



OBA: a phase 2 clinical trial testing the drug candidate BIO101 (20E) to limit the loss of muscle mass and function induced by semaglutide in patients with obesity.



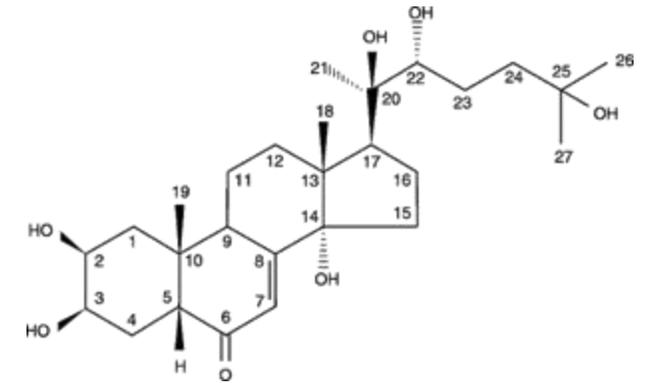
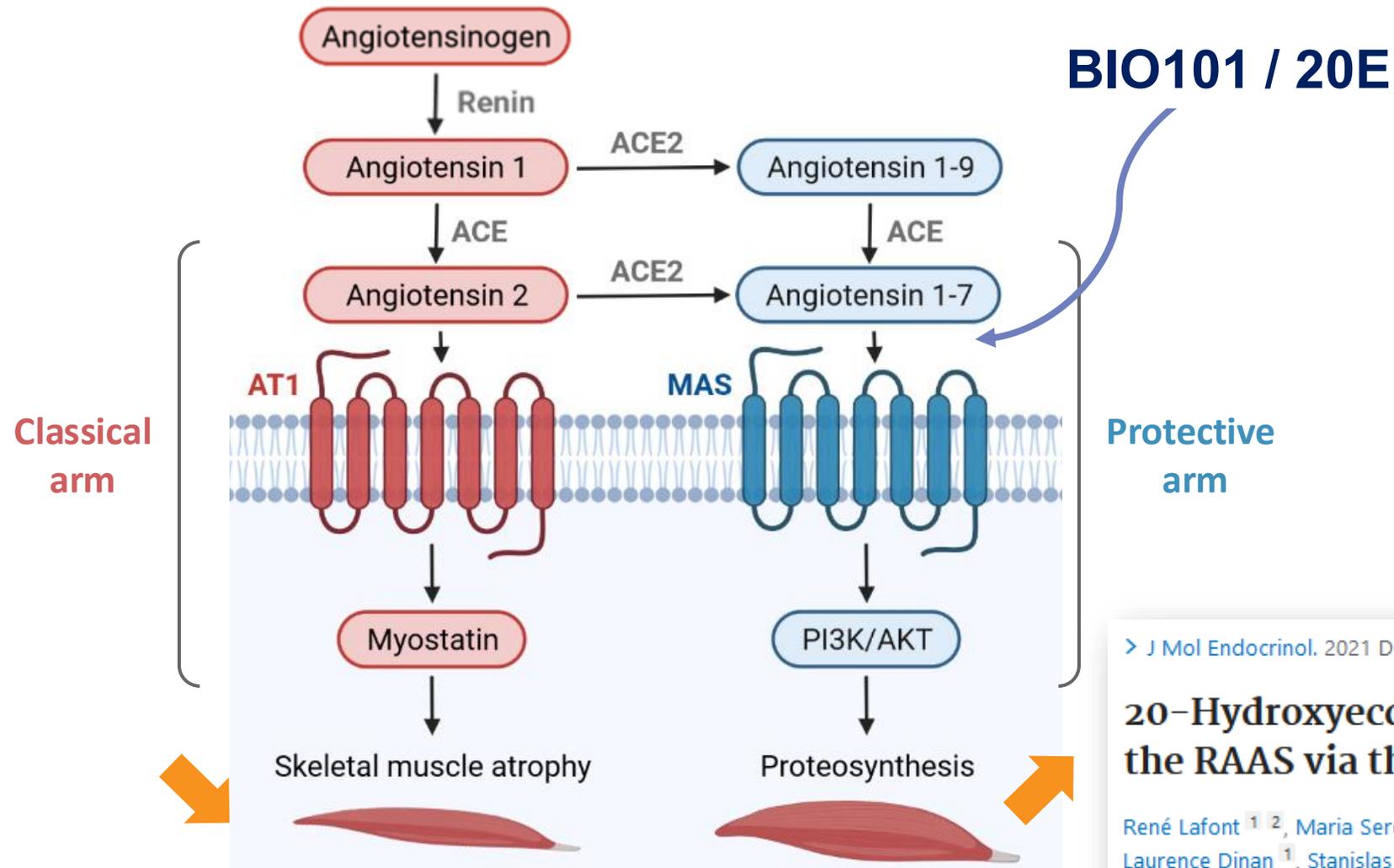
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**Abstract
No: 0673**

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Clinical Research Lead



BIO101, a MAS receptor activator with beneficial effect on muscle



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

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Affiliations + expand

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

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= 36

*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 68mg/kg (drinking water): «COMBO»

