

BIO101: a drug candidate to reduce GLP-1RA-induced muscle mass or function loss in patients with obesity.



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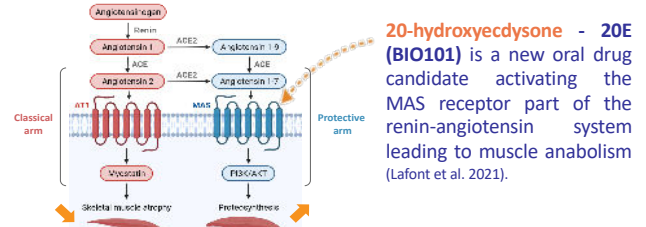
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Introduction

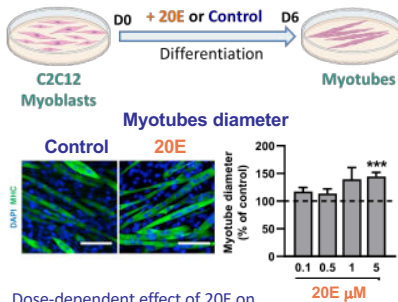
GLP-1 receptor agonists (GLP-1RAs), also named incretins, effectively reduce body weight, however up to 40% of the total lost weight is lean body mass, which includes loss of skeletal muscle mass. Similar levels of weight loss with bariatric surgery are associated with clinically significant reductions in muscle mass and strength. Combining skeletal muscle-targeted drug candidates with GLP-1RAs may preserve skeletal muscle mass and function. BIO101 (20-hydroxyecdysone; 20E), an oral MAS receptor activator, could be a promising treatment to prevent the loss of muscle mass or strength in patients with obesity or overweight treated with GLP-1RAs.

20-hydroxyecdysone - 20E (BIO101) mode of action



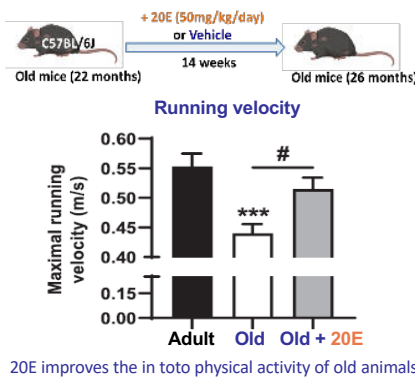
20E effects on myocytes

In vitro 20E has pro-differentiating effects in murine and human myocytes, increasing myotubes diameter (Serova et al. 2024).



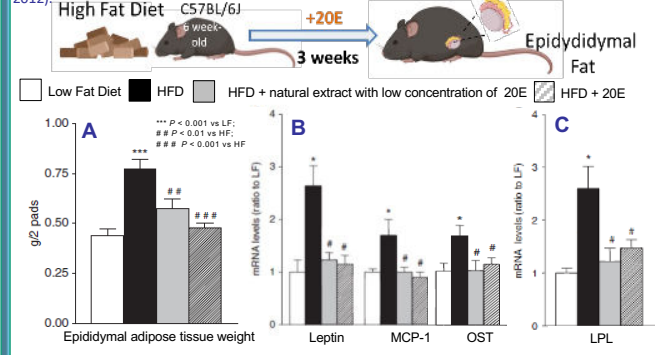
20E on muscular activity in old mice

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



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

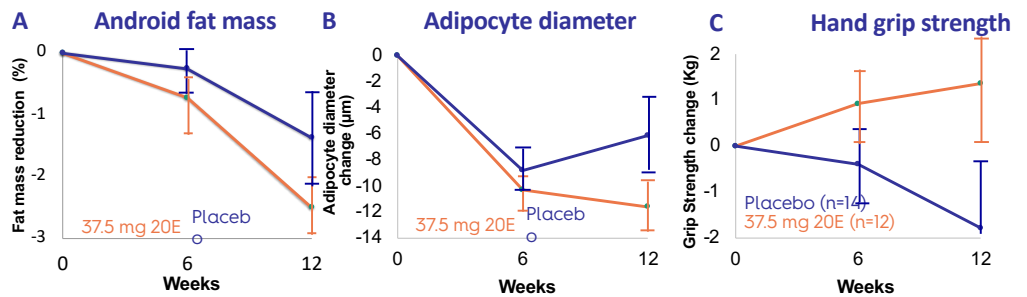
In HFD mice, 20E limited epididymal adipose tissue weight (A), reduced expression of leptin, MCP-1, and of osteopontin (OST) involved in insulin resistance (B) and lipoprotein lipase involved in lipid storage (C) (Foucault et al. 2012).



Quinolia : a randomized placebo-controlled study with a quinoa extract containing 20E (37.5 mg) in 58 subjects with obesity or overweight.

Patients were on 6-week hypocaloric dieting followed by a 6-week stabilisation dieting

- 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 ($p=0.032$).
- 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 ($n=12$ [20E] vs. 14 [placebo] $p=0.097$).



BA : a randomized placebo-controlled study with 20E 350 mg B.I.D in patients with obesity or overweight treated with semaglutide

Trial design:

Double-blind, randomized, placebo-controlled parallel group clinical trial with even distribution (1:1 : 20E 350mg BID vs. placebo). For efficacy, a study with 164 patients will have 80% power to detect a reduction of 75% in the expected deterioration of 7.5% in muscle strength in the placebo group.

Main Study Endpoints:

Primary Endpoint:

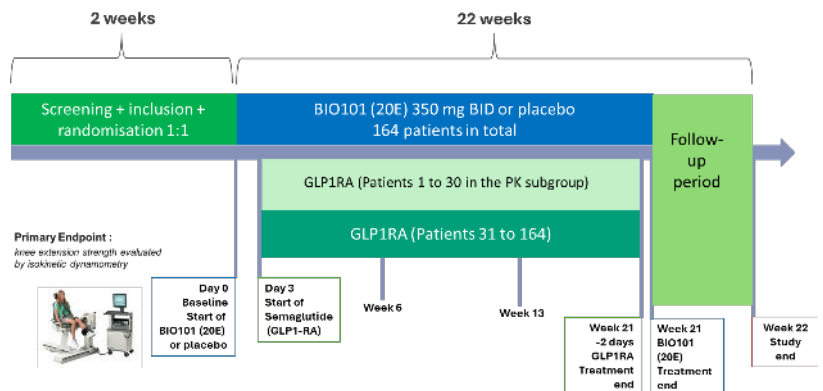
Muscle strength (knee extension determined by isokinetic dynamometry).

Main Secondary endpoints:

6MWD and 5XST, Hand grip test, Body composition : lean body and fat mass, Questionnaires : SF-36 and WQOL-Lite-CT physical function score, Body weight, BMI, Waist circumference. Safety and biomarkers expression.

Patient Population and main eligibility criteria:

- Age 18 years and older, patients with obesity (BMI ≥ 30) or overweight (BMI ≥ 27) with one or more weight-related sequelae (e.g. hypertension).
- Willing to participate and able to sign an ICF.
- Start of treatment with semaglutide for weight loss 3 days after the start of administration of the study treatment.
- Willing to maintain a diet with average intake of at least 1 gr/kg body weight protein daily and at least 150 minutes of activity per week.



Take home message:

BIO101 (20E) is a promising oral treatment to reduce the potential loss of muscle strength in patients with obesity treated with GLP-1RAs:

- Beneficial effects on adipocytes and muscles in preclinical models *in vitro* and *in vivo*.
- Statistically significant beneficial effects of low dose 20E in target patient population.
- Biophytis plans to start the Phase 2 OBA clinical trial in Q1 2025.**