Testosteronology Society™ Peptide Resource

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Audience:
This resource is intended for clinicians with a foundational understanding of physiology, endocrinology, and pharmacology who are seeking to expand or solidify their knowledge base regarding the clinical evaluation and contextual use of therapeutic peptides in adult patients.

Scope:
This document focuses on a high-level, evidence-based review of selected peptide therapies relevant to metabolic, endocrine, and performance-adjacent clinical care. It emphasizes pharmacologic mechanisms, safety considerations, regulatory context, and available human and preclinical data. It does not provide prescriptive treatment algorithms, compounding guidance, or dosing protocols, nor does it address complex scenarios such as athletic enhancement, fertility preservation, pediatric use, or management of patients with significant comorbidities that may complicate clinical decision-making.

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Definition:

A class of pharmaceuticals that is composed of a series of amino acids usually with a larger molecule size than small molecule pharmaceuticals and smaller molecule size than biologics.

History:

The first therapeutic peptide, insulin, was isolated in 1921. It was originally derived from bovine (cow) or porcine (pig) sources.
Peptides became more popular in the 1950s-1990s with nearly 40 peptides being approved worldwide.
2000-present: Recombinant technology pushed peptide development even further. By 2019, 10 of the top 200 drugs with the top sales included non-insulin peptides.

Pharmacology/Medicinal Chemistry[1]:

Sequences of peptides and large molecular size
Peptides shine in treating conditions that require large surface interactions such as Protein-Protein interactions with extracellular receptors compared to small molecules that can penetrate into the cell and exhibit intracellular actions.

Peptides have 2 drawbacks:

1. Membrane impermeability: Peptides inherently cannot cross cellular membranes due to their large size so their actions are limited to extracellular targets.
2. Poor In vivo stability: Due to the nature of peptides having a structure of sequences of amino acids joined together by amide bonds, peptides are prone to hydrolysis and destruction inside the body. Thus making it very challenging to formulate in an oral tablet. Most peptides are administered by injection which can present a challenge in adherence for those who have a fear of needles.

General uses of peptides:

- Medical (Ex. Insulin, GH, GLP-1s, glucagon, leuprolide,…etc)
- Performance (BPC-157, Growth Hormone secretagogues, Thymosin Alpha 1, PT 141,…Etc)

Introduction to GLP-1, GIP, and Glucagon:

1. Glucagon-like-peptide-1 (GLP-1)[1]:

Peptide produced and secreted by L cells in the intestines after ingestion of a meal and stimulates insulin release, delays gastric emptying, suppresses the appetite, and protects the heart. Therapeutic Effects: Reduces fasting and post prandial blood glucose, weight loss, cardio protection.

2. Glucose dependent insulinotropic polypeptide (GIP)[1]

Peptide Produced and secreted by K cells in the duodenum and jejunum. It was originally reported to Inhibit gastric secretion. GIP Potentiates insulin release and weight loss in combination with GLP-1s

3. Glucagon[1]

Peptide produced and secreted by alpha cells in the pancreas to maintain glucose homeostasis —> Gluconeogenesis & glycogenolysis and lipolysis & inhibiting lipogenesis. Promotes satiety and increase energy expenditure.

Therapeutic effects: Lipid catabolism, increase energy expenditure, reduce food intake.

Effects of GLP-1, GIP, and Glucagon on Different Tissues in the Body[1]			
Body Tissue/Peptide	**GLP-1**	**GIP**	**Glucagon**
Serum	• Inc insulin • Dec glucagon • Dec glucose	• Inc insulin • Decrease glucose	• Inc insulin
Stomach	• Dec gastric emptying • Dec pp glucose	• Dec gastric acid secretion	X
Brain	• Inc satiety • Dec body weight	• Dec food intake • Dec body weight	• Dec food intake • Dec body weight
Heart	• Decrease CVD risk	X	X
Fat Cells	X	• Inc energy expenditure	• Inc energy expenditure
Liver	X	X	• Inc gluconeogenesis • Dec lipogenesis • Inc lipolysis

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GLP-1 Receptor Agonists:

Semaglutide (Ozempic/Wegovy):
Indications:

- Glycemic Control as an adjunct to diet and exercise in T2DM (Ozempic)[2]

Considered first line therapy for glycemic control in patients with ASCVD or high risk for ASCVD[3].

- Reduce the risk of MACE reduction in patients with established CVD with T2DM, overweight or obesity (Ozempic & Wegovy)[2,4].

- Reduce the risk of sustained eGFR decline, ESRD, and CV death in patients with CKD and T2DM (Ozempic)[2].

Considered an alternative to SGLT2i for glycemic control in patients with CKD[3].

- Reduce excess body weight and maintain weight loss long term in patients age 12 years-old and older with obesity or overweight adults with at lease one weight-related comorbid condition. (Wegovy)[4]

68 weeks of therapy at 2.4 mg reported a change in weight of -12.44% compared with placebo. 86.4%, 69.1%, 50.5%, and 32.1% of participants lost 5,%, 10%, 15%, and 20% of their initial bodyweight respectively[5].

GLP-1/GIP:

Tirzepatide (Mounjaro/Zepbound):
Indications:

- Glycemic Control as an adjunct to diet and exercise in T2DM (Mounjaro)[6].

Very high glucose lowering efficacy and is considered first line in glycemic control for patients with T2DM. CVD and CKD benefits not established yet[3].

- Reduce excess body weight and maintain weight loss long term in adults with obesity or overweight adults with at lease one weight-related comorbid condition (Zepbound)[7].

See Figure 1 and 2 below[8]

- Treat moderate to severe OSA in adults with obesity (Zepbound)[7].

Significant improvements in apnea-hypoxic index (AHI) and sleep disturbances. Reduction in OSA related CV risk factors.

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GLP-1/GIP/Glucagon:

Retatrutide.
Not FDA approved for any indications yet. Currently undergoing Phase 3 clinical trials set to end in 2026.
Unprecedented at weight loss from Phase 2 clinical trial results (Figure 3 and 4)[10].

Dosing

- Semaglutide (Ozempic)[2]

Start at 0.25 mg/week x 4 weeks then increase to 0.5 mg/week based on glycemic control.
Can increase to 1 mg/week after 4 weeks on 0.5 mg/week.
Can increase to a max of 2 mg/week after 4 weeks on 1 mg/week.

