

# Ibutamoren mesylate

(aka MK-677, MK-0677, L-163,191)

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# Contents of Presentation

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What is Ibutamoren and how does it work?

What are the clinical effects of Ibutamoren?

What are the serum biomarker effects of Ibutamoren?

Take Home Message

# What is Ibutamoren and how does it work?

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# Growth Hormone Releasing Peptides (GHRPs)

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-Growth Hormone Releasing Peptides (GHRPs) are synthetic forms of the natural hormone Ghrelin.

-Ghrelin is a hormone that is secreted from the lining of the stomach, increases hunger, (28-amino acid)

-These simple short-chained amino acid peptide strings (5-amino acids) possess most of the positive characteristics of Ghrelin (such as effecting GH secretion) and few of the negative properties (such as Ghrelin's lipogenic behavior (i.e. conversion of glucose to fatty acids)).

# Growth Hormone Secretagogue (GHS)

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-GHRPs belong to a broader class of compounds all of which share the common trait of being able to bind to the Growth Hormone Secretagogue Receptor (GHS-R) and effect GH release.

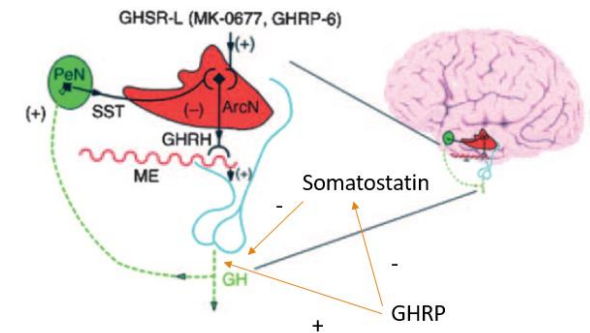
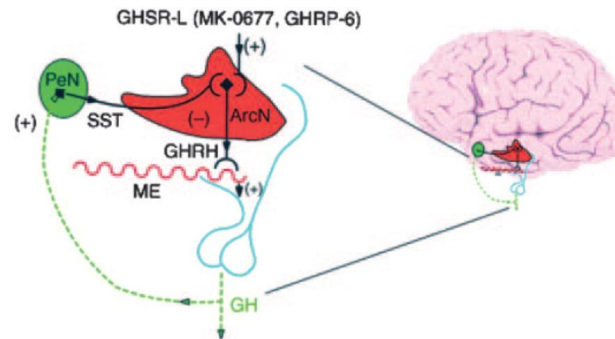
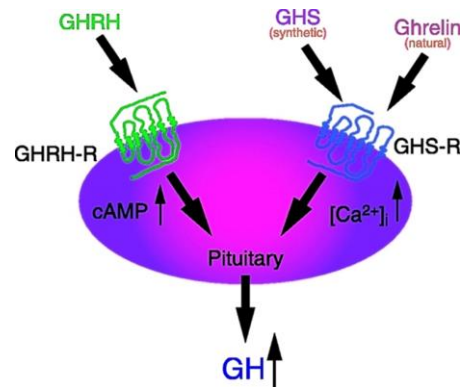
-These compounds include the synthetic peptides (GHRP-6, GHRP-1, GHRP-2, Hexarelin, Ipamorelin) and smaller synthetic non-peptide molecular compounds such as **ibutamoren** as well as the natural ligand Ghrelin.

-This broad class which includes all of the above but not Growth Hormone Releasing Hormone (GHRH) is termed Growth Hormone Secretagogues (GHSs).

# GHS- 3 main pathways of action

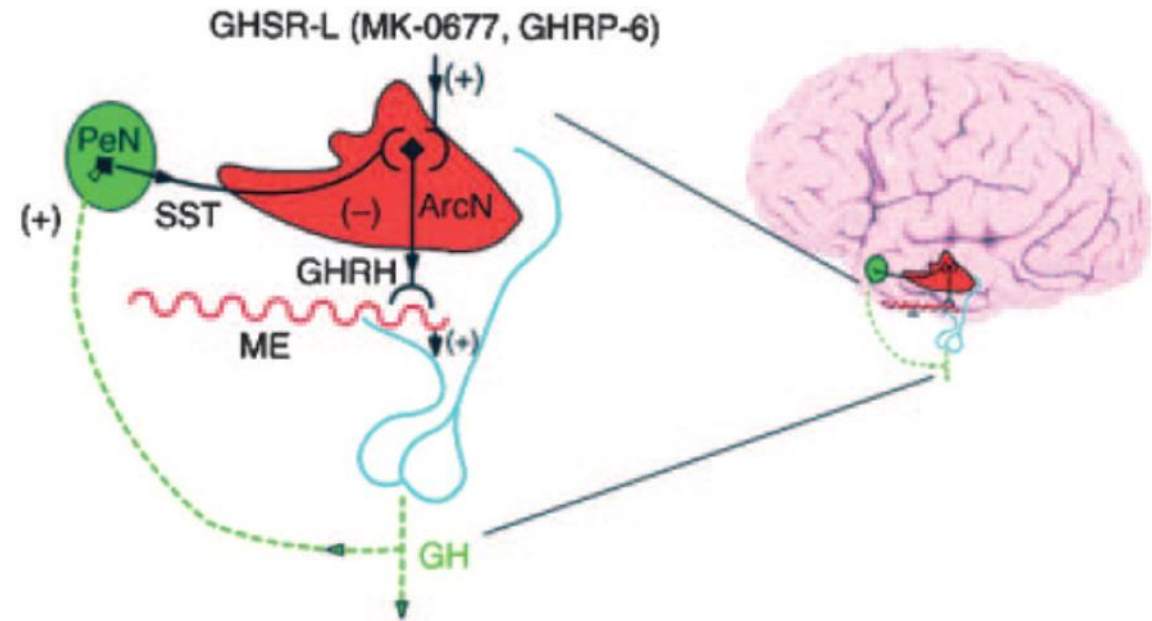
-These Growth Hormone Secretagogues (GHSs) exert their effect on increasing GH output in 3 main pathways.

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# GHS- 1st Pathway

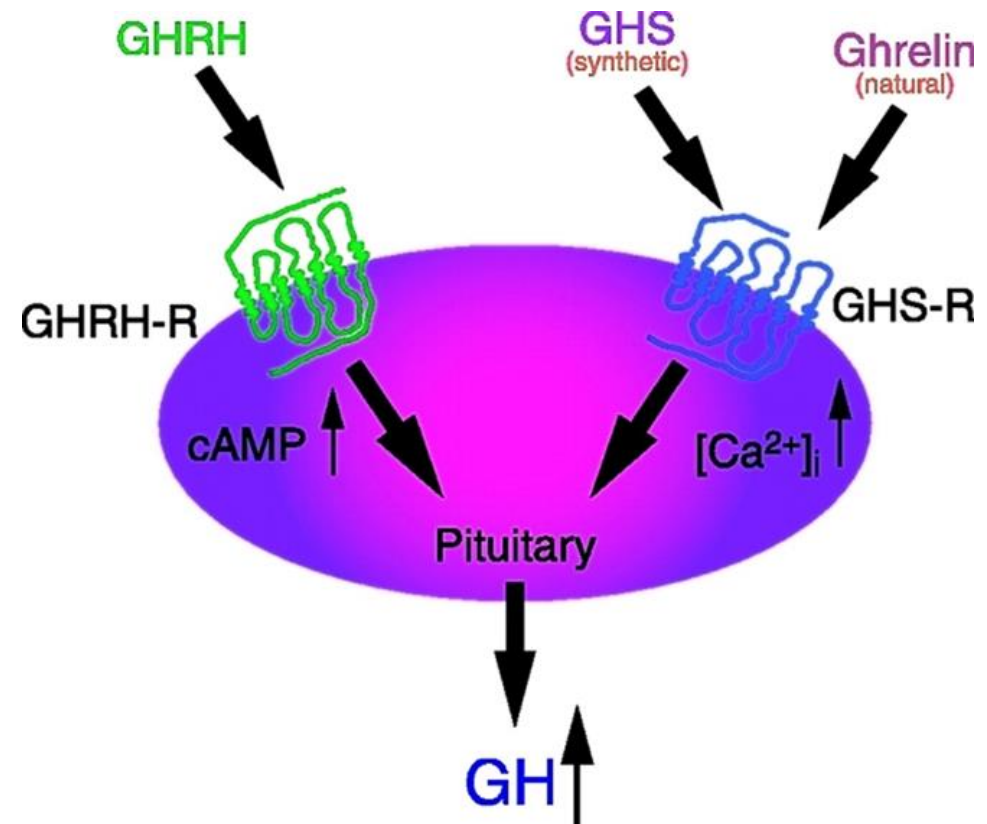
- First they INDIRECTLY increase growth hormone (GH) secretion by inducing Growth Hormone Releasing Hormone (GHRH) release from the hypothalamus in the brain.
- GHRH once released makes its way to the Growth Hormone Releasing Hormone Receptors (GHRH-R) in cells within the pituitary (a gland just below the brain) where it binds and exerts its direct influence in signaling GH release.



