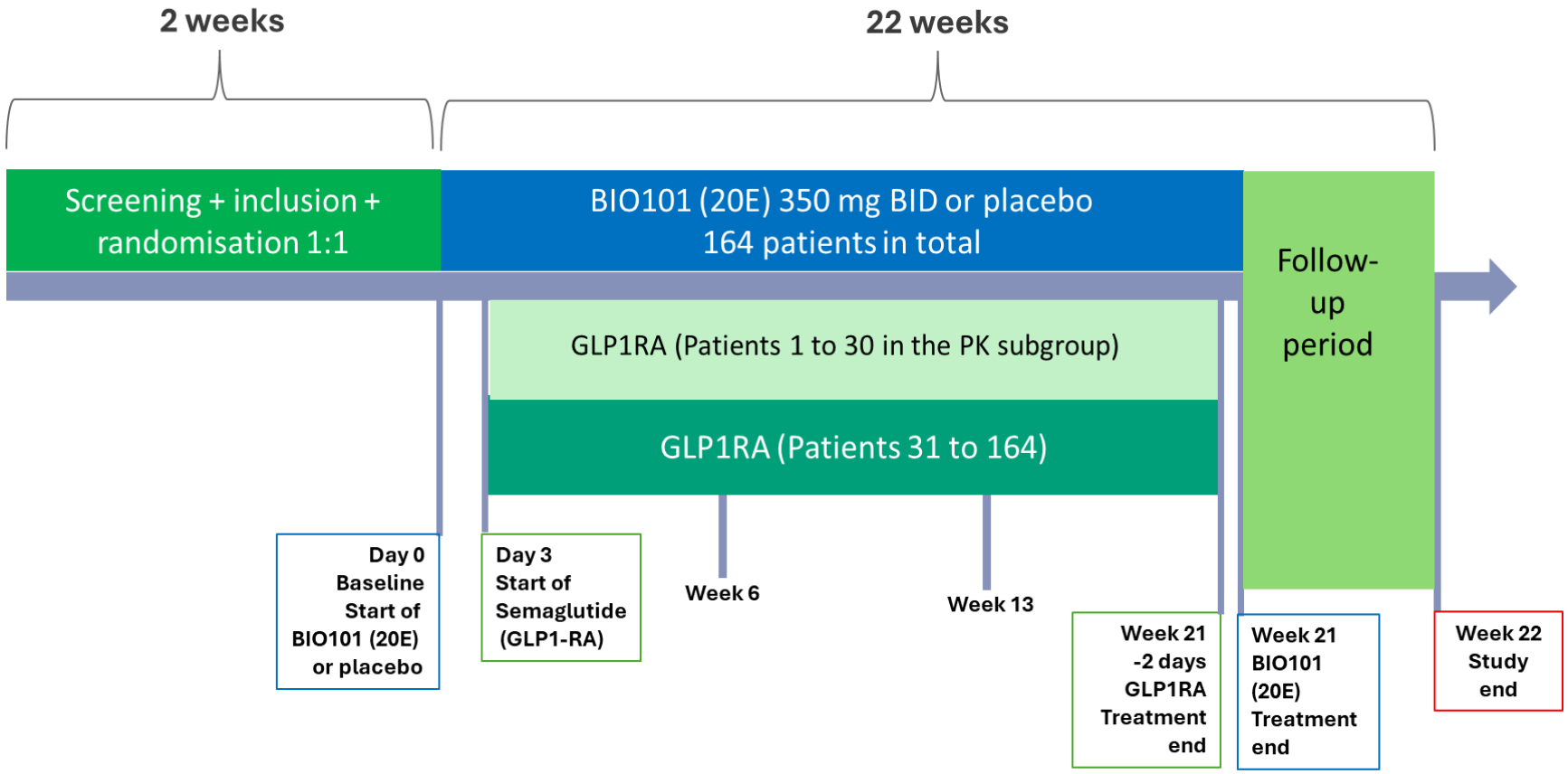
⇒ **Nominally significant treatment effect versus placebo p=0.0037 for the PP population at Month 6**

Source : CSR SARA INT

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

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 :

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:

- History or present cholelithiasis or cholecystectomy
- Presence of contra-indications to semaglutide
- **Current diabetes (both insulin dependent and T2DM)**
- 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
- **BMI >40**
- Clinically significant liver disease, ALT/AST >5x ULN, or total bilirubin > 2x ULN
- Clinical
- 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
- Use of antipsychotics, amphetamines, or other treatments that can affect weight
- History of major depressive disorder within the last 2 years
- Lifetime history of suicide attempt or suicidal behavior in the last month
- History or current gastroparesis (from medical history)

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

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 Insulin sensitivity, glucose control, blood pressure	HOMA, (fasted insulin + glucose) + Hba1c, LDL, HDL, triglycerides Blood pressure: SBP+DBP

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Questions and discussion

Thank you for your attention!

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