3 Peptides (and a Bonus 4th) for Wellness

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September, 2019
Using Peptides to Increase HGH
Disclosure

The following potential conflict of interest relationships are germane to my presentation.

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Consultant: N/A

Status of FDA devices used for the material being presented: N/A

Status of off label use of devices, drugs or other materials that constitute the subject of this presentation: N/A
You've got to accentuate the positive
Eliminate the negative
Latch on to the affirmative
Don't mess with Mister In-Between

Growth Hormone Mimetics
Accentuate the Positive - Eliminate the Negative

*Positive GH Characteristics*

- Improved:
  - Lean Body Mass
  - Strength
  - Energy
  - Mood

- Positive Outcomes:
  - TBI
  - CV Performance
  - Cancer Outcomes
  - Autism
  - Schizophrenia

*Negative GH Characteristics*

- Paresthesia's
- Arthralgias
- Glucose Intolerance
- Edema
- “Addiction”
- Legalities
**Latch onto the Affirmative**

**GH Stimulators**
- GHRH
- Exercise
- Ghrelin
- Amino Acids
- Blood glucose
- Fatty acids

**GH Inhibitors**
- Somatostatin the “off switch”
- Lethargy
- Ghrelin
- Amino Acids
- Blood Glucose
- Fatty Acids
Accentuate the Positive

- **Growth Hormone Releasing Hormone (GHRH)**
  - Stimulates synthesis and release of GH via
  - Somatotroph cells of the anterior pituitary gland.
GHRH discovered from a tumor causing acromegaly

- Growth Hormone Releasing Hormone (GHRH) is a 44 amino acid peptide hormone produced in the arcuate nucleus of the hypothalamus (1982)

- Thorner M, JCEM Volume 84, Issue 12, 1 December 1999, Pages 4671-4676
One needs a working pituitary gland for GHRH/ GHRP to work
Growth Hormone Releasing Hormone

- Amino Acids 1-29 are the active part of the hormone to stimulate Growth Hormone
- Degraded by DPP4 enzyme
- Down Regulates:
  - Inflammatory cytokines IL-2, IL-6, and IL-10
GHRH-Accentuate the Positive

- Cardioprotective
  - Remodel and Repair Cardiac Tissue Post MI
- Inhibits Sarcopenia
- Preserves Pituitary Function Post TBI
- Promotes Wound Healing
- Reduces Obesity
- Improves HIV S/S and Outcome
- Improves Testicular Function/Testosterone Production
- Preserves Fertility
- Mediates GABA Neurons (Promotes non-REM Sleep)
- Stimulates Telomerase

Kanashiro-Takeuchi RM¹,², Szalontay L³, Schally AV¹,³,⁴,⁵,⁶, et. Al., New therapeutic approach to heart failure due to myocardial infarction based on targeting growth hormone-releasing hormone receptor. Oncotarget. 2015;6(12):9728-39.
GHRH-Recognize the Negative

❖ May Promote Cancer Cell Proliferation
  ❖ Prostate
  ❖ Ectopic Acromegaly
  ❖ Thyroid Cancer
  ❖ Melanoma
  ❖ Lymphoma
  ❖ Breast Cancer

❖ Worsen S/S Diabetes Mellitus Type 1
❖ May increase fat levels
  ❖ Lowers Ghrelin, Adiponectin, Leptin

GHRH Isoforms

- Sermorelin*
- CJC -1295*
- GHRH
- Modified GRF (1-29)
- Tesamorelin*
Sermorelin (Modified GHRH)

- Synthetic Aminos 1-29 of GHRH
- FDA Approved in 1991 for diagnosis treatment of GH deficiency in children
- 16 children with short stature were treated with GHRH 1-29 for 9 months
- A significant improvement in height velocity was observed in the children
- SubQ 30 μg/kg per day

Sermorelin (Modified GHRH)

- Increase Strength
- Improved Energy
- Improved Mental Sharpness
- Improved Sense of Well Being
- Increase Lean Muscle Mass/Reduces Body Fat

Dose: 0.2 - 0.3 mcg subQ injection at bedtime

- Side effects (< 1%):
  - Injection Site Reaction
  - Headache
  - Dysphagia
  - Vertigo
  - Somu lance
  - Urticaria
In the USA, the GHRH of choice has been Sermorelin.