# GHS- 2nd Pathway

-Second these GHS also make there way to those same pituitary cells where they themselves bind to a Growth Hormone Secretagogue Receptor (GHS-R) and exert a DIRECT influence in signaling GH release.

-This signaling uses a different mode of action distinct from that of GHRH. As a consequence both bound GHRH & bound GHS can exert their positive influence concurrently resulting in synergistic growth hormone (GH) release.

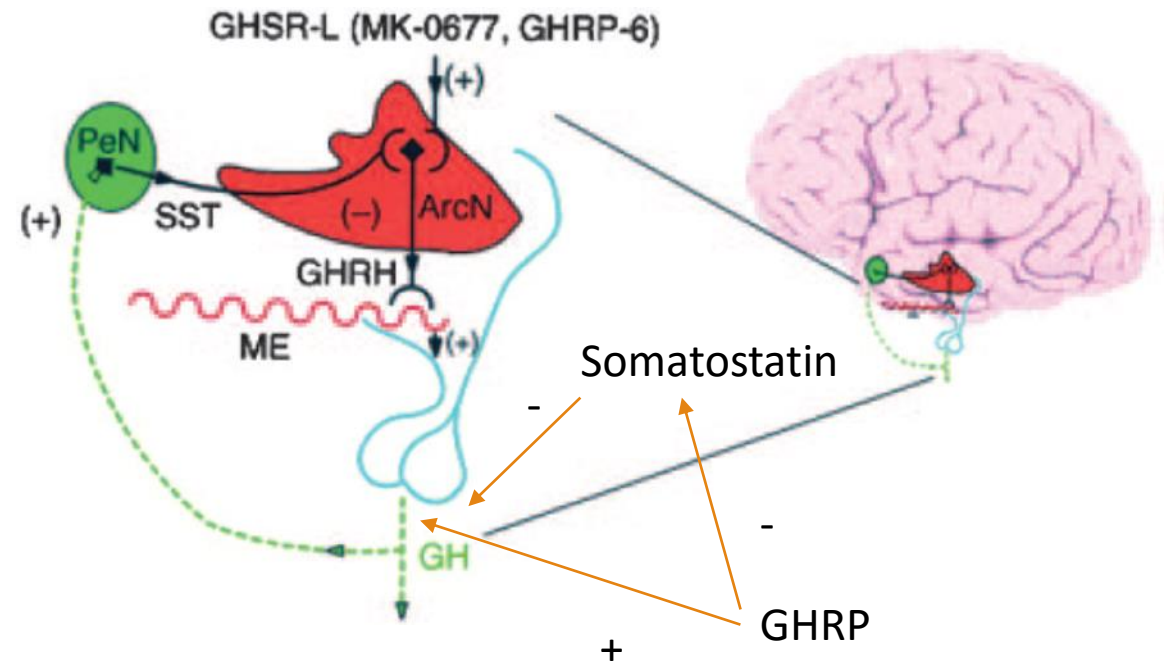




# GHS- 3rd Pathway

-Third they INDIRECTLY increase GH secretion by reducing release of Somatostatin (the GH inhibiting hormone) from the hypothalamus

-DIRECTLY by reducing the magnitude of Somatostatin's inhibiting action once it binds to its receptor on the pituitary cells.



# A 4th Pathway (not widely known)

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Direct effects, not through GH or IGF-1 on muscle

New findings strongly suggest that GHRP-2 (which extends to Ibutamoren) has significant direct effects on muscle cells (myocytes) in skeletal muscle (Yamamoto et al. 2008). Two proteins which specifically in muscle tissue and are responsible for the degradation of muscular protein, Atrogin-1 and MuRF1, have been linked to a diverse range of conditions that are characterized by muscle atrophy (Bodine et al. 2001)(Gomes et al. 2001)(Lecker et al. 2004). GHRP-2 acts through the growth hormone secretagogue receptor (GHSR1a) to suppress the expression of these muscle degrading proteins, Atrogin-1 and MuRF1. The reduction of activity and expression of these proteins might ultimately lead to less muscular atrophy (Yamamoto et al. 2008). Thus the effects of Ibutamoren are elicited directly on muscle cells, in addition to GH or IGF-1.

# GHS- Summary

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- Growth Hormone Secretagogues (GHS) turn up the positive signal to release GHRH
- Turn down the negative signal to release the inhibiting hormone Somatostatin
- Speak directly to the growth hormone releasing pituitary cells themselves to encourage them to release GH
- Speak directly to the growth hormone releasing pituitary cells themselves to encourage them to ignore Somatostatin's message to stop releasing GH

# Quick Note: Sermorelin

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- Sermorelin works synergistically with Ibutamoren
- Sermorelin is a truncated version of GHRH

## GHRH

YADAIFTNS<sub>9</sub> YRKVLGQLSA<sub>19</sub> RKLLQDIMSR<sub>29</sub> QQGESNQERG<sub>39</sub> ARARL<sub>44</sub>

## Sermorelin

YADAIFTNS<sub>9</sub> YRKVLGQLSA<sub>19</sub> RKLLQDIMSR<sub>29</sub>

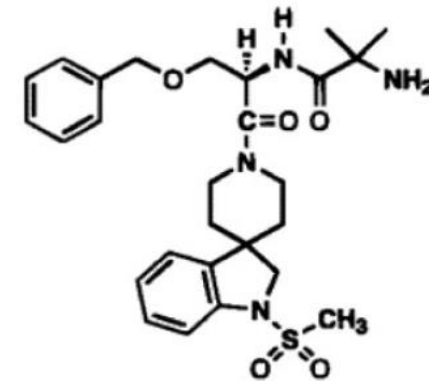


Each letter represents an amino acid

# Oral GHS: Ibutamoren

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- Based on the effectiveness of GHRPs smaller non-peptide molecules were created in an effort to mimic the GH releasing effects of with high oral bioavailability.
- Ibutamoren was eventually created as a non-peptide compound with sustained GH release and higher oral bioavailability



8 L-163,191; MK-0677 ( $EC_{50} = 1.3 \text{ nM}$ )

# General Overview: Ibutamoren

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- Ibutamoren (developmental names MK-677, MK-0677, L-163,191)
- non-peptidic growth hormone secretagogue
- modeled form peptidic structure of GHRP-6 (a peptidic secretagogue)
- long-acting (IGF-1 levels remain elevated in humans with a single oral dose for up to 24 hours)

# General Overview: Ibutamoren (Cont.)

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- orally-active
- selective agonist of the ghrelin receptor (GHSR)
- growth hormone secretagogue
- mimic of the growth hormone (GH)-stimulating action of the endogenous hormone ghrelin

