Potential to Optimize Weight Loss with Enobosarm: Augment Reduction of Fat Mass while Preserving Muscle in Older Patients with Obesity

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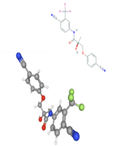
INTRODUCTION

There is a need for a drug when combined with a GLP-1 receptor agonist (RA) can prevent muscle loss, while preferentially reducing fat resulting in high quality weight loss. Older sarcopenic obese patients receiving a GLP-1 RA are at the highest risk for muscle atrophy and muscle weakness leading to frailty. Enobosarm, a novel oral selective androgen receptor modulator, has been studied in 5 clinical muscle studies involving 968 older men, postmenopausal women, and older patients who have muscle loss due to advanced cancer. The totality of the clinical data demonstrates that enobosarm therapy results in dose-dependent reductions in fat mass and increases in muscle mass with improvement in physical function.

Enobosarm is a novel oral selective androgen receptor modulator (SARM) designed to reduce fat mass and increase lean mass (muscle and bone)

- Enobosarm (Ostarine, MK2866, GTx-024) is a nonsteroidal, selective androgen receptor modulator[1,2]
- Data from clinical trials and preclinical studies support enobosarm's potential:
  - Once-a-day oral dosing
  - Activates the androgen receptor, a well-established mechanism
  - Tissue selective
    - Improves muscle mass and physical function[2,4]
    - Stimulates lipolysis, inhibits lipogenesis, and decreases fat mass[7,8]
    - Builds and heals bone-potential to treat bone loss/osteoporosis[3-5]
  - Safety
    - Lack of masculinizing effects
    - Not converted to estrogen or dihydrotestosterone
    - No liver toxicity



Chemical structure of enobosarm

AIM & METHOD

A placebo-controlled Phase 3 clinical trial was conducted by GTx, Inc.* evaluating oral daily 3mg enobosarm dose for the treatment of muscle wasting in advanced lung cancer patients undergoing chemotherapy. A post-hoc analysis was performed to assess body composition by DXA scan in a subset of older (≥60 years) patients with obesity (BMI ≥ 30kg/m2) at 12 and 21 weeks. Loss of appetite occurs with advanced cancer inducing a hypocaloric state.

* Global world-wide rights for enobosarm licensed to Veru, Inc.

RESULTS

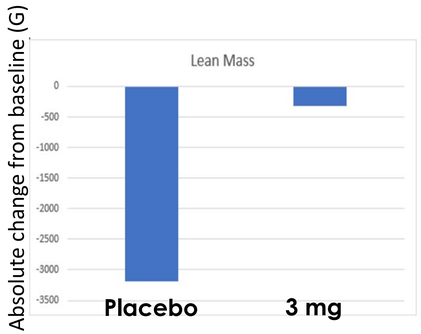
At 12 weeks, enobosarm 3mg treated subjects had maintained while placebo lost total lean body mass (n=29). Enobosarm 3mg treated subjects had a 5.77% reduction in fat mass compared to placebo (n=29). By 21 weeks, enobosarm 3mg treatment resulted in a 14.4% total fat mass loss, a 0.35% increase in total lean mass, and a 4.5% loss of DXA body weight compared to placebo (n=24) (Figure 1).

Enobosarm was generally well tolerated with no increase in frequency of gastrointestinal side effects compared to placebo.

Figure 1. Post-hoc analysis of subpopulation older subjects (≥60 years of age) with obesity (BMI ≥ 30)

Total lean mass

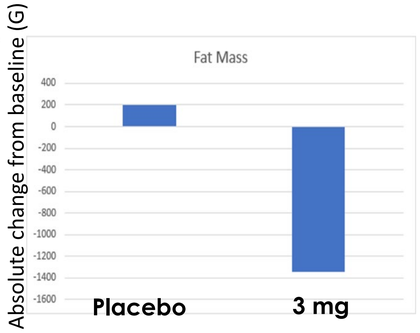
Up to week 12 visit



Placebo N=15, Treated N=14
Placebo corrected % change = +4.96%

Total fat mass

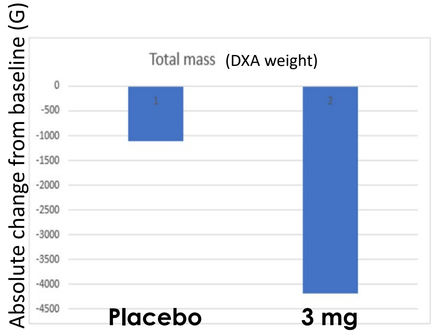
Up to week 12 visit



Placebo N=15, Treated N=14
Placebo corrected % change = -5.77%

Total body weight

Up to week 21 visit



Placebo N=12, Treated N=12
Placebo corrected % change = -4.51%

CONCLUSIONS

In a subset post-hoc analysis of older obese patients, enobosarm therapy resulted in reductions in fat mass while preserving lean body mass (muscle) leading to greater high quality weight loss.

A Phase 2b randomized controlled trial is currently underway to evaluate the safety and efficacy of enobosarm in preserving muscle mass and augmenting fat loss in at risk sarcopenic obese or overweight older patients receiving a GLP-1 RA for weight loss.

ACKNOWLEDGEMENTS

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