Treatment period (4 weeks)

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

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- Spontaneous activity: Actimeter
- Endurance test: treadmill

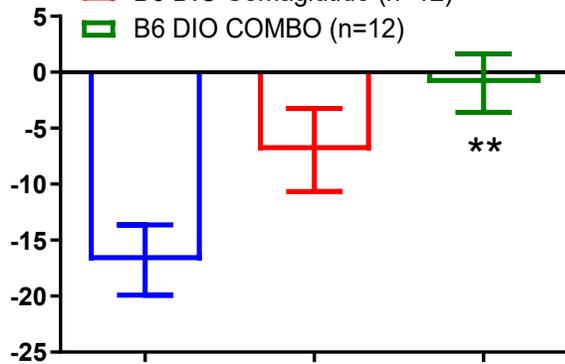
- *In situ* tests: EDL (contractility analysis)

A

Grip test (strength)

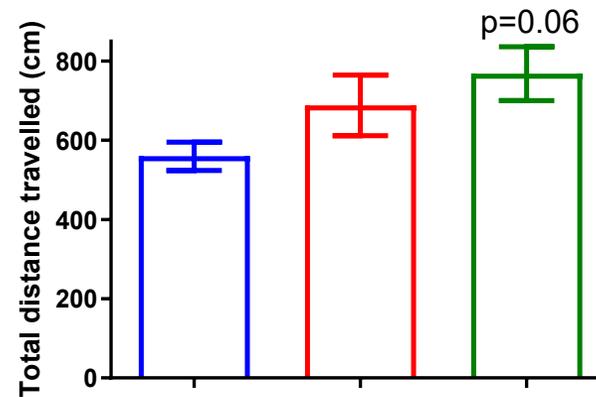
- B6 DIO untreated (n=12)
- B6 DIO Semaglutide (n=12)
- B6 DIO COMBO (n=12)

Variation of four limbs grip strength (% of loss compared to baseline)



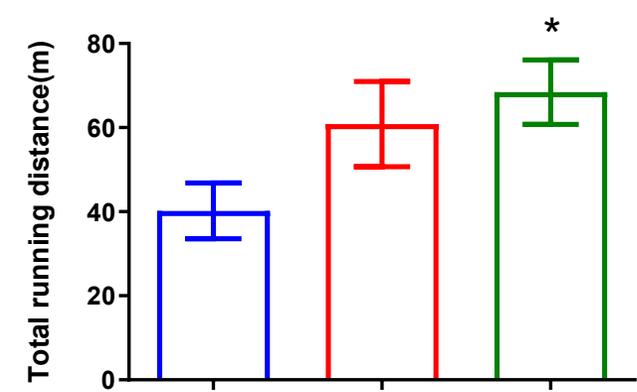
B

Spontaneous activity



C

Endurance test

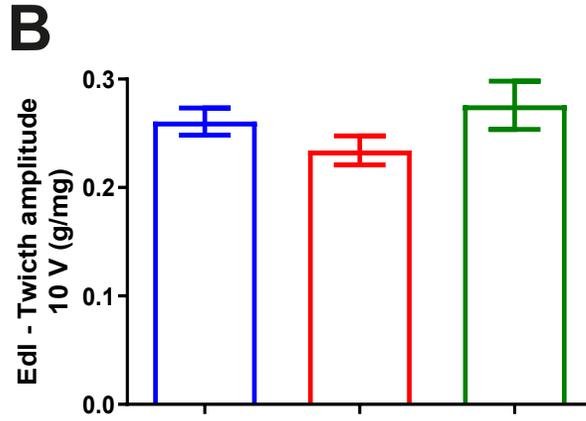
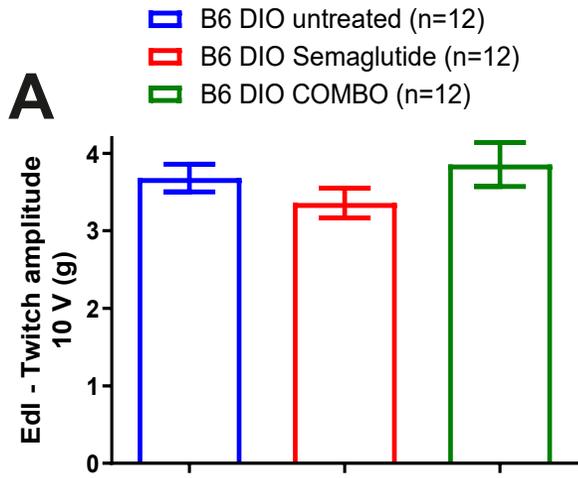


➤ Combination treatment (BIO101 + Semaglutide) significantly improves *in toto* tests compared to untreated mice