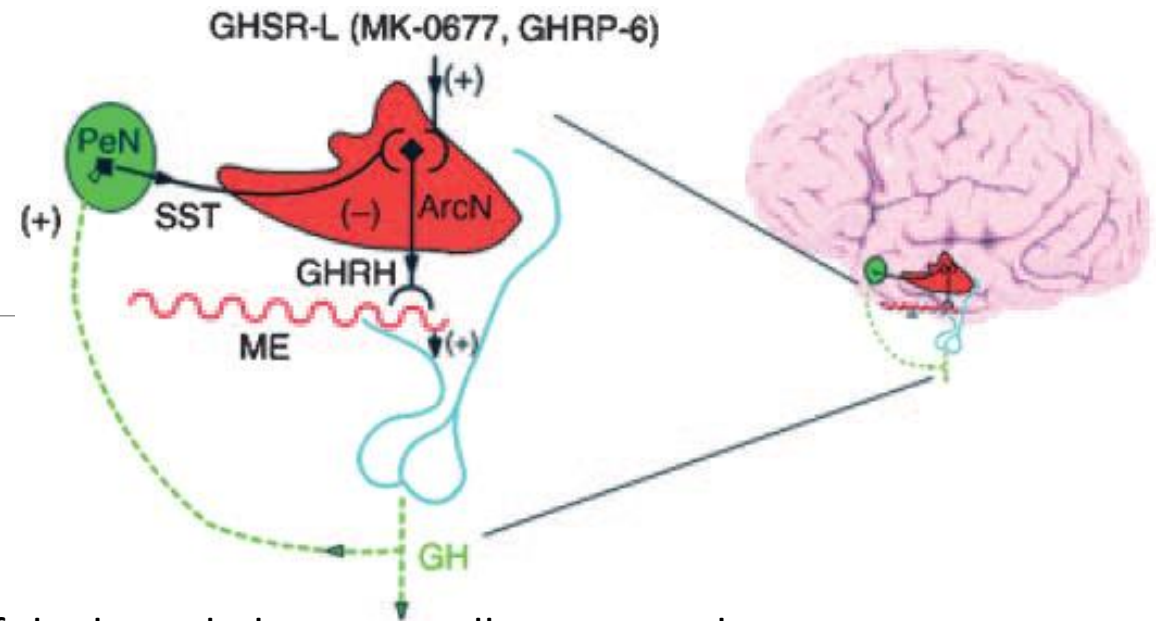
# General Overview: Ibutamoren (Cont.)

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- increases the release of, and produces sustained increases in plasma levels of GH and IGF-1, (affects several other hormones as well)
- potential treatment for reduced levels of GH and IGF-1, such as in children or elderly adults with growth hormone deficiency
- human studies have shown it to increase both muscle mass and bone mineral density
- promising therapy for the treatment of frailty in the elderly
- alters metabolism of body fat and so may have application in the treatment of obesity



# The Complex Axis: Ibutamoren



## GH-mediated negative feedback

1. periventricular nucleus (**PeN**) - composite structure of the hypothalamus, small neurons releases...
2. somatostatin (**sst**) - which inhibits the secretion of growth hormone from somatotrope cells, somatostatin action is inhibited by a...
3. GHSR-L, GHS receptor ligand (**GHSR-L**) - essentially Ibutamoren, GHRP or Ghrelin in the...
4. arcuate nucleus (**ArcN**) - which is a aggregation of neurons in the mediobasal hypothalamus, which releases...
5. growth hormone releasing hormone (**GHRH**) – (essentially Sermorelin) which is inhibited by somatostatin, GHRH acts through the..
6. median eminence (**ME**) - part of hypothalamus from which regulatory hormones are released. It is of great physiological importance, as it is integral to the hypophyseal portal system, which connects the hypothalamus with the pituitary gland communicating with somatotrope cells

# What are the clinical effects of Ibutamoren?

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# Clinical Effects: Ibutamoren

PubMed ID	Subject Characteristics	Subjects	Date	Main Findings
(Chapman et al. 1996)	Healthy Subjects	32	1996	Enhanced Pulsatile GH Release, Increased Circulating Concentrations of GH And IGF-I, Restored Serum IGF-I Concentrations
(Copinschi et al. 1996)	Healthy Young Men	9	1996	Increases Circulating IGF-I, Increases Of GH Pulse Frequency, Enhancement of IV And REM Sleep
(Copinschi et al. 1997)	Healthy Young and Older Adults	8	1997	Improved Sleep Quality IV, REM, And REM Latency

# Clinical Effects: Ibutamoren (cont.)

(Chapman et al. 1997)	Severely GH-Deficient Men	9	1997	Increased GH, IGF-I, And IGFBP-3 (Modest Relative To Responses Seen With Exogenous GH)
(Svensson, Ohlsson, et al. 1998)	Obese Males, 19-49 Years of Age	24	1998	Increases Markers Of Both Bone Resorption And Formation
(Svensson, Lonn, et al. 1998)	Obese Males, 18-50 Years of Age	24	1998	Increase In Fat-Free Mass
(Murphy et al. 1998)	Healthy Volunteers, 24-39 Years of Age	8	1998	Reverses Diet-Induced Nitrogen Wasting

# Clinical Effects: Ibutamoren (cont.)

(Svensson, Carlsson, et al. 1999)	Obese Males	24	1999	Increased Serum Free T3 After 8 Weeks, Affects Regulation Of Adipose Tissue Mass and Fuel Metabolism
(Murphy et al. 1999)	Elderly Adults (65 Years or Older)	187	1999	Elevations In Biochemical Markers Of Bone Resorption and Formation
(Svensson, Jansson, et al. 1999)	Obese Males, 18-50 Years of Age	24	1999	Decreased LDL-C/HDL-C Ratio
(Codner et al. 2001)	Prepubertal Children (15 Male, 3 Female) With Idiopathic GH Deficiency	18	2001	Increase GH, IGF-I, And IGFBP-3 Levels In Some Children With GH Deficiency

# Clinical Effects: Ibutamoren (cont.)

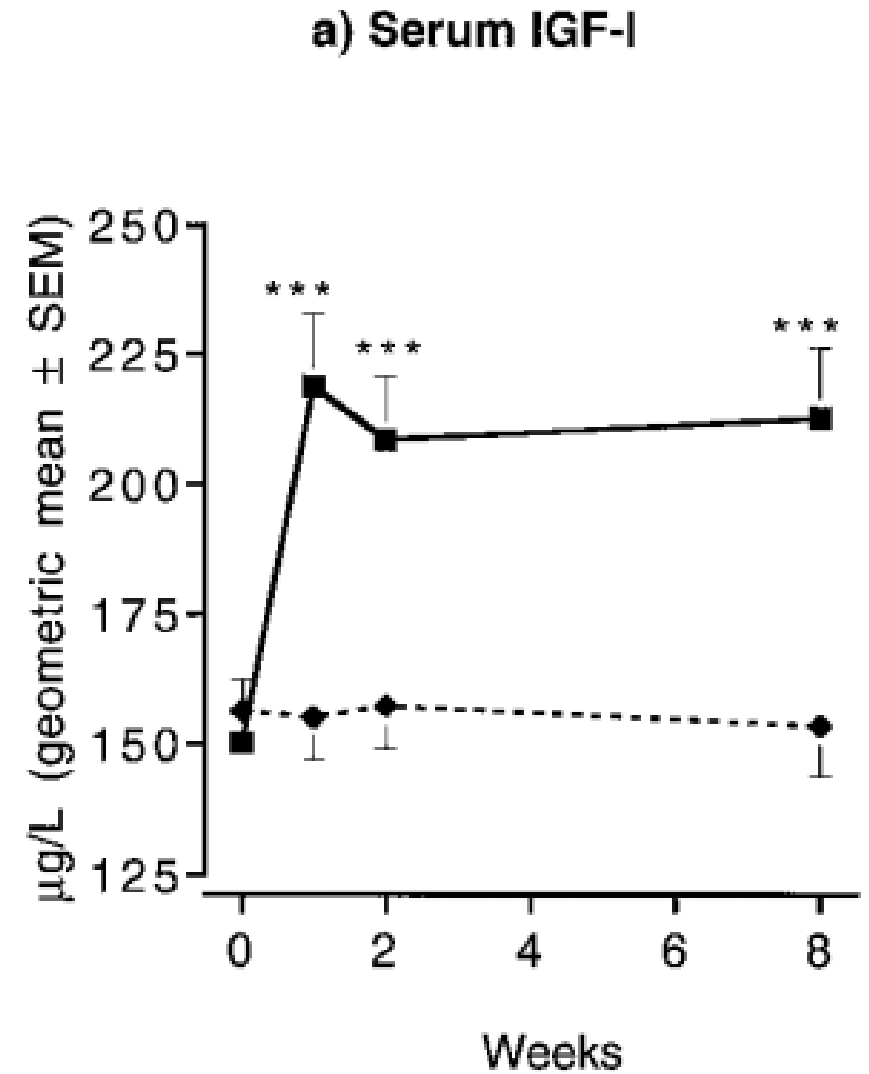
(Murphy et al. 2001)	Women With Postmenopausal Osteoporosis	292	2001	Attenuated The Indirect Suppressive Effect Of Drug (Alendronate) On Bone Formation
(Bach et al. 2004)	Hip-Fracture Patients Who Were Aged 65 And Older	161	2004	Increased Serum IGF-I, No Significant Functional Improvement
(Sevigny et al. 2008)	Patients With Mild to Moderate Ad	563	2008	Ineffective At Slowing The Rate of Progression Of Alzheimer Disease
(Adunsky et al. 2011)	Elderly Hip Fracture Patients	123	2011	Increase In Plasma IGF-1 Levels Was Not Paralleled By Improvement, Unfavorable Safety Profile In This Patient Population.