- Semaglutide (Wegovy)[4]

Start at 0.25 mg/week x 4 weeks then 0.5 mg/week x 4 weeks then 1 mg/week x 4 weeks then 1.7 mg/week (maintenance) based on treatment response
Can increase to a maximum of 2.4 mg/week after 4 weeks on 1.7 mg/week dose.

- Tirzepatide (Mounjaro and Zepbound)[6,7]:

Start at 2.5 mg/week x 4 weeks then increase to 5 mg/week based on treatment response.

Can increase in 2.5 mg/week increments every 4 weeks for a maximum dose of 15 mg/week.
The recommended treatment dose of Zepbound for OSA is 10 or 15 mg/week[7].

- Retatrutide[10]:

Has not passed FDA approval yet. Still undergoing clinical trials. Participants in a Phase 2 trial were started on 1 mg, 2 mg or 4 mg and a portion of the participants escalated up to 4 mg, 8 mg, or 12 mg using a gradual dose escalation every 4 weeks to a maximum of 12 mg.

Microdosing[11]

- No evidence-based protocol for microdosing semaglutide or tirzepatide. No data in clinical benefit or safety of microdosing upon conducting a literature review.
- There might be benefits to microdosing in patients that cannot tolerate adverse effects especially when titrating the dose.
- Need a high level of health literacy as dose errors can be common when microdosing.

Safety[2,4,6,7,11]

Adverse Reactions at Highest Doses (%)[% Placebo] Top 5 Most Occurring					
Ozempic[2]	Nausea (20%)[6%]	Vomiting (9%)[2%]	Diarrhea (2%)[2%]	Abdominal Pain (6%)[5%]	Constipation (3%)[1.5%]
Wegovy[4]	Nausea (44%)[16%]	Diarrhea (30%)[16%]	Vomiting (24%)[6%]	Constipation (24%)[11%]	Abdominal Pain (20%)[10%]
Mounjaro[6]	Nausea (18%)[4%]	Diarrhea (17%)[9%]	Decreased Appetite (11%)[1%]	Vomiting (9%)[2%]	Constipation (7%)[1%]
Zepbound[7]	Nausea (28%)[8%]	Diarrhea (23%)[8%]	Vomiting (13%)[2%]	Constipation (11%)[5%]	Abdominal Pain (10%)[5%]
Retatrutide[11]	Nausea (45%)[11%]	Decreased Appetite (29%)[9%]	Diarrhea (15%)[11%]	Vomiting (19%)[1%]	Constipation (16%)[3%]

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Contraindications:
Ozempic/Wegovy/Mounjaro/Zepbound[2,4,6,7]

- Personal or FH of Medullary Thyroid Carcinoma (MTC) or Multiple Endocrine Neoplasia Type 2 (MEN 2)
- Hypersensitivity to any of the active or inactive ingredients.

Warnings:
Ozempic/Wegovy/Mounjaro/Zepbound[2,4,6,7]

- Risk of thyroid C-Cell Tumors
- Acute Pancreatitis
- Diabetic Retinopathy
- Sharing Pens Between Patients
- Hypoglycemia
- AKI
- Severe GI Adverse Events - Avoid ins severe gastroparesis.
- Hypersensitivity Reactions
- Acute Gallbladder Disease
- Pulmonary Aspiration During General Anesthesia - Due to delayed gastric Emptying
- Increased Resting Heart Rate (Wegovy only)
- Suicidal Ideation and Behavior (Wegovy and Zepbound)

Place in Therapy (TRT)

- More data is needed in our TRT population specifically. However, the metabolic effects of GLP-1s and GLP-1/GIPs can be very beneficial in patients with hypogonadism.
- In addition, they can be very beneficial in overweight patients who are pre diabetic and patients with T2DM who are taking TRT.
- Wegovy and Ozempic have shown benefits in CV protection which is very beneficial in patients who are taking TRT.
- Ozempic has proven its benefits in CKD which is another potential target population who can be prescribed TRT.
- Zepbound can potentially be beneficial in patients with OSA who take TRT. Treating their OSA could reduce hypoxic drive which can help control their erythrocytosis.
- Overall, we would recommend the use of these medications for their indicated uses as they overlap well with our TRT population.

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BPC-157

Introduction

- BPC-157 names

BPC-157 also known as PL 14736, PL-10, Bepecin, or Pentadecapeptide

- Sources

BPC-157 is a human gastric juice-derived is a stable gastric pentadecapeptide that had its debut introduction and review in the Journal of Physiology in 1993. Since its introduction, it has been shown the ability to heal various types of tissues in rat studies including but not limited to tendon, ligament, muscle and bone[1].

- Structure of BPC

BPC-157 has a 15 amino acid fragment structure (Gly-Glu-Pro-Pro-Pro-Gly-Lys-Pro-Ala-Asp-Asp-Ala-Gly-Leu-Val)[2]. The structure of BPC-157 is as follows[3].

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Animal trials of BPC-157

Gastric pentadecapeptide BPC 157 accelerates healing of transected rat Achilles tendon and in vitro stimulates tendocytes growth[4].	
Population	Male Wistar albino rats. 280-320 g body weight randomly assigned to groups
Groups	• Right achilles tendon transverse transection 0.5 cm proximal to calcaneal insertion. • Sham operation; skin lesion only. • Non-operated healthy rats.
Intervention	• Saline • 10 mcg/kg BPC-157 in saline intraperitoneal once daily. • 10 ng/kg BPC-157 in saline intraperitoneal once daily. • 10 pg/kg BPC-157 in saline intraperitoneal once daily. • Dose 1: 30 mins after surgery. • Last dose 24 hours prior to autopsy (14 days total)
Results	Compared with placebo, significant improvement in achilles tendon recovery measures in all measures (biochemical, microscopic, and macroscopic).

Effective Therapy of Transected Quadriceps Muscle in Rat: Gastric Pentadecapeptide BPC 157[5]	
Population	Male Wistar albino rats, 280–320 g body weight randomly assigned to groups
Groups	• Right quadriceps completely transected transversely 1 cm proximal to the patella.

	• Sham operation; skin lesion only. • Non-operated healthy rats.
Intervention	• Saline • 10 mcg/kg BPC-157 in saline intraperitoneal once daily. • 10 ng/kg BPC-157 in saline intraperitoneal once daily. • 10 pg/kg BPC-157 in saline intraperitoneal once daily. • Dose 1: 30 mins after surgery. • Last dose 24 hours prior to assessment procedure. • Assessment on day 1-17, 14, 21, 28, and 72
Results	• Prompt functional and biomechanics improvement, advanced quality of improved muscle healing, and reached normal values.
Conclusions	• BPC-157 (at all 3 regimens) induced postransection healing promptly and maintained the healing along with full functional restoration in a transected muscle in rats.