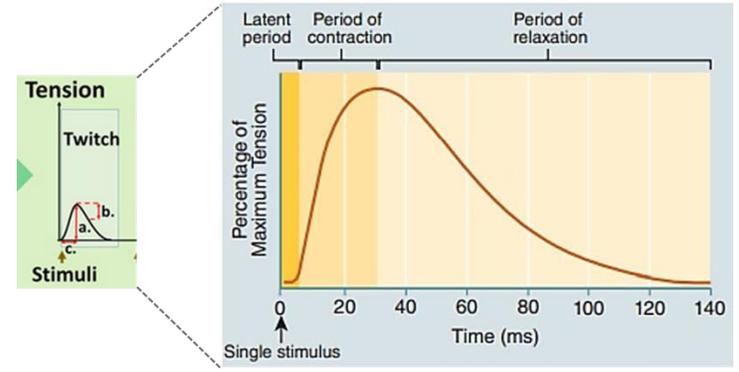
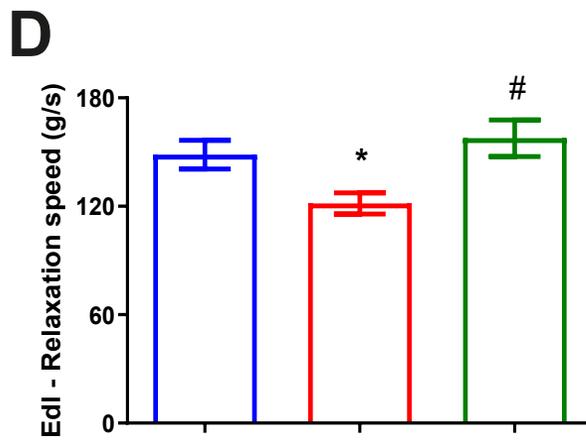
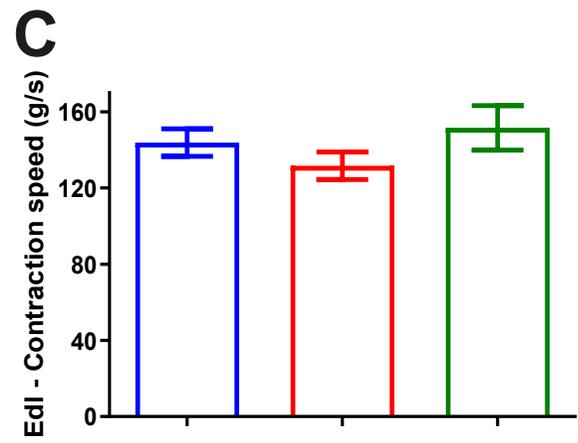
Preclinical BIO101 (20E) efficacy in Diet Induced Obese (DIO) mice (II)

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

Twitch amplitude



Twitch kinetic

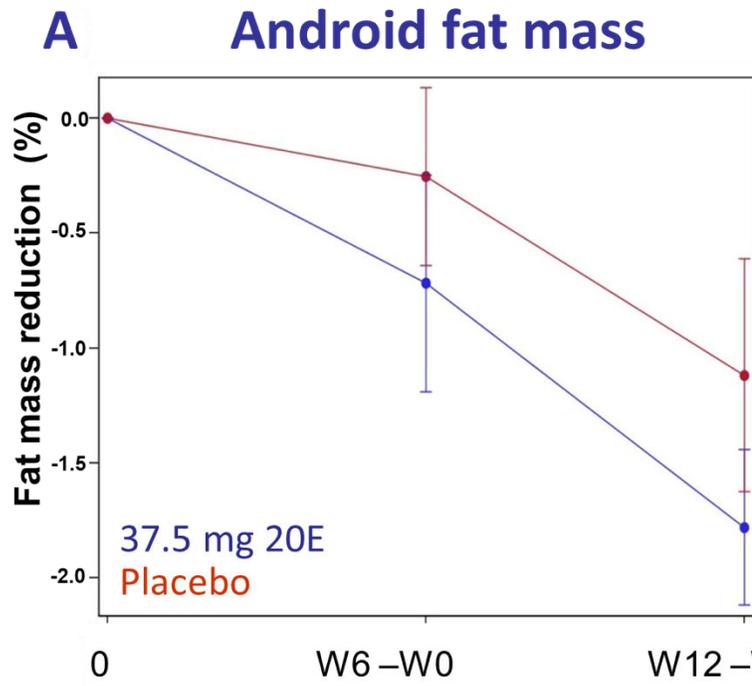


➤ **Combination treatment (BIO101+ Semaglutide) tends to revert contraction amplitude alterations due to Semaglutide alone.**