# What are the serum biomarker effects of Ibutamoren?

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# IGF-1

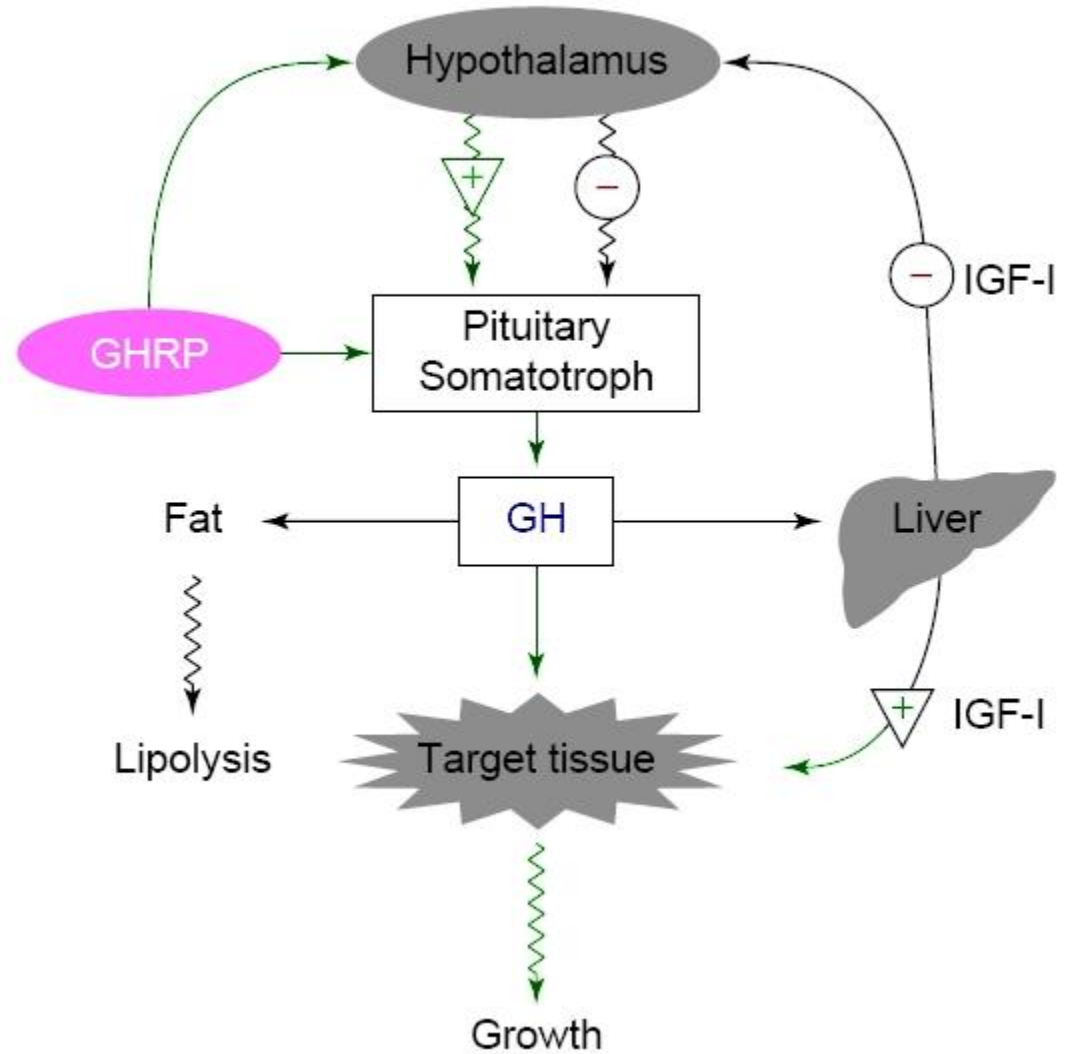
-serum concentrations of IGF-I during 2-month treatment with Ibutamoren (25 mg) or placebo daily in obese males.



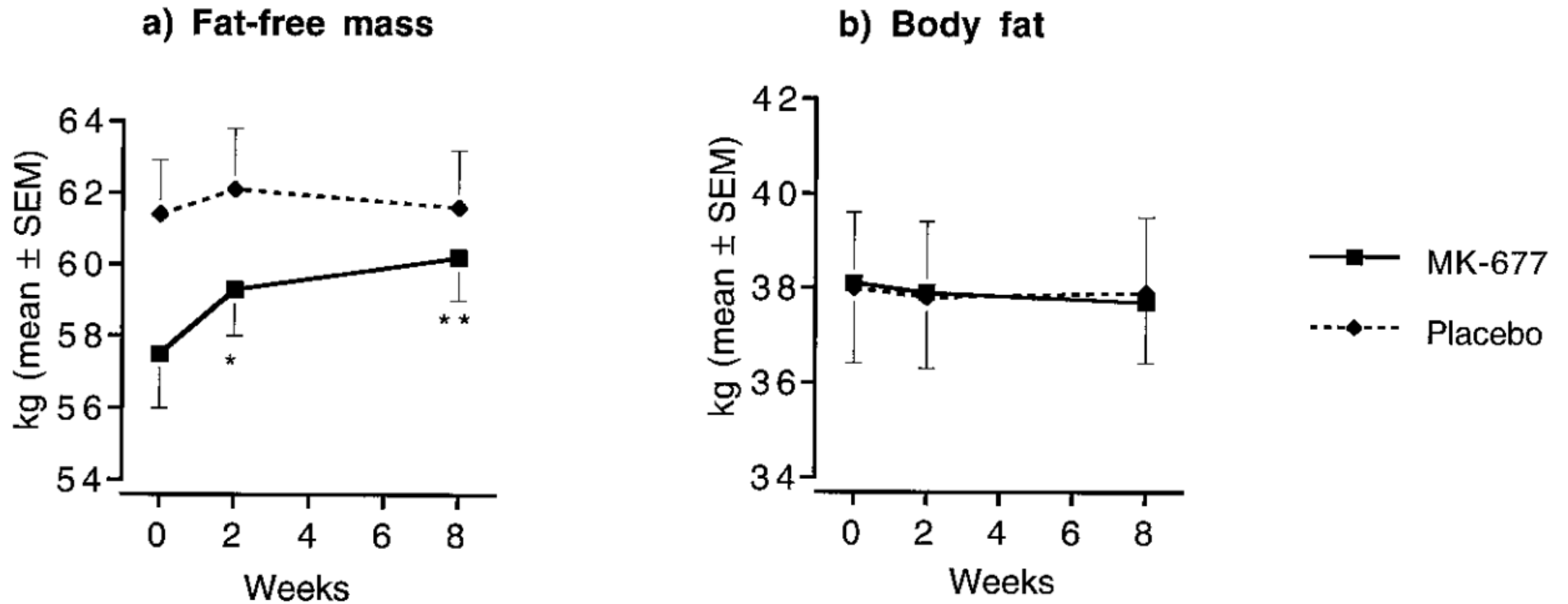


# Axis: Ibutamoren

-hyperstimulation of the GH/IGF-I axis by high doses of Ibutamoren (GHS) is prevented by IGF-I-mediated negative feedback



# Body Composition



# IGF-1 Binding Proteins

\*  $p < 0.01$ , †  $p \leq 0.001$ , ‡  $p < 0.05$ .