Pentadecapeptide BPC 157 (PL 14736) Improves Ligament Healing in the Rat[6].	
Population	Male Wistar Albino rats. 400 g body weight randomly assigned to groups
Groups	• MCL injury to the knee. 5-7 mm incision, MCL was transected to the joint line. • Sham operation; skin lesion only. • Non-operated healthy rats.
Intervention	• Saline • 10 mcg/kg BW or 10 ng/kg BPC-157 in saline intraperitoneal once daily. • 1 mcg BPC-157 dissolved in 1g cream and applied to as a thin layer locally to injury site. • 1.92 mcg/12 mL of drinking water administered PO. • Dose 1: 30 mins after surgery. • Last dose 24 hours prior to autopsy (90 days total)
Results	• All BPC-157 regimens demonstrated consistent and extensive improvement. • Biomechanic, macroscopic and microscopic function reached pre injury levels with BPC-157 administration.
Conclusions	BPC-157 administration IP, topically, or PO can improve ligament healing in rats.

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Phase I, Pilot Study in Healthy Volunteers, to Assess the Safety and Pharmacokinetics of PCO-02, Which Active Ingredient is BPC-157, a Penta-deca-peptide From Gastric Source[7].		
Population	42 healthy male or female adults ages 18-35 Single site in Hospital Angeles Tijuana Duration: 6 months	
Groups	Phase 1a PCO-02 tablets containing 1 mg BPC-157 • 3 groups of 14 subjects (6:1 PCO-02:placebo) • Single dose PO 1, 3, or 6 PCO-02 tablets or placebo	Phase 1b PCO-02 tablets containing 1 mg BPC-157 • 3 PCO-02 tablets PO TID x 2 weeks or placebo
Intervention	Phase 1a • 24 hour admission to the hospital	Phase 1b • Ambulatory

	• Fasted before and after administration. • Serial blood and urine tests to determine pharmacokinetics and safety. • Return after 1 week for clinical assessment and labs	• Subjects will return to clinic on day 0, 7 and 14 for safety and pharmacokinetics assessment.
Results	Results not posted. Trial canceled 5/23/2016	

Pharmacology[2]
- Intrinsic muscle/tendon Damage repair:
- Mechanisms:
- VEGFR2
- Effect on growth factors
- Nitric Acid (NO)
- Prostaglandins
- Fibroblast proliferation

Therapeutics[2-7]
- Evidence of efficacy (Animal studies, no human RCTs available).
- Route of administration (Why PO is viable even though BPC-157 is a peptide). Most peptides (Ex. Insulin and GLP-1 Agonists) get deactivated in the GI tract d/t gastric acid. However, BPC-157 has been shown to be active even with PO administration.
- Dosage
- Oral No human studies but rat studies showed 10 mcg/kg which is roughly equivalent to 1.6 mcg/kg in humans[8].
- Injection: Based on a pharmacist who works in a compounding pharmacy (Jessica Beal, PharmD), doses are typically 150-300 mcg SubQ QDAY.

Safety[2-7]
- Insufficient evidence but rat studies showed no negative adverse effects.

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Legal Status and Potential Sources:
- FDA Category 2[9]
- Definition of Category 2: Significant safety risks identified by the FDA pending further evaluation. The FDA would consider taking action against a compounder for drug products with BPC-157 bulk substance.
- The reason the FDA categorized BPC-157 as category 2 is due to no or limited safety information for the proposed route of administration. The FDA lacks sufficient information to know whether BPC-157 an cause harm in the event of administration in humans[8].

Conclusion and application to practice:
Animal data shows potential benefits. However, the lack of human studies and the difficulty of sourcing BPC-157 through legitimate means makes it a difficult drug to recommend use for our patients in an evidence-based practice.

Growth Hormone Secretagogues (GHS):

Definition[12]:
GHS are a variety of synthetic peptide and non-peptide agents that can stimulate endogenous growth hormone release through interactions with the hypothalmic-pituitary-somatropic axis.

History[12]:
Therapeutic GH has been shown to increase lean body mass, decrease adiposity and improve lipid profile. However, GH use has been restricted due to the 1988 and 1990 amendments of the Food, Drug and Cosmetic act. The amendments made it illegal to use GH in the USA other than to treat a disease or other recognized medical condition. The only labeled indication to use GH is for Growth hormone deficiency in children and adults.

GH is also extremely cost prohibitive costing thousands of dollars monthly in the USA.

Mechanism of GH release in the body[13]
Mechanism of action of GHS:
GHS stimulate endogenous GH release through mimicking growth hormone release hormone (GHRH) or through their interaction with Ghrelin

Examples of GHS include[14]:

Sermorelin

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GHRH analog derived from the first 29 amino acids of the GHRH protein. Sermorelin impacts the hypothalmic-pituitary-somatropic access directly.

Sermorelin trials[14]
Limited data in hypogonadal men

- 10 older men (age 60-78) were administered either 0.5 mg or 1 mg of sermorelin twice daily for 14 days. Sermorelin was then held for 14 days and given again for another 14 days. GH, IGF-1, IGFB-3, T levels, body weight, BMI and waist-hip ratios were compared to 9 younger men (age 2-33)
- Results: High dose sermorelin elevated mean 24-hour, peak amplitude, and area under the peak GH. IGF-1 levels were elevated and approached those of younger men. IGF-1 levels remained above baseline even after 2 weeks after holding sermorelin. T levels were improved but no statistically significant.
- Conclusions: Sermorelin is effective at increasing GH and IGF-1 levels in older men with reduced IGF-1 levels.