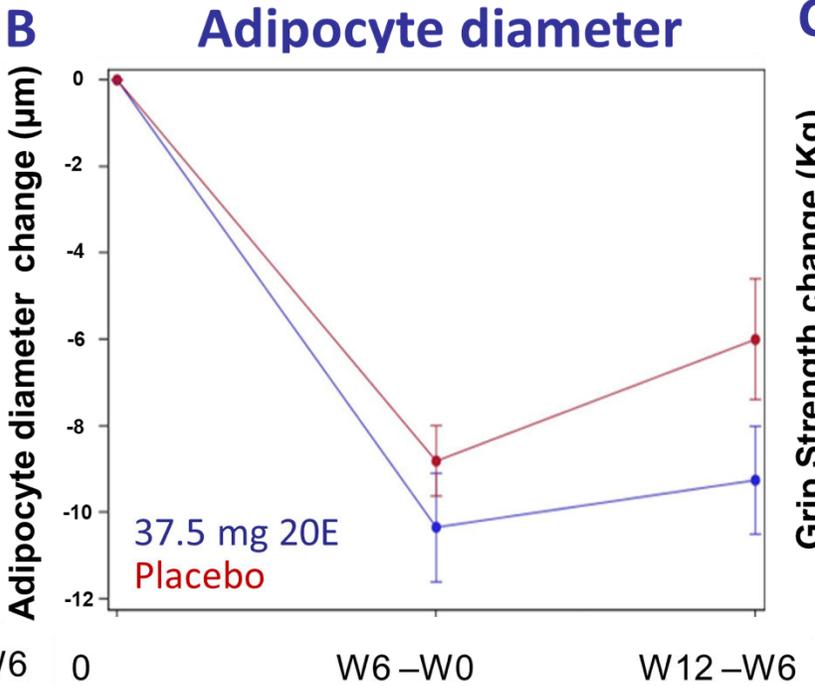
➤ **Combination treatment (BIO101+ Semaglutide) reverts contraction kinetic alterations due to Semaglutide alone.**

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

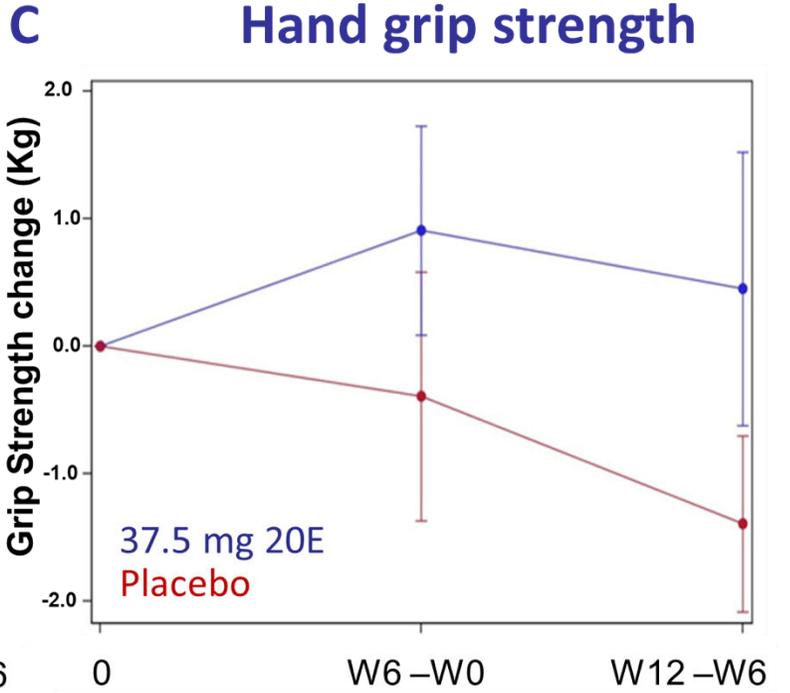
Patients were on 6-week hypocaloric dieting followed by a 6-week stabilisation dieting (n= 12 [20E] vs. 14 [placebo])



Quinoa extract containing 37.5mg of 20E significantly decreased android fat mass ($p=0.039$).



Quinoa extract containing 37.5mg of 20E induced a statistically significant reduction in adipocyte diameter, over the entire trial period ($p=0.032$).