<i>Variable</i>	<i>Baseline</i>	<i>2 weeks</i>	<i>8 weeks</i>
Serum IGF-I (ng/ml)			
MK-677	150.3 (12.1)	208.5 (12.2)*	212.8 (13.6)*
placebo	156.4 (8.2)	157.3 (8.0)	153.5 (9.7)
Serum IGFBP-3 (mg/l)			
MK-677	2.8 (0.1)	3.5 (0.1)*	3.2 (0.2)*
placebo	2.8 (0.1)	2.7 (0.1)	2.7 (0.1)
Serum IGFBP-4 (ng/ml)			
MK-677	358.5 (21.6)	443.1 (25.7)*	406.3 (18.1)
placebo	407.8 (16.7)	400.8 (16.4)	442.8 (14.3)
Serum IGFBP-5 (ng/ml)			
MK-677	390.2 (24.5)	549.0 (18.6)*	545.7 (17.8)†
placebo	367.8 (13.0)	387.1 (14.0)	429.9 (18.3)

# Collagen/Bone Formation Markers

<i>Variable</i>	<i>Baseline</i>	<i>2 weeks</i>	<i>8 weeks</i>
Type I procollagen propeptide ( $\mu\text{g/l}$ )		* $p < 0.01$ , $^{\dagger}p \leq 0.001$ , $^{\ddagger}p < 0.05$ .	
MK-677	108.5 (27.1)	132.2 (23.4)*	147.8 (39.8) $^{\dagger}$
placebo	107.1 (8.3)	112.6 (8.4)	114.3 (9.0)
P-III-NP (kU/l)			
MK-677	0.46 (0.04)	0.59 (0.05) $^{\dagger}$	0.63 (0.04) $^{\dagger}$
placebo	0.43 (0.04)	0.43 (0.03)	0.41 (0.03)
Osteocalcin ( $\mu\text{g/l}$ )			
MK-677	9.09 (0.66)	9.12 (0.65)	10.38 (0.73)*
placebo	10.60 (0.68)	10.63 (0.68)	10.83 (0.58)
Type I collagen telopeptide ( $\mu\text{g/l}$ )			
MK-677	3.97 (0.54)	4.69 (0.62) $^{\dagger}$	4.84 (0.57) $^{\dagger}$
placebo	4.16 (0.47)	3.83 (0.36)	3.86 (0.42)

# Collagen/Bone Formation Markers

\* $p < 0.01$ ,  $^{\dagger}p \leq 0.001$ ,  $^{\ddagger}p < 0.05$ .

Urine hydroxyproline/ creatinine ( $10^{-3}$ )			
MK-677	12.00 (0.71)	15.83 (1.50)*	14.42 (0.71) $^{\ddagger}$
placebo	12.75 (0.94)	12.45 (1.16)	11.83 (1.11)
Urine calcium/creatinine (mmol/mmol)			
MK-677	0.26 (0.02)	0.43 (0.04) $^{\ddagger}$	0.35 (0.03) $^{\ddagger}$
placebo	0.28 (0.04)	0.30 (0.05)	0.27 (0.03)
Serum calcium (mmol/l)			
MK-677	2.31 (0.03)	2.34 (0.03) $^{\ddagger}$	2.30 (0.02)
placebo	2.31 (0.02)	2.26 (0.02)	2.29 (0.02)
Serum intact PTH (ng/l)			
MK-677	40.6 (4.7)	38.2 (3.2)	44.1 (4.9)
placebo	44.9 (5.2)	45.8 (5.2)	46.4 (5.2)

# Growth Hormone and Prolactin

Variable	Initiation of treatment	2 weeks	8 weeks
Peak GH (mIU/L)			
MK-677	65.4 (13.1) <sup>a</sup>	17.0 (3.3) <sup>a</sup>	14.3 (3.9) <sup>a</sup>
Placebo	2.0 (0.8)	1.5 (0.8)	0.9 (0.4)
GH AUC (mIU·h/L)			
MK-677	144.4 (32.1) <sup>a</sup>	33.1 (5.0) <sup>a</sup>	29.0 (7.5) <sup>a</sup>
Placebo	7.1 (2.2)	5.8 (2.3)	3.8 (1.0)
Peak PRL (mIU/L)			
MK-677	737 (59) <sup>a</sup>	358 (24)	372 (35)
Placebo	224 (29)	290 (51)	282 (50)
PRL AUC (mIU·h/L)			
MK-677	3565 (259) <sup>a</sup>	2135 (157) <sup>a</sup>	2015 (196) <sup>b</sup>
Placebo	1097 (143)	1261 (170)	1252 (162)

<sup>a</sup>  $P < 0.001$ .

<sup>b</sup>  $P < 0.01$ .

<sup>c</sup>  $P < 0.05$ .