Effects of Single Nightly Injections of Growth Hormone-Releasing Hormone (GHRH 1-29) in Healthy Elderly Men[15]	
Population	11 healthy men age 64-79 Baseline IGF-1 < 250 mcg/L
Study Protocol	2 days of admission to General Clinical Research Center (GCRC) of the Johns Hopkins Bayview Medical Center (JHBMC). Day 1:

	• Fasted blood tests including IGF-I, IGF binding protein-3 (IGFBP-3), GH-binding protein (GHBP), glucose, and lipids. • NMRS of the flexor digitorum superficialis muscle of the dominant arm and DXA scan. • 1 rep max testing of 6 exercises (latissimus pull-down, leg extension, bench press, leg curl, shoulder press, and upright row) and endurance testing (number of abdominal crunches in 30 secs) • 24-hour urine specimens to test creatinine, C peptide and nitrogen. • Blood tests every 20 mins from 8am to 8pm Day 2: • 2 hour - 75 g glucose tolerance test with insulin, glucose and GH assays. • Skeletal muscle biopsy obtained from the right vastus lateralis muscle
Intervention	• 2 mg GHRH SubQ every night x 6 weeks • BP, serum IGF-1 and BG after 2 weeks. • Readmission for the same protocol tests after 6 weeks while continuing GHRH administration. • BP, serum, IGF-1 and BG after study conclusion.
Results	12. GHRH administration doubled the 12-hour mean GH and the mean area under GH peaks for nocturnal GH release. 13. Increase in GH release was confined to 2 hours after administration gf GHRH 14. 2 men did not receive the final GHRH dose had similar GH secretory profiles to pretreatment baseline. 15. Baseline serum IGF-1 did not increase significantly after 2 and 6 weeks of GHRH. 16. Mean IGF-1 levels at 2 weeks of treatment was higher than 2 weeks post treatment. 17. No effects of GHRH on body composition 18. Highly significant increase in strength for the upright row, less significant increase in the shoulder press, leg curl and abdominal crunch. No effect on other exercises. 19. No significant effects on muscle energy metabolism, muscle fiber panel, glucose and insulin tolerance, or other hormones.
Conclusions	GHRH can temporarily increase pituitary GH release when administering 2 mg SubQ nightly to older adults and more clinical investigation is needed to evaluate the effects of GHRH.

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Another study[14] evaluated the duration of long term administration of sermorelin to men and women (ages 55-71) for 5 months (4 weeks of placebo followed by 16 weeks of sermorelin 10 mcg/kg SubQ nightly.
This study showed significant increases in GH release for the 2 hours after administration and 12 hour men GH levels.
Interestingly, this study showed an increase in lean body mass for men (1.26 kg) and an increase in skin thickness in both genders. While there was no change in T levels in men, there was a significant increase in insulin sensitivity and libido.

Conclusions: Long term administration of GHRH can increase GH and IGF-1 in older adults along with an increase in lean body mass in men.

CJC 1295

CJC 1295 is another GHRH analog that has been synthetically modified to enable it to bind to endogenous albumin upon SubQ administration and become more resistant to proteolytic cleavage extending its half-life and duration of action[16].

Trials on dogs and pigs showed that physiological GH secretion was maintained and IGF levels were increased for several days after CJC 1295 administration[16].

Two double blind randomized control trials in healthy adult subjects were performed:

Prolonged Stimulation of Growth Hormone (GH) and Insulin-Like Growth Factor I Secretion by CJC-1295, a Long-Acting Analog of GH-Releasing Hormone, in Healthy Adults - Study 1[16]					
Population	42 Healthy men and women ages 21-61 with a BMI of 30 or less				
Study Protocol	• Four sequential dose escalation groups, 5:1 active:placebo • 1 cohort receiving the same dose • Serum GH measured on D0 60, 30, 15 mins before administration, 15, 30, 60 mins after, 2, 3, 4, 6, 8, 10, 12, 24 hours, every 8 hours on D2-D3, and D4, 5, 6, 7, 9, 11, 14, 21, and 28. • CJC 1295 and IGF-1 levels on D0, 1, 2, 3, 4, 5, 7, 9, 11, 14, 21, and 28. • Serial clinical evaluations (vital signs, adverse events, and physical examination) and laboratory safety assessments (serum chemistry, hematology, and urinalysis) on D28				
Intervention	30 mcg/kg (n=5 + 1 placebo SubQ	60 mcg/kg (n=5 + 1 placebo) SubQ	125 mcg/kg (n=5 + 1 placebo) SubQ	250 mcg/kg (n=5 + 1 placebo) SubQ	125 mcg/kg (n = 15 + 3 placebo) SubQ
Results	• Mean half life of CJC 1295 = 5.8-8.1 days • Mean serum GH increased by 2-10 fold through D6 compared to stable serum Gh in placebo. Significant increases only in the 60, 125, and 250 mcg/kg dose groups in a dose-dependent manner. • Median Serum GH peaked 1 hour after injection in all groups except the 250 mcg/kg group with the peak occurring 4 hours after injection (mean 0.5-4 hours). • Elevated IGF-1 levels compared to baseline (0.5-3 fold) for 9-11 days post injection. Dose dependent. Significant only in 60, 125, 250 mcg/kg/dose. Levels exceeded normal range only in 250 mcg/kg group. • IGF-1 levels peaked 2-3 days after administration and 4 days after the highest dose. Levels plateaued for 7 days and then decreased towards baseline. Remained elevated for at least 2 weeks in the highest dose.				
Adverse Events	• 94% in CJC 1295 groups (n=33) vs 29% in placebo (n=2), all mild to moderate and none required medical intervention. • Injection site reactions in 70% of patients receiving CJC 1295 lasting up to 5 days. More severe or prolonged in higher doses. • Headache (63%), diarrhea (43%), systemic vasodilatory reactions (30%) all more common at higher doses 125 and 25 mcg/kg.				

Prolonged Stimulation of Growth Hormone (GH) and Insulin-Like Growth Factor I Secretion by CJC-1295, a Long-Acting Analog of GH-Releasing Hormone, in Healthy Adults - Study 2[16]	
Population	24 Healthy men and women ages 21-61 with a BMI of 30 or less
Study Protocol	• Four sequential dosing cohorts 5:1 active:placebo receiving more than 1 injection • Same sample collection as Study 1 with more post injection sampling on D7 (groups 3 and 4), and D14, and a final sample collection on D49

	• Serial clinical evaluations (vital signs, adverse events, and physical examination) and laboratory safety assessments (serum chemistry, hematology, and urinalysis) on D49			
Intervention	30 mcg/kg x 2 [D0,14) (n=5 + 1 placebo) SubQ	60 mcg/kg x 2 [D0,14] (n=5 + 1 placebo) SubQ	30 mcg/kg x 3 [D0,7,14) (n=5 + 1 placebo) SubQ	60 mcg/kg x 3 [D0,7,14) (n=5 + 1 placebo) SubQ
Results	• Mean half life of CJC 1295 = 5.4-9.2 days • IGF-1 levels increased within 8 hours of injection and remained above baseline through D28. Levels remainder elevated before there second and 3rd doses in all groups but only remained significant in group 4 • No significant increases in serum cortisol, prolactin, TSH, LH, after single injection gf 60 mcg/kg.			
Adverse Events	• Mild injection site reactions in all treated groups. • Flushing in 100% of the patients treated with 60 mcg/kg and 40% in 30 mcg/kg			

Conclusions from both studies:
- CJC 1295 has the potential to increase endogenous GH secretion and elevate IGF-1 levels at the studied doses.
- Both single and multiple doses of CJC 1295 over 2 weeks were safe and well tolerated at 30 mcg/kg or 60 mcg/kg.
- More research is needed to evaluate its role in performance boosting for athletes and the general patient population.