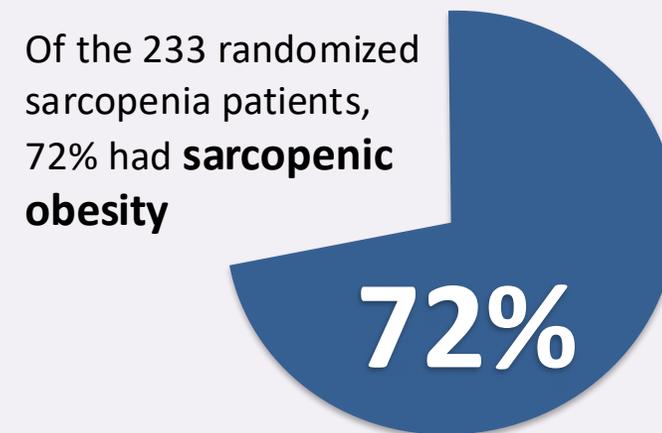
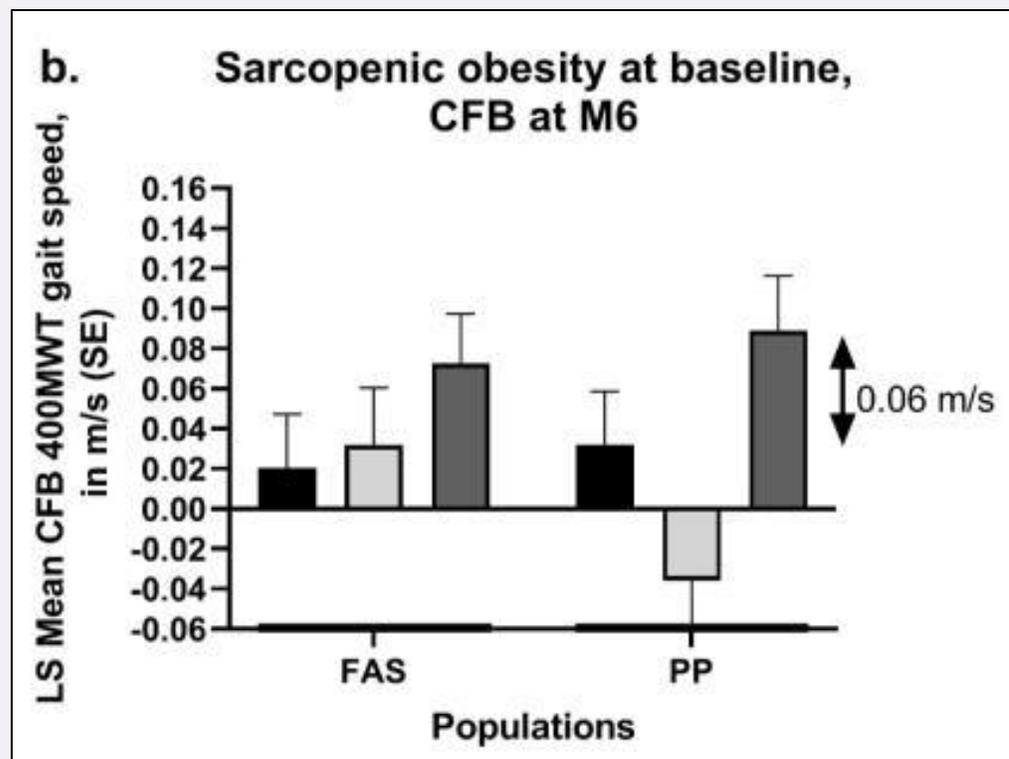
Quinoa extract containing 37.5mg of 20E induced a trend for improvement in handgrip strength in the subpopulation who lost > 5% of their initial body mass during the weight loss phase ($p=0.097$).



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



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



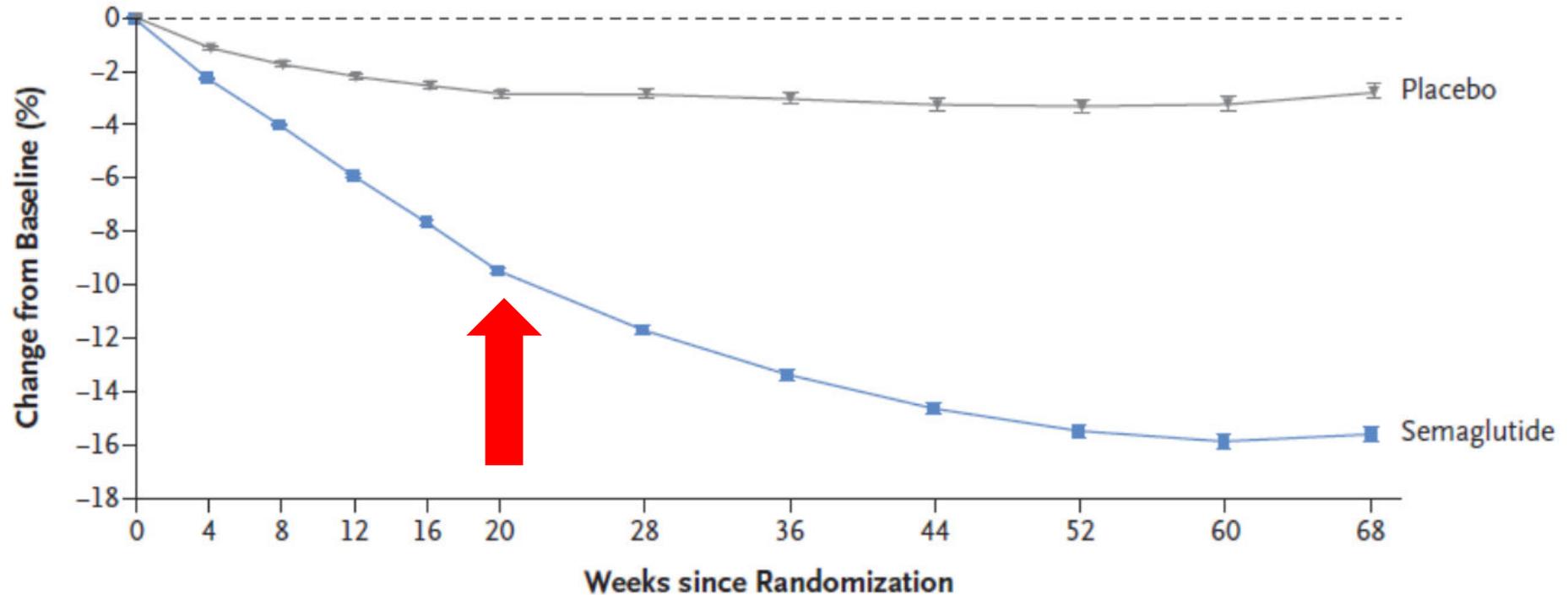
⇒ **Nominally significant treatment effect versus placebo**
p=0.0037 for the PP population at Month 6



Study Rationale : duration and primary endpoint

- Semaglutide is at steady state at W21
- ~ 2/3 of effect of semaglutide @W68 realized after 20 weeks
- Meta-analysis (Zibellini et al.) found 7.5% knee extension strength loss with a mean weight loss of 9 kg.