# Growth Hormone

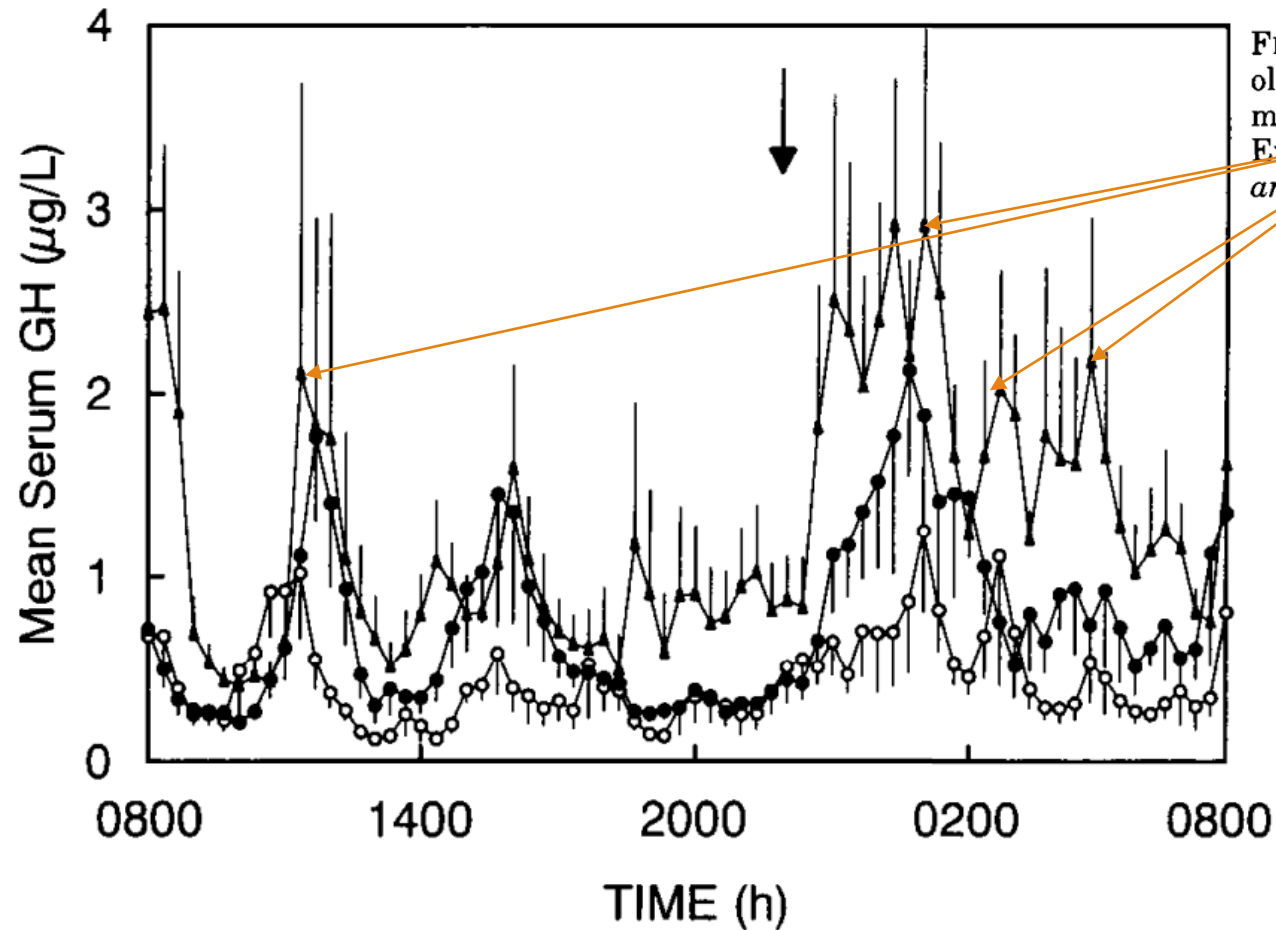


FIG. 2. Mean ( $\pm$ se) serum GH concentrations (micrograms per L) in older subjects after 2 weeks of treatment with placebo ( $\circ$ ;  $n = 10$ ), 10 mg/day MK-677 ( $\bullet$ ;  $n = 12$ ), and 25 mg/day MK-677 ( $\blacktriangle$ ;  $n = 10$ ). Evening treatment time (between 2200–2300 h) is indicated by an arrow.

# hypothalamic–pituitary–adrenal axis (HPA)

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Peak cortisol (nmol/L)			
MK-677	634 (34) <sup>a</sup>	329 (21)	357 (30)
Placebo	313 (20)	329 (28)	296 (15)
Cortisol AUC (nmol·h/L)			
MK-677	3439 (235) <sup>a</sup>	1977 (109)	2129 (129)
Placebo	1901 (108)	1971 (116)	1806 (90)
Urinary free cortisol/creatinine ratio (10 <sup>-6</sup> )			
MK-677	26.2 (3.0)	17.7 (2.0)	21.4 (3.3)
Placebo	18.5 (2.6)	14.9 (2.2)	15.4 (1.3)
17-OHCS/creatinine ratio (10 <sup>-3</sup> )			
MK-677	6.0 (0.5)	6.2 (0.7)	6.8 (0.6)
Placebo	3.8 (0.3)	3.6 (0.4)	4.1 (0.4)

<sup>a</sup>  $P < 0.001$ .

<sup>b</sup>  $P < 0.01$ .

<sup>c</sup>  $P < 0.05$ .



# hypothalamic–pituitary–thyroid axis (HPT)

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Variable	Initiation of treatment	2 weeks	8 weeks
Peak TSH (mU/l)		* $P < 0.05$ ; ** $P < 0.01$ ; † $P = 0.05$ †† $P < 0.09$ .	
MK-677	1.94 (0.18)	2.17 (0.20)	2.17 (0.18)*
Placebo	1.54 (0.23)	1.72 (0.27)	1.62 (0.18)
Free T3 (pmol/l)			
MK-677	5.66 (0.15)	5.71 (0.17)	6.04 (0.19)*
Placebo	5.66 (0.13)	5.55 (0.09)	5.78 (0.15)
Free T4 (pmol/l)			
MK-677	17.1 (0.7)	15.1 (0.6)†	16.5 (0.7)
Placebo	17.1 (1.0)	16.4 (1.0)	16.7 (1.0)
Free T3/T4 (pmol/pmol)			
MK-677	0.33 (0.01)	0.38 (0.02)*	0.37 (0.01)††
Placebo	0.34 (0.02)	0.35 (0.02)	0.36 (0.02)

# hypothalamic–pituitary–gonadal axis (HPG)

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\*  $P < 0.05$ ; \*\*  $P < 0.01$ ; †  $P = 0.05$  ††  $P < 0.09$ .

Total testosterone (nmol/l)

MK-677 22.4 (1.4)

19.7 (1.6)\*

20.7 (1.8)\*

Placebo 19.8 (2.0)

20.4 (1.9)

21.6 (1.9)

SHBG (nmol/l)

MK-677 24.1 (3.0)

20.9 (2.9)\*\*

21.6 (2.8)†

Placebo 21.6 (2.8)

21.8 (3.5)

22.3 (3.6)

Total testosterone/SHBG ratio (nmol/nmol)

MK-677 1.09 (0.13)

1.12 (0.14)

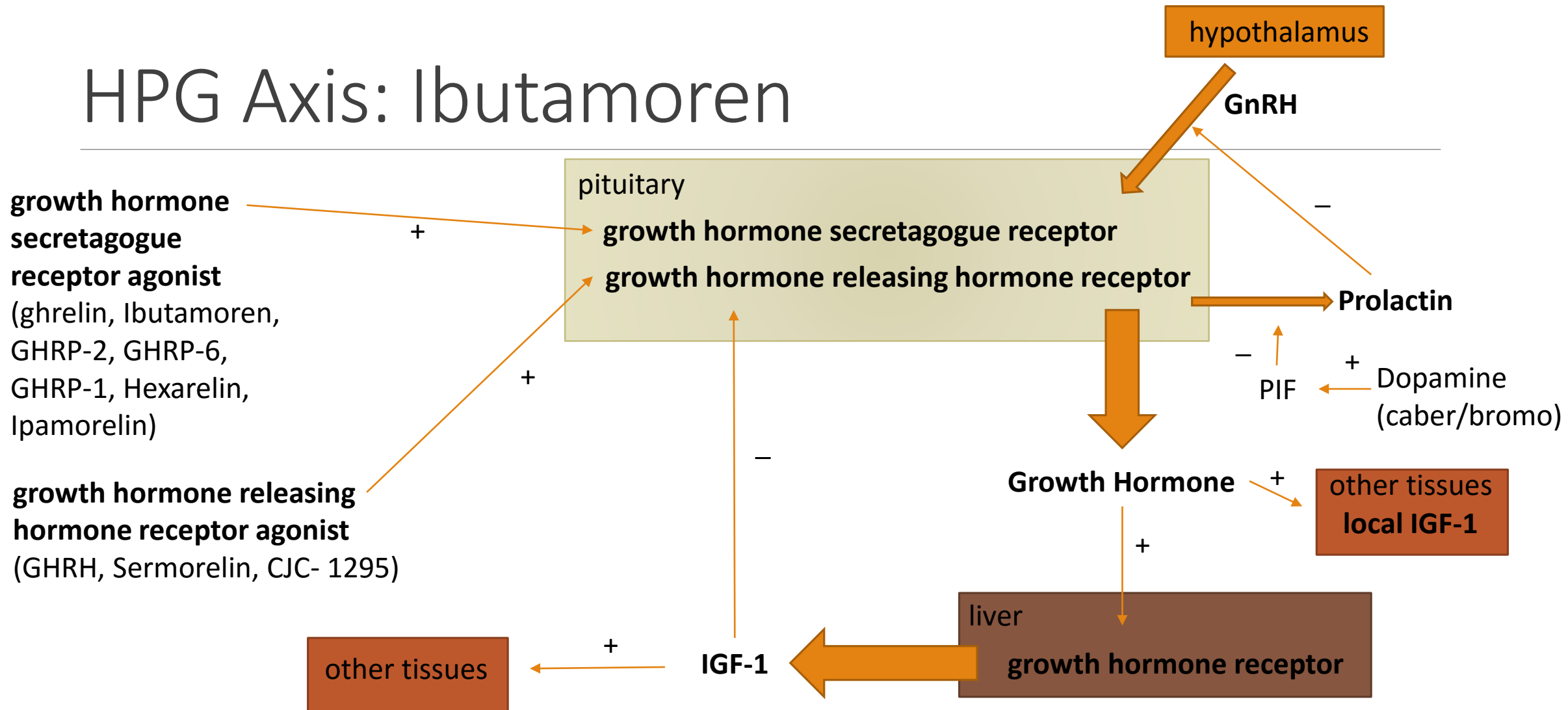
1.12 (0.14)