GHRP-2 & GHRP-6

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Short synthetic amino acids that trigger GH secretion through interactions with receptors at the pituitary and hypothalamus. They primarily interact with growth hormone secretagogue receptor 1a (ghrelin receptor) located primarily in the brain along with the pancreas, thyroid, adrenal gland and adipose tissue and CD36 located in endothelial cells, immune cells, adipocytes, cardiac and skeletal muscle, and hepatocytes[12].

GHRP-6 was the first GHRP to be studied in humans which led to developing other GHRPs like GHRP-2. GHRP-6 was found to provoke a significant hunger response in patients which may highlight its interactions with the ghrelin receptors[12].

Human trial[17]:
This is a parallell-cohort, double blind, perspective randomized trial on 24 young healthy men which evaluated GHRP-2 in acutely hypogonadal men.

The subjects were administered a 30 minute infusion (IV) of 30 g L-arginine followed by either a 1 mcg/kg GHRH or 3 mcg/kg bolus (IV) GHRP-2. Blood was then drawn every 10 minutes for 6 hours

The results showed that increased abdominal visceral fat decreased the efficacy of GHRH and increased IGF-1 levels increased the efficacy of GHRH whereas GHRP-2 was not affected by abdominal visceral fat or IGF-1 levels. The results also showed that GHRP-2 induced a 2-fold greater increase in pulsatile GH secretion.

<u>However, I doubt the applicability of this study to the every day athlete due to difficulty of replication of acute hypogonadism in the real world, the challenges of IV administration in real life and the short duration of the trial (6 hours).</u>

Ipamorelin

Synthetic Pentapeptide that is a selective ghrelin/GHS receptor agonist binding to the GHSR-1a receptor the same receptor GHRP-6 & GHRP-2 bind to. Binding to the GHSR-1 will release GH from the pituitary which can regulate appetite, fat processing, and energy usage[12].

With that there is a potential therapeutic use to stimulate the GI tract and ipamorelin has been tested in rodents with induced ileus[12].

In a 9 week trial of ipamorelin compared to GH, female GH-deficient and GH-intact mice were injected with 250 mcg/kg, 1.75 mg/kg hGH or placebo twice daily. The results were as follows:

1. GH-Deficient mice experienced a bodyweight increase of 15.3% with ipamorelin and 95.5% with GH
2. GH-Intact mice experienced a bodyweight increase of 16.9% with ipamorelin and 27.5% with GH.
3. Weight gain only in the first 1-2 weeks with ipamorelin compared to 9 weeks with GH.
4. Relative dissected organ weight remained the same with ipamorelin compared to increase in liver weight with GH.
5. Mice treated with ipamorelin experienced an increase in body fat percentages whereas GH showed no effect.
6. No adverse effects reported.

The results suggest that ipamorelin functions independent from GH, ipamorelin will not cause organomegly compared to GH, and ipamorelin has adiposegenic effects.

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Recommendations for Practice Site:
More research and trials into human administration to evaluate safety and efficacy in humans is needed before recommending the use of this medication. In addition, complications with sourcing ipamorelin through legitimate sources makes it more difficult to recommend the use of this peptide in patients.

TB4 and TB500

Thymosin Beta-4 (TB4) is a peptide that consists of 43 amino acids. It was found to have anti-inflammatory, anti-apoptotic, and anti-fibrotic activity highlighting the potential in therapeutic applications for promoting angiogenesis at ischemic sites and tissue repair[18].

TB4 has been explored as a therapeutic option for myocardial infarctions due to cardiovascular research demonstrating its role in improving blood supply, reducing myocardial injury, promoting tissue repair in the myocardium, and improving microvascular obstruction[18].

In addition to its positive healing effects on cardiomyocytes, TB4 is also known to promote dermal healing, corneal wound healing, neuron survival. TB4 has shown the potential to possess benefits beyond just CV protection and healing post MI[19].

A randomized, placebo-controlled, single and multiple dose study of intravenous thymosin beta4 in healthy volunteers - Phase 1a (Single Dose)[20]

Population	• Inclusion: Male or female subjects ages 18-79 in good health, no underlying medical conditions. • Exclusion: malignancy or increased risk of malignancy, tobacco use, safety labs or vitals out of range (ex. ECG), eGFR < 80 mL/min/1.7 m^2, use of any medications.			
Study Protocol	• Randomized, double blind, placebo-controlled to evaluate safety, tolerability and kinetics • 4 cohorts of subjects - 10 subjects per cohort • Single dose placebo or active drug at a 4:1 ratio • Admission on day -1 and discharge on day 2 of administration. • Single dose of TB4 administered on day 1 • Vital signs, CBC, Chem, and UA on days 1, 2, 7, 14, and 28 • Physical exam on days -1, 1, 2, 7, 14, and 28 • PK samples on day 1 and day 2, serum antibodies at screening and day 28 • Cancer follow up call 6 months after for those who did not participate in 1b			
Intervention	42 mg IV x1	140 mg IV x1	420 mg IV x1	1260 mg IV x1
Adverse Events	• 18 total, 15 unrelated to drug or placebo, 1 who received placebo and had leukocytosis, 1 who received 140 mg and had dizziness that persisted for 7 days, 1 who received placebo and had a headache 3 hours after dose and persisted for 18 hours. • No clinically significant findings on ECG • No serious AE, no withdrawals due to AE, no deaths, no cancers in 6 month follow up call for those who didn't participate in 1b.			
Pharmacokinetics	• Cmax and AUClast are proportionate to the dose. • Half life increases with dose • Clearance is independent of dose.			
	Half life: 0.95 hour	Half life: 1.2 hour	Half life: 1.9 hour	Half life: 2.1 hour