In Australia, the GHRH of choice is CJC 1295. Another name for CJC 1295 is ModGRF129.
CJC- 1295 (modified GHRH)

- Is a modified GHRH 1-29
- CJC 1295 has four amino acid substitutions in GHRH(1-29) to enhance activity and render it resistant to degradation by proteolytic enzymes
- Elevates GH and Igf-1 up to 6 days

- Half Life:
  - Sermorelin- 10 minutes
  - CJC 1295-30 minutes
  - CJC 1295 with DAC-6 days (Drug affinity complex)

CJC- 1295 (modified GHRH)

- CJC 1295 can be compounded in two forms (DAC and non-DAC).
- Drug affinity complex (DAC) prevents enzymatic degradation thus increasing the half-life.
- Using CJC 1295-NON-DAC daily (between 6-8pm) provides a more effective GH spike at 1:00am.
CJC- 1295 (modified GHRH)
Daily Subcutaneous injection

❖ Usual Dose CJC 1295 w DAC 0.5 cc IM weekly
❖ Range 30 to 250 mcg/kg
❖ IGF-I levels increased for up to 28 days w 1 injection
❖ Half life about 7 days
❖ No serious adverse reactions were reported

2006 Mar;91(3):799-805
✓ Increase Strength
✓ Improved Muscle Tone
✓ Improved Sleep
✓ Improved Sense of Well Being
✓ Strengthens Immune System

Dose: 0.5 cc subQ injection weekly

• Perras B, et al Psychoneuroendocrinology 1999
  Oct;24(7):743-57
• https://www.slideshare.net/NeoBio/current-research-findings-regarding-cjc1295

● Side effects (< 1%):
  - Hot Flash Post Injection
  - Fatigue
  - Edema
  - Headache
  - Diarrhea
  - Urticaria
CJC 1295 DAC - 1 possible death

- CJC-1295 DAC - phase II trial for lipodystrophy in HIV patients
- July 2006 study 1 death from a heart attack.
- 12 week study done in Argentina

- The deceased patient received the 11th weekly dose and approximately two hours later, the patient complained of chest discomfort and an ECG confirmed an acute myocardial infarction; death occurred approximately 1 hour later.
There is no evidence of any cardiotoxic effects of CJC 1295 DAC in previous preclinical or clinical studies.

http://www.natap.org/2006/newsUpdates/081106_02.htm

The attending physician stated that his most likely explanation for the event was the patient had asymptomatic coronary artery disease with plaque rupture and occlusion.
Tesamorelin - GHRH

- 44 amino acids of human GHRH with the addition of a *trans*-3-hexenoic acid group

- Tesamorelin, developed by the Canadian pharmaceutical company Theratechnologies

- Brand name - "Egrifta"

- Stabilized against dipeptidyl peptidase IV (DPP4) degradation

- Half life of 30 minutes

- GHRH half life of 7 min
Tesamorelin- GHRH

- 2010 FDA approved Tesamorelin for HIV lipodystrophy
Tesamorelin- GHRH

- Harvard Study- in Healthy Men
- Tesamorelin 2 mg sc once daily for 2 wk
- Raises IGF-1 level by 182


<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>2 weeks</th>
<th>4 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>IGF-1</td>
<td>148</td>
<td>329</td>
<td>161</td>
</tr>
</tbody>
</table>
Tesamorelin - GHRH

- Reduces Triglycerides
- Reduces Visceral Adipose Tissue
- Reduces Carotid Intima Media Size
- Improves Cognition in people over 60 years

Tesamorelin and Fatty Infiltration of the Liver

- Phase III trials of 806 HIV-infected patients with abdominal obesity and elevated liver enzymes

- Significant visceral adipose tissue reduction with Tesamorelin was associated with improved liver enzymes