A Body Weight Change from Baseline by Week, Observed In-Trial Data



No. at Risk

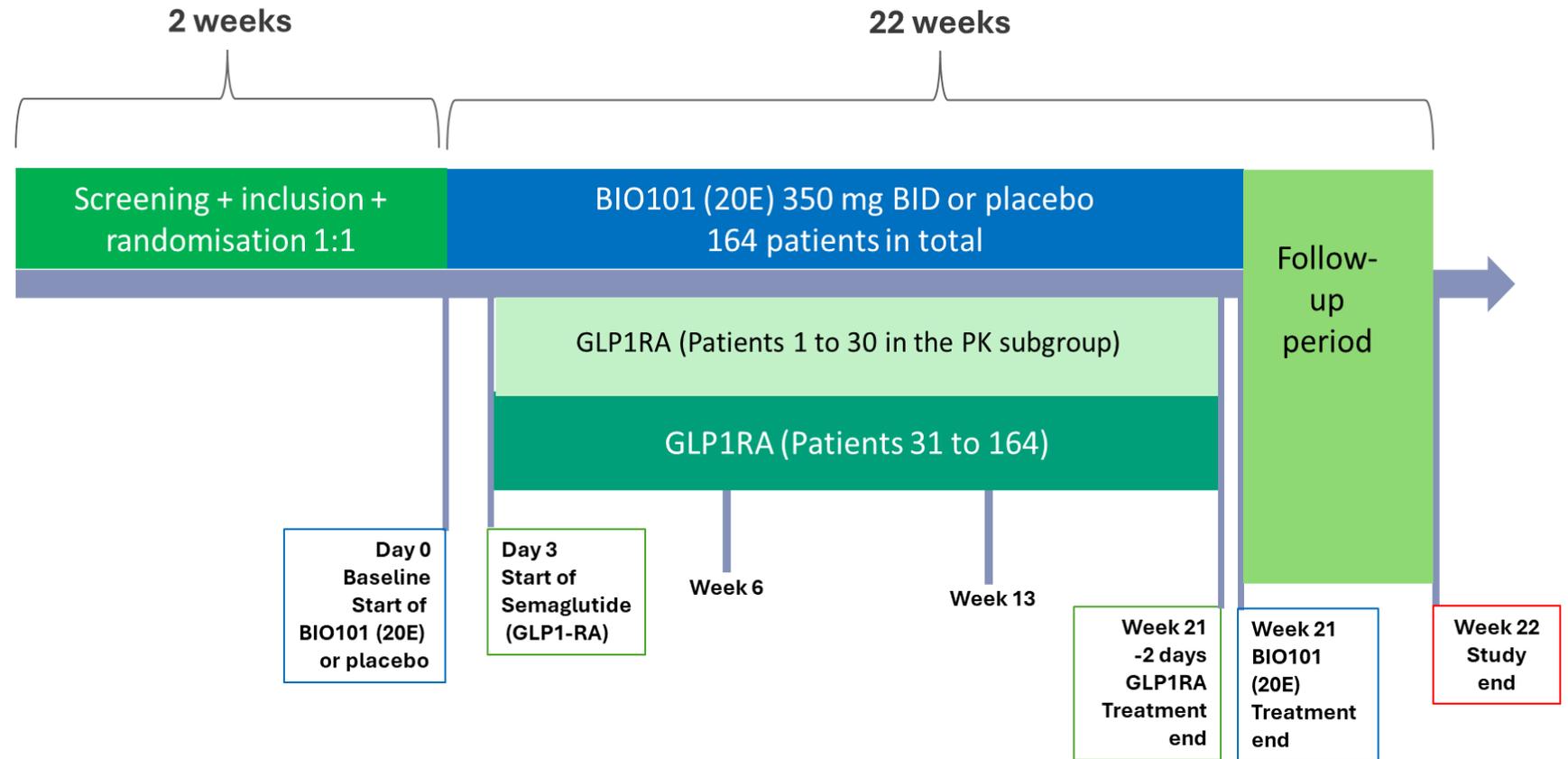
Placebo	655	649	641	619	615	603	592	571	554	549	540	577
Semaglutide	1306	1290	1281	1262	1252	1248	1232	1228	1207	1203	1190	1212



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 sequelae (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 g/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
- Patients with obesity due to other endocrine 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



Secondary and exploratory Objectives

Endpoints

To explore the efficacy of 20E on another measure of muscle strength	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 6MWD • 5XSST • Stair climb
To explore 20E effect on body composition	<ul style="list-style-type: none"> • DXA: appendicular and total lean body mass and fat mass (central reading)
To explore 20E effect on health related QoL	<ul style="list-style-type: none"> • SF-36 • WQoL- Lite CT Physical Function score and total score
To explore 20E effect on body weight and anthropometry	<ul style="list-style-type: none"> • 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