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A randomized, placebo-controlled, single and multiple dose study of intravenous thymosin beta4 in healthy volunteers - Phase 1b (Multiple Dose)[20]				
Population	• Inclusion: Male or female subjects ages 18-79 in good health, no underlying medical conditions. • Exclusion: malignancy or increased risk of malignancy, tobacco use, safety labs or vitals out of range (ex. ECG), eGFR < 80 mL/min/1.7 m^2, use of any medications.			
Study Protocol	• Randomized, double blind, placebo-controlled to evaluate safety, tolerability and kinetics. • 10 subjects in each cohort • Subjects from Phase 1a were requalified or subjects of the same demographics were recruited instead • Admission on day -1 until Day 15 • TB4 or placebo was administered IV QDAY x 14 days • Safety labs, EKG, vital signs, evaluation of AE, and physical exam intermittently. • PK samples on days 1, 2, and 12-15, serum antibodies at screening and day 28 • Outpatient evaluation on days 21, 28, and 42, and de novo cancer follow up call 6 months after day 42.			
Intervention	42 mg IV QDAY x14	140 mg IV QDAY x14	420 mg IV QDAY x14	1260 mg IV QDAY x14
Adverse Events	• 64 total AEs, frequency varied with increased dose, 62 TEAEs, 55 of the 63 were ruled unrelated to the study • Most common AE was headache in all dose groups including placebo • 1 subject with feverish feeling at 140 mg dose, one with elevated GGT at 1260 mg dose, 1 subject with nausea in the placebo group, and 1 subject with headache, elevated PTT/INR in placebo group. • No clinically significant finding on ECG study • No reported cancers at 6 month follow up call			

Pharmacokinetics	Not published

Conclusion:
Single IV and multiple IV dosing of 14 days are potentially safe and tolerable with no dose limiting toxicity or serious AE at the range of 42 mg/dose to 1260 mg/dose.

Recommendations:
While TB4 is one of the most widely and extensively researched peptides, most research has been done in vitro and in vivo in animals. Pharmacokinetic trials have been completed in humans and proven to be safe and tolerable in humans at 0.25 mcg/kg-25 mcg/kg doses and doses of 42, 140, 420, or 1260 mg all intravenously[18,19,20]. More research is needed on efficacy and safety and using routes of administration that can be utilized in an outpatient setting.

TB500 is a synthetic peptide that is a considered a fragment of the active site in TB4.

KPV:

KPV is a tripeptide (Lys-Pro-Val) that composes the C-terminal section of alpha-melanocyte stimulating hormone. KPV exhibits anti-inflammatory activity and has been trialed in vitro and in mice in vivo. The trials indicated KPV's potential therapeutic benefits in potentially treating Inflammatory bowel disease (IBD) and ulcerative colitis through its anti-inflammatory mechanisms[21,22].

Recommendations:
KPV has shown potential in vivo and in mice but has not been yet evaluated in humans for safety and efficacy and will need further evaluation before recommending its use in humans to treat inflammatory conditions.

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GHK-Cu

GHK-Cu is a tripeptide that can be found in human plasma and can also be released from injured tissue. In 2010, GHK-Cu was found to be able to up-regulate or down-regulate a large number of human genes connecting it to many of its effect to those genomic effects. GHK-Cu affects 31.2% of the human genome with a change of 50% or more[23].

GHK-Cu has been explored or shown to have the following therapeutic benefits[23]:

1. Skin Regeneration
2. Cosmetic Use: Clinical studies on humans have been done in 1998-2002.

- A study of GHK-Cu in 71 women for 12 weeks with mild to advanced photoaging has shown positive effects in increasing skin density, thickness, reducing elasticity, improving clarity, and reducing lines and wrinkles.
- A study of GHK-Cu in 41 women with mild to advanced photoaging applied around the eyes for 12 weeks has shown to perform better than Vitamin K or placebo.
- A study of GHK-Cu in women applied to the thigh for 12 weeks was shown to improve collagen production by 70% compared to 50% with Vitamin C and 40% with retinoic acid.

3. Wound Healing: GHK has been shown to improve wound healing in animals such as rabbits and rats.
4. Blood Vessel and nerve growth stimulation
5. Nerve Outgrowth promotion in cell cultures and rat experiments
6. Anti-oxidant and anti-inflammatory effects in animal experiments
7. COPD and Lung Injury: GHK-Cu was tested in vitro and was shown to restore function of lung fibroblasts. In addition, GHK-Cu was shown to protect mice lung tissue from damage and suppressed

inflammatory cells infiltrating in the lungs. Finally, GHK-Cu was shown to decrease TNF-1 and IL-6 production.
8. Blocking Cortisone Effects: Systemic GHK-Cu was shown to block cortisone-induced inhibition of wound healing in mice, rats and, pigs.
9. Suppressing Fibrinogen: Fibrinogen was shown to be the single most powerful risk of CVD in men and women surpassing lipoprotein cholesterol. GHK-Cu suppression of IL-6 production can reduce fibrinogen.
10. Skin remodeling and anticancer
11. Ubiquitin Proteosome System
12. Anti-pain, Anti-anxiety, and Anti-Aggression: GHK-Cu has been shown to have effects on pain, anxiety and aggression in rat experiments.

Conclusion and recommendations for practice:
GHK-Cu has been shown safe and effective to improve skin healing in humans and has the potential for many more positive effects. However, more trials must be completed before recommending its use for anything other than topical cosmetic use for skin.

Tesamorelin

Human growth hormone releasing factor (GHRF) made of 44 amino acids that binds and stimulates human GRF receptors with a similar potency to endogenous GRF. GHRF or GHRH is a peptide that is released by the hypothalamus that signals to the pituitary to release endogenous GH in its pulsatile mechanism. GH has both anabolic and lipolytic functions in the body and affects many tissues. It also increases IGF-1 levels in the body[24].

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Tesamorelin is manufactured under the name brand name EGRIFTA WR and is indicated for the reduction of excess abdominal fat in HIV-infected adults with lipodystrophy[24].

Recommended dose is 1.28 mg (0.16 mL) SubQ QDAY[24]

Contraindications[24]:
- Disruption of the Hypothalmic-pituitary axis
- Active malignancy
- Hypersensitivity
- Pregnant women due to potential for fetal harm and no benefit in modifying visceral adipose tissue.