Tesamorelin and Insulin Resistance

- A 12-week randomized, placebo-controlled n=53
- Concern that GHS increases blood glucose because of decreases in insulin sensitivity.
- 3 treatment groups: placebo, 1 and 2 mg tesamorelin
- Diabetics with oral hypoglycemic Rx with or without insulin
- Total Cholesterol and non HDL significantly improved with Tesamorelin
- Dose-dependent increase in IGF1.
  - 33 ng/mL for the 1 mg
  - 2 mg increase of 66 ng/ml
- Tesamorelin did not alter insulin response or glycemic control
Tesamorelin and Cognition

• Randomized, double-blind, placebo controlled
• N = 152, age 55 to 87
• Tesamorelin 1 mg/day x 20 weeks

Tesamorelin - Dosing Protocol

- 1 mg injected at bedtime subcutaneously 5-6/7 days a week

- Compounded with Trehalose instead of Manitol
Growth Hormone Releasing Peptides- since 1984 (not GHRH)

- Growth Hormone Releasing Peptides (GHRP) Induces release GH from hypothalamus and pituitary
- Growth hormone releasing peptide-6 (GHRP 6) - Hexapeptide (6 amino acids)
- GHRP 6-first GHRP discovered

GHRP-”Ghrelin-esque”

- GHRP acts on Ghrelin receptor
- Antagonizes somatostatin
- Stimulates release of GHRH

- ↑ GH release from somatotrophs in anterior Pituitary
- Ghrelin binds to GHS-R (GH secretagogue receptor)
- ↑ GHRH neuron excitability ▼ GABA inhibitory inputs =
- ↑ GHRH release.
GHRP’s

- Ghrelin stimulates production of NO from endothelial cells
- Muscle repair similar to muscle IGFs
- Anti-inflammatory
- Exhibits anti-cancer effects

GH-releasing peptide-2 administration prevents liver inflammatory response in endotoxemia, Miriam Granado, AJP-Endo January 2008 vol. 294 no. 1 E131-E141
Growth Hormone Axis -2

Endocrinology and Metabolism Clinics - Volume 41, Issue 2 (June 2012)
Different GHRP’s

- GHRP-1
- GHRP-2*
- GHRP-4
- GHRP-5
- GHRP-6*

- Alexamorelin
- Ipamorelin*
- Hexarelin*
- Ghrelin

GHRP 6

- Transient increase in cortisol
- Restores GH secretion in obesity
- Improves stage 2 sleep
- Anti-oxidant
- **Reduces Myocardial Necrosis in AMI by 50-78%**
- Side effect: Hunger

- Dosage: 200mcg daily (10 insulin units) SQ Monday-Friday
- Dosage: 150 mcg (2 Sprays am and hs 5x/week)
  - Half life is 2.5 hours
- Dosed with or without GHRH
- Use at night to improve sleep

GHRP 2

- Dosage 100mcg/d
- Dosed with or without GHRH

- Side effects:
  - Increases in cortisol, prolactin, ACTH
  - Increase in appetite – weight gain
  - Hypoglycemia


Another type of GHRP - Ipamorelin

- Ipamorelin-
  - Third generation GHRP
  - 5 Amino acids
- Increases GH via Ghrelin receptor
- Lowers somatostatin = Increased GH
Another type of GHRP- Ipamorelin

- Developed by Novo Nordisk
- Does not raise cortisol, prolactin or aldosterone
Hexarelin (GHRP not GHRH)

- 6 Amino acids
- IV, oral intranasal/ SubQ
- Activates Ghrelin receptor
  - Does not increase hunger
Hexarelin - second generation

- Hexarelin via IV, intranasal, oral and subcutaneous increases GH

- Similar potency of GHRP-2

- half-life of 55 min
- Mild elevation of IGF-1
Hexarelin—Bone loss

- Hexarelin improves bone density in gonadectomized male and in ovariectomized female rats


Hexarelin – Improves Insulin Resistance

- Significantly improves glucose and insulin intolerance
- Decreased triglycerides
- Increase in lean mass
- Study done in Insulin resistant MKR mice

Hexarelin

Cardiovascular benefit of acute myocardial infarction

- Hexarelin treatment (pre and post 0.3 mg/kg/day) preserves myocardial function
  - Significant improvement in LV function after 14 days treatment.