Placebo 1.03 (0.11)

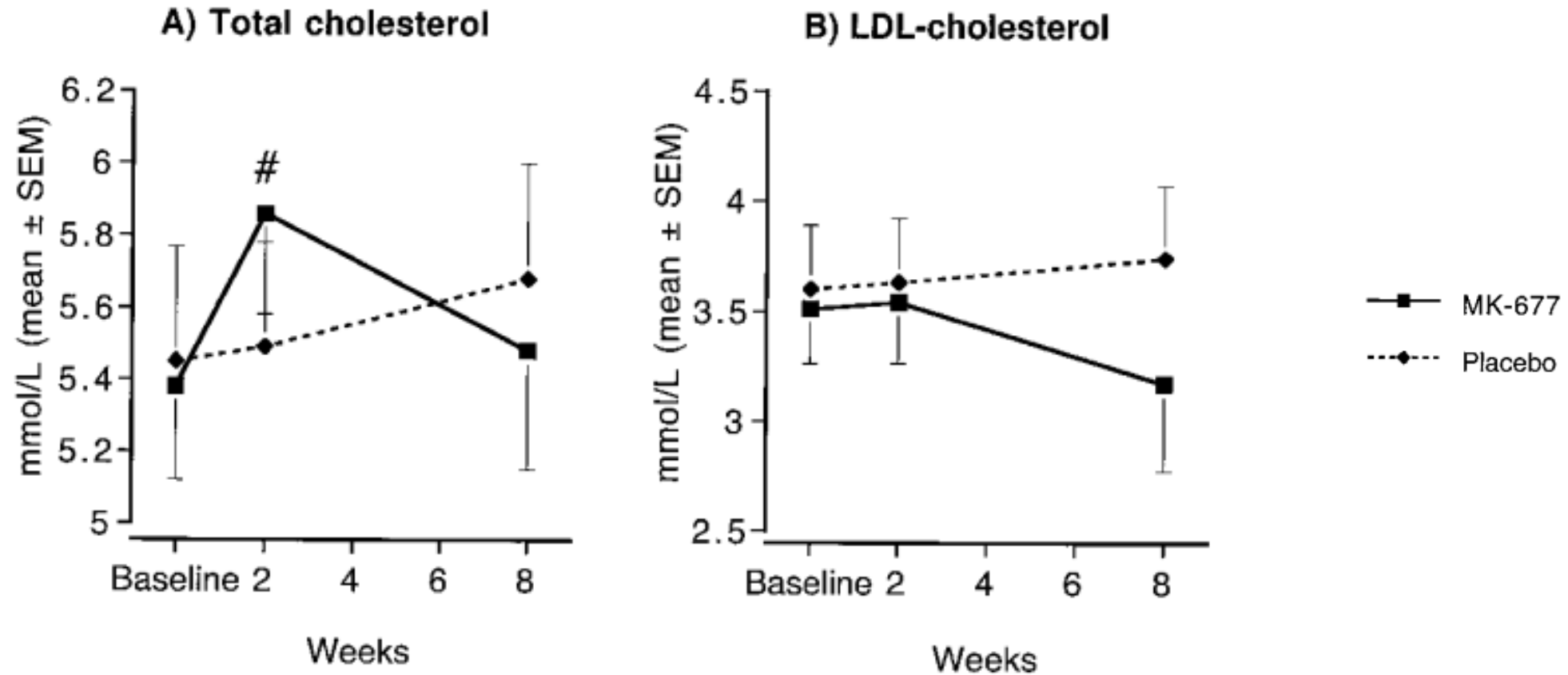
1.06 (0.14)

1.16 (0.16)

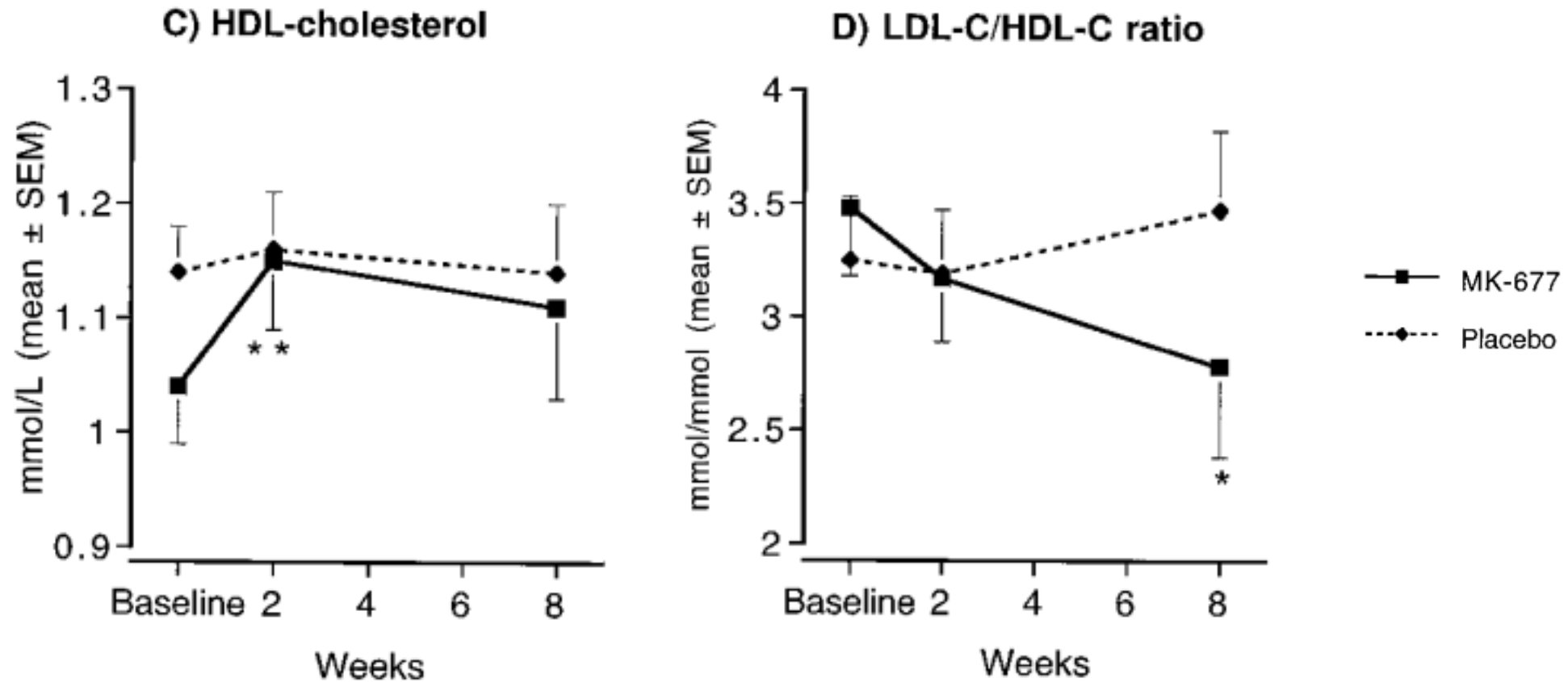
# HPG Axis: Ibutamoren



# Cholesterol and LDL



# HDL and LDL/HDL Ratio



# Lipoproteins

Variable	Baseline	2 weeks	8 weeks	<sup>a</sup> $P < 0.001$ . <sup>b</sup> $P < 0.01$ . <sup>c</sup> $P < 0.05$ .
Lp(a) (mg/L)				
MK-677	118.4 (89.2)	119.6 (91.2)	119.8 (95.1) <sup>a</sup>	
Placebo	109.3 (46.0)	109.6 (42.1)	100.3 (42.1)	
ApoA-1 (g/L)				
MK-677	1.27 (0.04)	1.42 (0.04) <sup>b</sup>	1.30 (0.06)	
Placebo	1.36 (0.03)	1.35 (0.04)	1.40 (0.05)	
ApoB (g/L)				
MK-677	1.28 (0.06)	1.37 (0.09) <sup>a</sup>	1.26 (0.10)	
Placebo	1.28 (0.08)	1.27 (0.08)	1.31 (0.09)	
ApoE (g/L)				
MK-677	0.038 (0.003)	0.045 (0.003) <sup>c</sup>	0.039 (0.003)	
Placebo	0.038 (0.003)	0.037 (0.003)	0.039 (0.003)	

# Lipoproteins and Lipids

Variable	Baseline	2 weeks	8 weeks
Mean LDL particle diameter (nm)			
MK-677	26.6 (0.32)	26.2 (0.42) <sup>a</sup>	27.2 (0.34)
Placebo	27.4 (0.39)	27.7 (0.31)	27.5 (0.37)
Triglycerides (mmol/L)			
MK-677	1.75 (0.20)	2.92 (0.63) <sup>a</sup>	2.12 (0.25)
Placebo	1.63 (0.25)	1.62 (0.18)	1.76 (0.21)
Abdominal LPL activity (mU/g adipose tissue)			
MK-677	141 (17)	ND	161 (15)
Placebo	171 (36)	ND	248 (47)
Gluteal LPL activity (mU/g adipose tissue)			
MK-677	120 (16)	ND	132 (21)
Placebo	190 (92)	ND	200 (30)

<sup>a</sup>  $P < 0.001$ .

