# Double-Blind, Multiple Ascending Dose, Safety, Pharmacokinetic and Body Composition Study of Enobosarm in Healthy Young and Older Men

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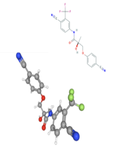
## INTRODUCTION

Enobosarm is a novel oral selective androgen receptor modulator that has been shown to increase lean mass and decrease fat mass. There is a need for a therapy that can prevent the loss of muscle mass, while further increasing fat loss in patients taking GLP-1 RA for weight loss, especially in older sarcopenic obese patients who are at-risk for developing muscle atrophy and muscle weakness leading to frailty.

**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[3,4]
    - 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 double-blind, randomized, placebo-controlled, single-center, multiple ascending dose Phase 1 study was conducted by GTx, Inc.* in normal-weight healthy young (18-45y; 27±7y) and older men (≥60y; 67±5y). The study was of sequential dose escalation design (young men 1, 3, 10 and 30 mg; older men 3 and 30 mg) with separate groups receiving oral dose of enobosarm vs matching placebo (n=72). The Phase 1 study assessed the safety and pharmacokinetics of a dose range that covers the projected clinical dose range of up to 3 mg per day. A DXA scan was obtained to assess early changes in body composition. A main objective of this study was to compare the effects of enobosarm in young healthy normal-weight men with that observed in older men.

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

## RESULTS

PK parameters were similar between young and older men. In the placebo groups, the changes in total lean mass and total fat mass were similar between the young and older men. There was a placebo corrected 2.13% and 3.98% increase in total lean mass with enobosarm 3 mg in the young and older men after 14 days of treatment, respectively. A placebo corrected 3.03% and 3.49% decrease in total fat mass with enobosarm 3 mg in young and older men, respectively (Table 2). Enobosarm was generally safe and well tolerated.

**Table 1. Baseline BMI and age in young and older men in the study (mean± SD).**

| Young men | Placebo | Enobosarm (3 mg) |
|---|---|---|
| N= | 12 | 9 |
| Age (years) | 27.16 (±7.09) | 26 (±7.87) |
| BMI (kg/m2) | 24.07 (±2.15) | 23.44 (±1.69) |
| **Older men** | **Placebo** | **Enobosarm (3 mg)** |
| N= | 5 | 9 |
| Age (years) | 68.4 (±5.45) | 67.77 (±5.24) |
| BMI (kg/m2) | 26.7 (±1.63) | 27.92 (±3.18) |

**Table 2. Total lean and fat mass changes in young and older men after 14 days of enobosarm or placebo treatment (mean± SD).**

| Young men | Placebo | Enobosarm (3 mg) |
|---|---|---|
| N= | 12 | 9 |
| Total lean mass (g) | -0.70% (±2.53%) | 1.43% (±2.37%) |
| Total fat mass (g) | 3.72% (±3.92%) | 0.69% (±3.02%) |
| **Older men** | **Placebo** | **Enobosarm (3 mg)** |
| N= | 5 | 9 |
| Total lean mass (g) | -0.95% (±2.04%) | 3.03% (±2.75%) |
| Total fat mass (g) | 2.33% (±4.47%) | -1.16% (±4.16%) |

## CONCLUSIONS

With short term 14-day exposure of enobosarm treatment, similar increases in total lean mass and decreases in total fat mass were observed in young and older men compared to placebo. While enobosarm was associated with positive body composition changes in men regardless of age, older men with lower lean mass and higher fat mass at baseline appear more likely to have greater benefit from enobosarm therapy.

An ongoing randomized controlled Phase 2b trial is enrolling to evaluate the safety and efficacy of enobosarm as a treatment to augment fat loss and to prevent muscle loss in sarcopenic obese or overweight elderly patients receiving a GLP-1 RA who are at-risk for developing muscle atrophy and muscle weakness.

## ACKNOWLEDGEMENTS

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## REFERENCES

1- Narayanan R et al. Mol Cell Endocrinol 2017|
2- Dalton JT et al. Curr Opin Support Palliat Care 7:345-351, 2013
3- Kamrakova M et al Calcif Tissue Int 106:147-157,2020
4- Hoffman DB et al. J Bone Metab 37:243-255, 2019
5- Kearbey JD et al Pharm Res 26:2471-2477, 2009
6- Dobs AS et al. Lancet Oncol 14:335-45, 2013
7- Dalton JT et al. J Cachexia Sarcopenia Muscle 2:153-161, 2011
8- Leciejewska N et al. J Phys and Pharma 70:525-533, 2019