- Hexarelin treatment (pre and post 0.3 mg/kg/day) reduces cardiac fibrosis

- Reduces TGF-1 expression

- Reduces troponin-I, IL-1b and TNF-a level
Hexarelin - Cardiovascular Benefit


- Subjects with dilated cardiomyopathy
- Ischemic cardiomyopathy
- IV bolus of 2 mcg/kg

- Left ventricular function improved in ischemic cardiomyopathy
- No improvement in dilated cardiomyopathy
**Hexarelin** Cardiovascular benefit in 30 min


<table>
<thead>
<tr>
<th>Group</th>
<th>LVEF (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Basal</td>
</tr>
<tr>
<td>Dilated CMP</td>
<td>16.7 ± 2.1</td>
</tr>
<tr>
<td>Ischemic CMP</td>
<td>22.6 ± 2.1</td>
</tr>
<tr>
<td>Normal subjects [41]</td>
<td>64.0 ± 1.5</td>
</tr>
<tr>
<td>GHD patients [41]</td>
<td>50.0 ± 1.9</td>
</tr>
</tbody>
</table>
Hexarelin - on Cortisol and Prolactin

- SQ use Hexarelin (1.5 micrograms/kg) 2/day x 16 weeks

- No increase ACTH, cortisol and prolactin


- IV use Hexarelin increases ACTH, Cortisol and Prolactin

Hexarelin – Dosing

- Suggested Dosing
  - 100 to 200 mcg SQ q hs 5 out 7 nights a week
  - 100-200 mcg SQ daily at bedtime and consider taking 1 month off after 3 months of Hexarelin
**Peptides Synergistic Effects on the Pituitary**

- CJC-1295
- TESOMORELIN
- SERMORELIN

Diagram:
- GHRH
- GHS (synthetic)
- Ghrelin (natural)
- GHRH-R
- GHS-R
- cAMP
- [Ca^{2+}]_i
- Pituitary
- GH

Additional Peptides:
- IPAMORELIN
- HEXARELIN
- GHRP6
- GHRP2
CJC 1295 with Ipamorelin

- CJC 1295 non DAC with Ipamorelin
  - 2000 mcg/ml each
- Starter dose: 100 mcg or 0.05 ml or 5 units SQ at HS Monday to Friday
- Side effect: Flushing
  - Within 5-10 minutes; Lasts 5-15 minutes
- Titrate to 200 mcg or 0.1 ml or 10 units SQ at bedtime
- Take 2 days off per week to prevent “burn out”
GHRH + GHRP (1 + 1 = 10!)
CJC 1295 with Ipamorelin

- CJC 1295 potentiated by GHRP
- Ipamorelin is most effective
- INCREASED LEAN MUSCLE MASS/STRENGTH
- DECREASED BODY FAT
- PROMOTES MUSCLE RECOVERY
- INCREASED ENERGY & OVERALL VITALITY
MK-677/Ibutamoren

• Oral Secretagogue

• Orphan Drug Status
  – Childrens Somatotropin Deficiency

• Increases in GH and IGF-1 levels in 8 days

• Improves Sleep
  – Increases Time in stage 4 deep sleep 50%,
  – Increases Time in REM sleep 20%

• Promotes Muscle

• Dose of 0.8 mg/kg oral q.d x 8 days

• Well tolerated
✓ Randomized, double blind, placebo controlled trial.
✓ 15 W & 17 M, 64-81 yr
✓ 10, or 25 mg MK-677
✓ 28-day study

<table>
<thead>
<tr>
<th>MK-677</th>
<th>Baseline IGF-1</th>
<th>2 weeks IGF-1</th>
<th>4 Weeks IGF-1</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mg</td>
<td>123 ug/l</td>
<td>164 ug/L</td>
<td>N.A.</td>
</tr>
<tr>
<td>25 mg</td>
<td>141 ug/L</td>
<td>219 ug/l</td>
<td>265 ug/L</td>
</tr>
</tbody>
</table>