Warnings and precautions[24]:
1. Malignancy
2. Elevated IGF-1
3. Fluid Retention: Think about testosterone and HF
4. Risk of DM and glucose intolerance
5. Hypersensitivity
6. Injection site reactions
7. Increased mortality in acute critical illness

Two Phase 3 Clinical Trials:

Visceral Fat Reduction with Tesamorelin Is Associated with Improved Liver Enzymes in HIV[25]		
Trial #	Trial 1 (Main Study)	Trial 2 (Extension Phase)
Population (N = 806)	Inclusion • Men and women with HIV ages 18-65 years-old	

	• Abdominal fat accumulation (Men: Waist circumference of >=95 cm and wait-hip ratio >= 0.94 and women with >= 94 cm and >= 0.88) • CD4 > 100 cells/mm^3 and HIV viral load < 10,000 copies/mL on stable ART >= 8 weeks. Exclusion: • Known history of DM requiring medication • Fasting BG >= 150 mg/dL • Any history of malignancy	
Population Baseline	• 64% of patients had AST or ALT > 30 U/L at study entry. • Male sex, race, viral hepatitis, lipid lowering therapy, ART regimen and testosterone use were all associated with increased liver enzymes. • Subjects with increased ALT or AST had a greater VAT, lower abdominal SAT, and lower limb fat.	
Study Design Phase 3 Trial	• 26 Weeks • Randomization 2:1 to tesamorelin 2 mg SubQ QDAY or placebo	• 26 Weeks • Subjects who received placebo were switched to tesamorelin and subjects who received tesamorelin were randomized to continue (T-T) or placebo (T-P)
Study Procedures	Baseline visit for subjects • History and Physical Exam • Abdominal CT scan to determine visceral and subcutaneous adipose tissue (VAT and SAT) • DXA scan to determine trunk and extremity fat • Viral hepatitis, ART regimen, use of testosterone and/or lipid lowering therapy via self-report • Fasting ALT and AST • Reassessment of the above parameters at 26 and 52 weeks • VAT responders >= 8% reduction in VAT	
Results	• Participants with baseline ALT or AST > 30 U/L who received tesamorelin had 69% VAT responders and 31% non-responders at 26 weeks. • Characteristics didn't play a role in response vs no response except viral hepatitis was less common among responders. • ALT decreased by 8.9 and AST by 3.8 in responders and increased by 1.4 and 0.4 in non-responders after 26 weeks respectively. • No decline in ALT or AST in subjects that received placebo and had an >= 8% decrease in VAT at 26 weeks.	• Of the 177 responders, 141 subjects had data after 26 weeks. Randomization: 104 T-T and 37 T-P • Significant reduction in ALT in T-T and T-P groups with no difference between the groups at 52 weeks. • ALT and AST did not return to baseline after 26 weeks in the T-P group. • VAT reaccumulated in the T-P group.
Conclusions	• Tesamorelin has potential clinical benefits in reducing VAT among HIV infected patients.	

Recommendations for Practice Site:

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Due to the cost of “Pharma-grade” tesamorelin and its need for further evaluation outside of its indicated use, I would not recommend its use in our TRT population. EGRIFTA WR costs $6,000-$8,000/month. More trials are needed in its safety and efficacy in TRT patients outside of HIV populations.

MOTS-c

Mitochondrial ORF of the 12S rRNA type-c (MOTS-c) is a 16 amino acid polypeptide encoded in the mitochondrial rRNA and localized to the mitochondria at resting conditions. Endogenous MOTS-c levels have been shown to increase 11.9x following exercise[26].

MOTS-c has potential positive effects on many conditions[26]:

1. MOTS-c and Aging:

Blood and skeletal muscle MOTS-c levels decrease with age endogenously. Blood MOTS-c levels in younger people are 11% and 21% higher than middle aged and older adults respectively.

2. MOTS-c and CVD:

- Rat studies have shown aerobic exercise and MOTS-c administration effects on protecting against cardiac dysfunction, improving heart structure and function and cardiac remodeling through increasing myocardial MOTS-c levels.
- Another study in diabetic rats showed that MOTS-c improved angiogenesis, inflammation and apoptosis. This suggests that MOTS-c might have the same effect as aerobic exercise in improving heart failure in patients with diabetes.

3. MOTS-c and insulin resistance:

- A study in male mice showed that MOTS-c administration can improve age-related insulin resistance through increasing intake of glucose into their soleus muscles.
- A study in older mice showed an increase in insulin sensitivity 7 days after MOTS-c administration to match the the insulin sensitivity in younger mice.
- MOTS-c has also been shown to improve blood glucose and prevent hyperinsulinemia in mice fed a high fat diet. MOTS-c was shown to affect muscle tissue directly making it a promising peptide to use for insulin resistance in muscles.

4. MOTS-c and Inflammation:

MOTS-c has also been shown to have anti-inflammatory and analgesic effects in mice through a significant increase in anti-inflammatory cytokines and a decrease in pro-inflammatory cytokines.

Conclusion and Recommendations:

Through those trials, MOTS-c has many potential benefits in humans. However more trials in humans are needed to recommend its use in humans in general and our TRT patients specifically.

AOD-9604

AOD-9604 is the C-terminal fragment of the hGH molecule using the amino acids 177-191. It is synthesized from the fragment of hGH that is mostly linked to stimulating lipolysis and inhibiting lipogenesis[27].

The mechanism of action for AOD-9604 has not been understood. It has been found to share some effect of GH while not stimulating IGF-1 production. It also shares many of the metabolic effects of GH like fat reduction without causing insulin resistance[27].

Six human clinical trials were performed using AOD-9604 and was shown to be safe and well tolerated using the IV or PO route. Some weight loss was observed with AOD-9604. Pharmacokinetic and toxicology studies in pigs and rats showed no toxicity and no immunogenicity[27].

Recommendation for Practice site:
AOD-9604 can theoretically be utilized for weight loss and lipolysis along with some effects of GH without increasing insulin resistance. However, difficulty sourcing it from legitimate sources and little trials being done in humans make it difficult to recommend its use in evidence based practice.

MK677

MK677 is the first PO ghrelin mimetic (GHS). It increases the pulsatile secretion of GH in humans. It has been shown to increase GH secretion of older adults to the level of younger adults[28].