Medical Affairs

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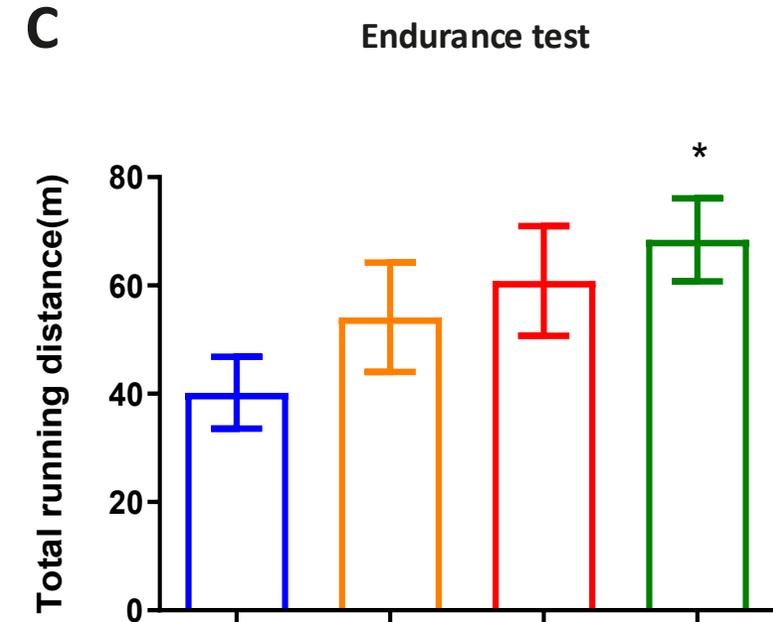
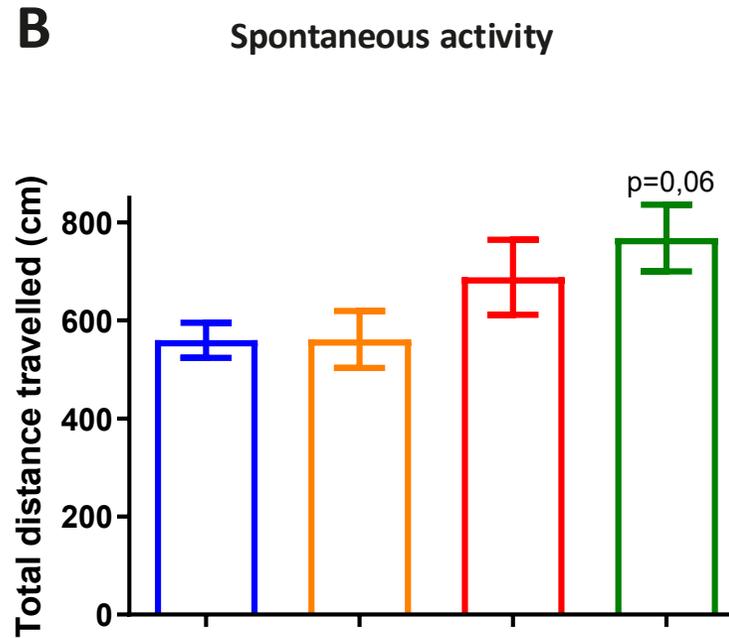
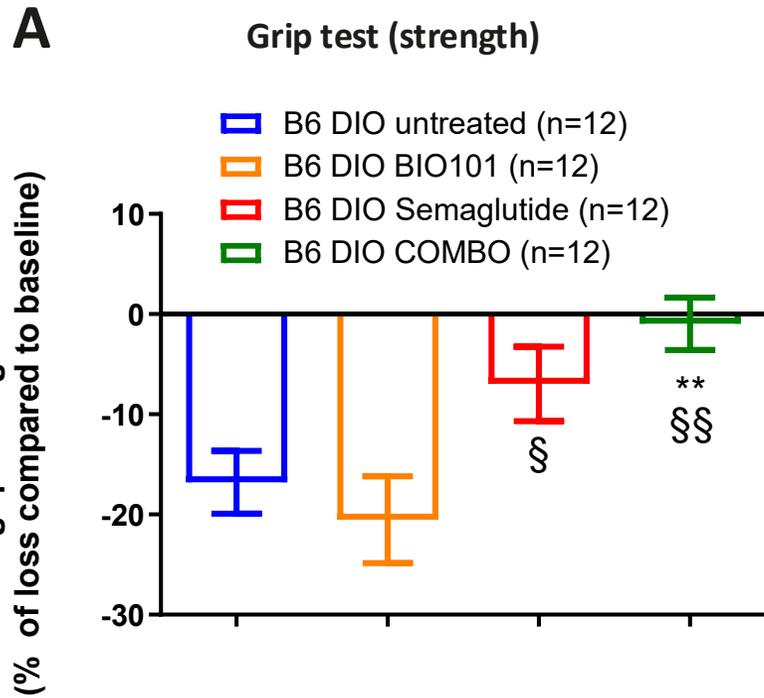
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Questions and discussion