<sup>b</sup>  $P < 0.01$ .

<sup>c</sup>  $P < 0.05$ .

# Body Parameters

Variable	Baseline	2 weeks	8 weeks	<sup>a</sup> $P < 0.001$ . <sup>b</sup> $P < 0.01$ . <sup>c</sup> $P < 0.05$ .
BW (kg)				
MK-677	99.3 (2.3)	100.9 (2.3) <sup>a</sup>	102.0 (2.4) <sup>b</sup>	
Placebo	103.4 (2.1)	102.8 (1.9)	103.1 (1.8)	
Sagittal diameter (cm)				
MK-677	26.2 (0.4)	ND	26.2 (0.7)	
Placebo	24.8 (0.4)	ND	25.0 (0.4)	
Visceral fat vol (L)				
MK-677	5.54 (0.58)	ND	5.32 (0.59)	
Placebo	4.79 (0.40)	ND	4.75 (0.39)	
TBN (kg)				
MK-677	1.85 (0.06)	1.91 (0.05)	1.92 (0.06)	
Placebo	2.02 (0.06)	1.96 (0.08)	2.07 (0.06)	
TBW (kg)				
MK-677	50.6 (1.9)	54.6 (1.2)	55.2 (1.6)	
Placebo	53.4 (1.0)	56.0 (1.7)	55.8 (1.5)	



# Cardiovascular Parameters

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Systolic blood pressure  
(mm Hg)

MK-677	131.2 (3.2)	129.1 (1.9)	134.1 (4.7)
Placebo	124.4 (3.1)	126.5 (3.4)	134.2 (3.4)

Diastolic blood pressure  
(mm Hg)

MK-677	78.8 (3.4)	79.0 (2.5)	83.7 (3.2) <sup>c</sup>
Placebo	80.6 (2.1)	78.8 (2.7)	79.0 (2.7)

Heart rate (beats/min)

MK-677	58.6 (2.7)	62.5 (3.6)	61.3 (3.0) <sup>c</sup>
Placebo	60.0 (2.5)	62.5 (2.3)	55.9 (1.8)

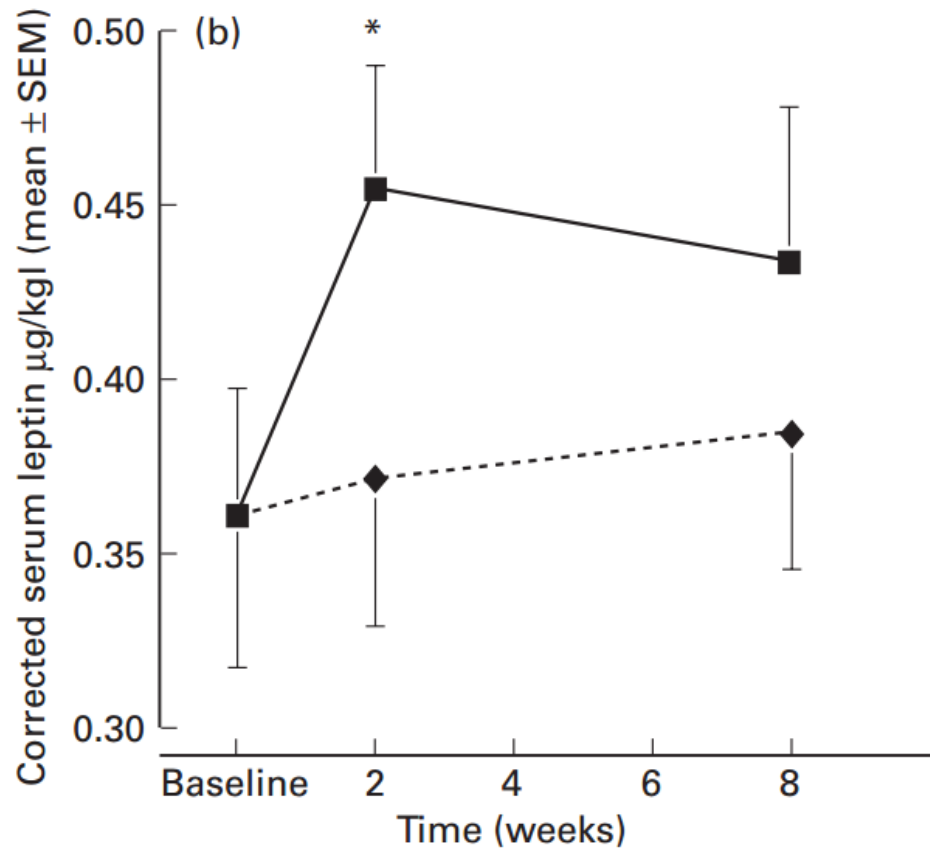
Values are presented as the mean ( $\pm$ SEM). *P* values are based on a between-group analysis of the percent change from baseline. ND, Not determined.

<sup>a</sup> *P* < 0.001.

<sup>b</sup> *P* < 0.01.

<sup>c</sup> *P* < 0.05.

# Leptin



In the steady-state condition, serum leptin reflects the amount of total body fat (Maffei et al., 1995; Considine et al., 1996)

Leptin improves peripheral (hepatic and skeletal muscle) insulin sensitivity and modulates pancreatic  $\beta$ -cell function. Leptin resistance is associated with reduction of leptin-mediated JAK–STAT signaling, and induction of suppressor of cytokine signaling-3 (SOCS-3). (PMID: 23266767)

**Fig. 1** (a) Serum leptin and (b) serum leptin corrected for total body fat during 2 months treatment with MK-677 25 mg (■) or placebo (◆) daily in obese males. In (b), leptin/body fat ratios are calculated by the use of previously reported total body fat values obtained by DEXA measurements (Svensson *et al.*, 1998). *P*-values are based on a between-group analysis of percentage change from baseline.  
\*  $P < 0.05$ .

# Appetite

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- increased in appetite by lbutamoren (PMID: 10468903) has been described
- could possibly have explained the transient leptin increase.
- systemic GHRP-6 injection activates cells containing neuropeptide Y (NPY) while leptin decreases NPY expression, in the arcuate nucleus of the rat hypothalamus (Schwartz et al., 1996; Dickson & Luckman, 1997).
- NPY, as well as the GHRP KP-102, stimulates feeding (Clark et al., 1984; Okada et al., 1996).
- however, the dietary questionnaires used in the present study did not detect any increase in food intake (Svensson et al., 1998).

# Take Home Message

Component	Change over 8 weeks (25mg Ibutamoren)	Meaning
IGF-1	41%	Lean Mass Support
Fat Free Mass	5%	Increase in Lean Tissue
Body Fat	-1%	Loss in Body Fat (kg)
Procollagen Peptide	36%	Tendon and Bone Strengthening/Repair
Free T3	7%	Body Regulation

Dosage recommendations:

-25mg to 50mg Ibutamoren HS

-(optional) 100 mcg Sermorelin TID, BID or QD

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