Trial in older adults:

Effects of an Oral Ghrelin Mimetic on Body Composition and Clinical Outcomes in Healthy Older Adults: A Randomized Trial[28].	
Population	• 71 subjects randomized • General population healthy men and women age >= 60 on or off HRT. • All caucasian except 1 Hispanic and 1 African American man. Exclusion Criteria: • BMI >= 35 kg/m^2 • Strenuous exercise > 60 mins/day • Smoking, DM, untreated HTN, H/O malignancy, thyroid disease, meds that can affect GH secretion.
Study Design	• Two-year, randomized, double-blind, modified crossover trial • Sep 1998 - Nov 2003 • MK677 or placebo (2:1 ratio) for 1 year. • Subjects who received MK677 were then randomized to placebo or MK677 for a second year.
Study Procedures	• Baseline and every 6 month x 2 years, admission for baseline & evaluation of body composition, body water, BMD, blood sampling, quality of life, tests of strength and function. • Standardized meals • Blood GH samples drawn Q10MIN x 24 hours
Intervention	MK677 25 mg PO QDAY
Results	• 65 subjects completed Year 1, 59 completed 18 months and 53 completed 24 months • 4 subjects were titrated back from 25 mg QDAY to 10 mg QDAY. • GH levels increased by 1.8x from baseline and serum IGF-1 by 1.5x, 22/43 subjects sustained IGF-1 levels similar to young adults. • Fat free mass -0.5 kg in placebo and +1.1 in MK677 by DXA. • Abdominal visceral fat +4.2 cm^2 in placebo and +8.4 cm^2 in MK677 and SubQ fat +1.3 and +18 respectively

RESTORATIVE ENDOCRINOLOGY SOCIETY™

	• Bodyweight +0.8 kg in placebo and +2.7 kg with MK677 • No difference in quality of life in both groups. • LDL +0.12 nmol/L in placebo and -0.14 in MK677 • Cortisol - 18 nmol/L in placebo and +47 in MK677 • No significant change in total T
Adverse Effects	• Increased appetite in 36% of subjects in placebo and 67% in MK677. • Mild, transient edema in 27% placebo and 44% MK677. • Transient muscle pain 9% and 33% and joint pain 77% and 58%
Conclusions	MK677 is promising in restoring endogenous GH pulsatile secretion in older adults compared to a high amplitude pulse seen in GH administration. More trials are needed to make a final recommendation.

SLU-PP-332

SLU-PP-332 is a small peptide and acts as a pan agonist of estrogen receptor Alpha (ERR). ERR is required for mitochondrial biogenesis in adult skeletal muscle and muscle regeneration suggesting its role in muscle adaptation to exercise[29].

SLU-PP-332 has been shown to replicate muscle response to exercise in maurine muscle cell lines in vitro and was shown to increase muscle endurance exercise capacity in mice. In human muscle cells taken from 20 women who self reported as active and inactive, SLU-PP-332 treatment induced a significant improvement in cellular metabolism and reduction of oxidative stress. In conclusion, ERR activation using SLU-PP-332 could be a promising strategy to preserve muscle in older adults and those with conditions causing muscular atrophy[29].

Recommendation for practice site:
More trials are needed in humans to recommend using SLU-PP-332 in our TRT patient population. Additionally, legitimate sourcing using manufactured product or compounding pharmacies is a challenge.

PT141

PT141 is also known as bremelanotide is a cyclic heptapeptide that acts as an analog of the endogenous peptide alpha-melanocyte-stimulating hormone. It has a high affinity for the MCR4 receptor. It was shown to work on physiological and neurobiological components of the female sexual function[30].

PT141 is available under the brand name VYLEESI and is indicated for the treatment of premenopausal women with HSDD not due to a comorbid medical or psychiatric condition, relationship problems, or the effects of a medication or substance[31].

Contraindications:
Uncontrolled HTN or known CVD[31].

Warnings and precautions[31]:
1. Transient increase in BP and decrease in HR.
2. Focal Hyperpigmentation; More than 8 monthly doses is not recommended
3. Nausea

Bremelanotide for the Treatment of Hypoactive Sexual Desire Disorder Two Randomized Phase 3 Trials[30]		
Trial #	Study 301 (NCT02333071)	Study 302 (NCT02338960)
Population	• 1267 Healthy Women age 18 and older in stable monogamous relationships with either a male or female partner. • Diagnosis of HSDD by an investigator or licensed healthcare provider for 6 months or longer, had previously normal sexual function for 2 years or more and were willing to engage in sexual activity once or more every month. Exclusions: • Pregnancy or nursing • Any other sexual dysfunction • Dx of depression, psychosis, bipolar, or substance use within 6 months. • Taking neuroleptics, lithium, antidepressants, mood stabilizers, benzos, cognitive enhancers, or GABA antagonists within 3 months.	
Intervention	Bremelanotide 1.7 mg SubQ for a maximum of 12 doses/4weeks and 1 doses/24 hours	
Study Design	Randomized, Double blind, Placebo-Controlled, Multicenter	
Study Procedures	• Monthly screening including physical exam, BP, vitals, EKG, labs AE monitoring, and Beck Scale for SI. • 4 week screening period (visit 1) • 4 week single-blind placebo only treatment where patients were expected to engage in sexual activity at least once (visit 2) • 1:1 randomization to placebo or bremelanotide x 24 weeks double blinded. • Observation and BP for self-administered in-clinic dose. 1 hour pre-dose and 1, 1.5, and 2 hour post-dose.	
Primary Endpoint	Change from baseline in FSFI-D score Change from baseline in score for being bothered by low sexual desire (FSDS-DAO), item 13.	
Secondary Endpoint	Change from baseline in satisfying sexual events within 16 hours of administration and reported for 72 hours.	
Results	• Statistically significant increases in sexual desire from baseline (P<0.001 for both trials) • Statistically significant decrease in distress related to low sexual desire (P<0.001 for trial 301 and P=0.005 for trial 302) • Changes observed for both coprimary endpoints at week 4 and sustained throughout treatment. • Greater number of responders compared to placebo for secondary endpoints	
Adverse Events	• Nausea, headache, flushing occurred > 10% than placebo • Nausea was the most common AE occurring in 44% of treatment and 1.3% of placebo. Median onset = 30 mins after dose and resolving 2.4 hours after, mild to moderate. • 8.1% discontinuation due to nausea and 3.5% reported vomiting. • One serious AE in trial 301 of nausea and headache resulting in overnight hospitalization. • Mean BP inc of 3 mmHg Systolic and 2 mmHg diastolic within 0-2 hours of administration and return to baseline within 8-10 hours. • No clinically significant effects on labs, EKG, weight, depression, or SI. • No difference in AE based on alcohol consumption.	
Conclusions	Bremelanotide can increase sexual desire and decrease distress related to sexual desire with a manageable side effect profile in premenopausal women with HSDD.	

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