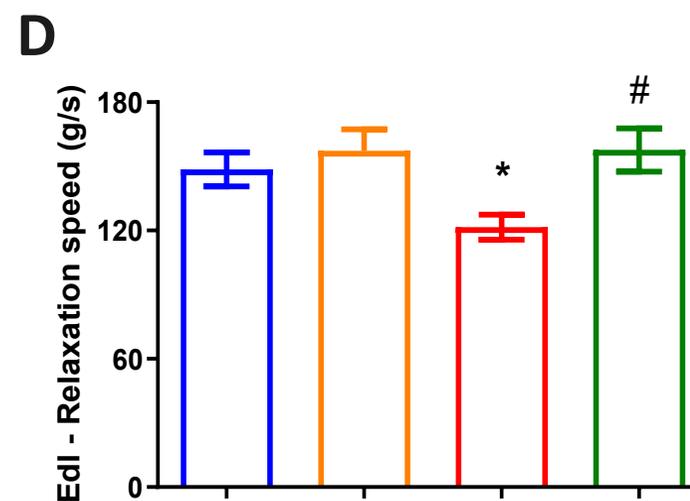
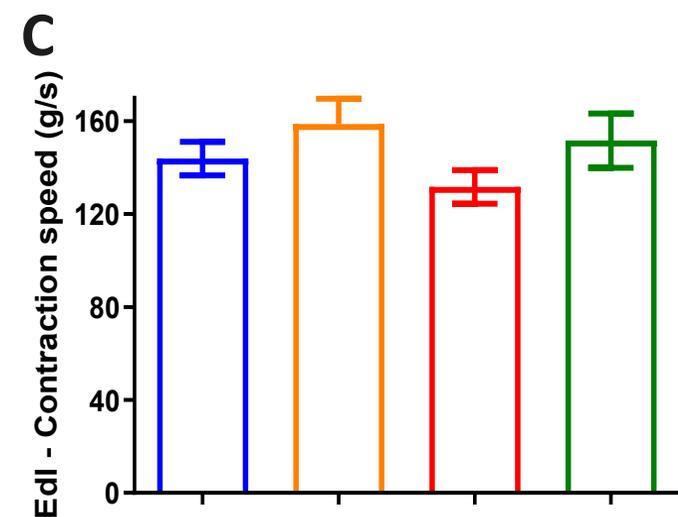
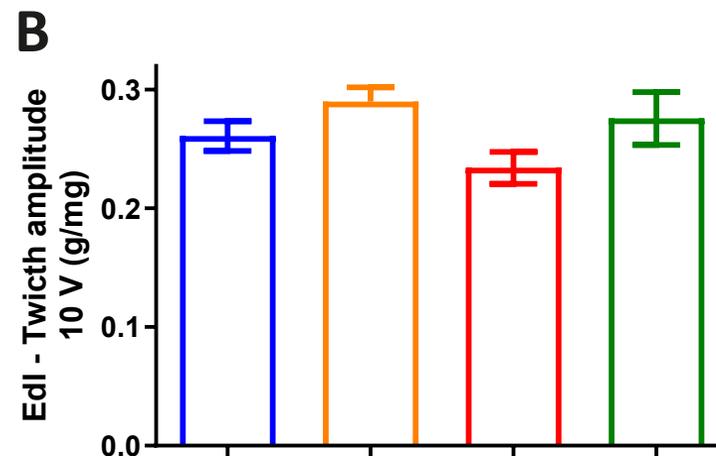
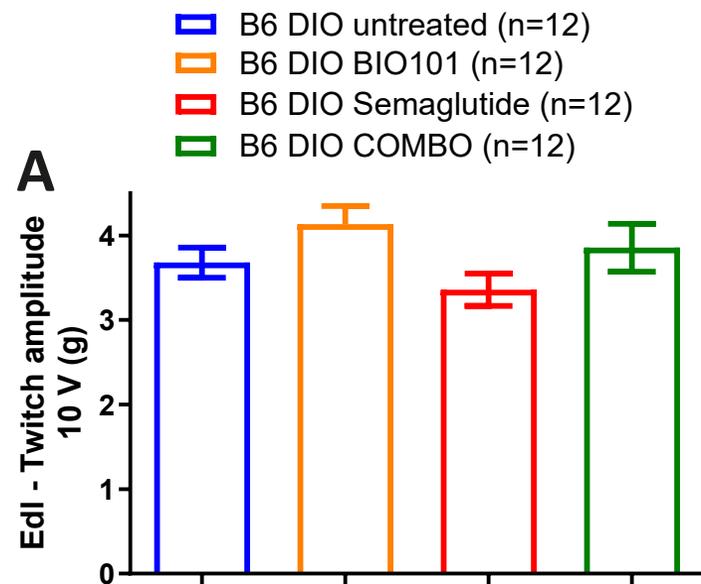
Preclinical 20E efficacy in Diet Induced Obese (DIO) mice (I)



With *p<0,05 and **p<0,01 compared to B6 DIO untreated group
With §p<0,05 and §§p<0,01 compared to B6 DIO BIO101 group

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

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



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

Thank you for your attention!

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