✓ Randomized, double blind, placebo controlled trial.
✓ 15 W & 17 M, 64-81 yr
✓ 10, or 25 mg MK-677
✓ 28-day study

✓ Increased Appetite
✓ Slight Rise in Insulin Resistance

<table>
<thead>
<tr>
<th>MK-667</th>
<th>Baseline Glucose mg/dL</th>
<th>4 weeks Glucose mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mg</td>
<td>97</td>
<td>113</td>
</tr>
<tr>
<td>25 mg</td>
<td>97</td>
<td>120</td>
</tr>
</tbody>
</table>

**MK-677-Muscle Mass**

- 25 mg/d
- Ages 61-81
- Double blind placebo controlled trial
- 2 years

- Body Weight Increased 0.8 kg vs. placebo
- Body Weight Increased 2.7 kg with MK-677

- Fat Free Mass decreased 0.5 kg-placebo
- Increased 1.1 kg w MK-677

- FBS 5 mg/dl
- LDL 5.4 mg/dl

- Side Effects: Appetite Increase, LE Edema, Muscle Pain
MK-677- Hip Fracture Study

- 25 mg/d x 24 weeks
- Double blind placebo-controlled trial
- 168 Patients
- IGF-1 $51.4$ ng/ml

- Muscle strength and performance
  - Stair Climb- $12.5$ W vs. Placebo
  - Repeated Chair Rise
  - 6-minute walk-Speed $0.7$ m/s

Side Effects:

- FBS (8 mg/dl)
- HbA1c (0.4)
- Hunger

Contraindicated w CHF

Combining 2 GHRP + GHRH

- GHRP 2, 6 + Semorelean
- Combine GHRP-2 + GHRP 6 + Sermorelin =
- IGF-1 80 ng/ml (50%)

Conclusion

- The GH-releasing activity of GHRPs is synergistic with that of GHRH
- GHRPs are pleiotropic peptides with major effects on GH, nutrition, cardiovascular and metabolism
- Generally very well tolerated
- Use the Peptides at bedtime
- Recommend to take it 5 nights a week
Isn’t This Great? Wherever You Are, That’s the Place to Be.

Using Peptides to Increase HGH

Fast Times At Ridgemont High

Damon’s Third Rule of Dating
BPC-157
• Isolated pure gastric juice from surgically prepared dogs.
• Calmed the gastrointestinal tract.
• Treated dyspepsia, gastritis, diarrhea, constipation, heartburn, poor appetite
• Stimulated red blood cell production.
  – Determined 12 years after his death to be intrinsic factor. Pavlov’s “drug” relieved pernicious anemia.
BPC 157
Mechanism of Action

...not just protect the brain from damage, but actually help replace and revitalize damaged cells.

...significantly accelerate bone healing

...protect and promote the health of the intestinal tract

...promote and accelerate wound repair

promote and restores healthy arteries and veins.

...protect the liver and promote its regenerative capacity

...speed up the repair and regeneration of muscle and cartilage tissue

...reduce and reverse cardiac (=heart) damage.
BPC 157 Mechanism of Action

• BPC-157 promotes new vascular formation.

• Stimulates NO production.

• Stimulates angiogenic cytokines VEGF, FGF, and TGF-b

• Upregulates Anti-Inflammatory Gene Transcription Factor


L. BRCIC1, I. BRCIC2, M. STARESINIC3, T. NOVINSCAK3, P. SIKIRIC3, S. SEIWERTH1, MODULATORY EFFECT OF GASTRIC PENTADECAPEPTIDE BPC 157 ON ANGIOGENESIS IN MUSCLE AND TENDON HEALING 1Institute of Pathology, University of Zagreb Medical School, Zagreb, Croatia; 2. Clinical Department of Pathology and Cytology, University Hospital Center Zagreb, Zagreb, Croatia; 3. Department of Pharmacology, University of Zagreb Medical School, Zagreb, Croatia
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**BPC 157 Mechanism of Action**

- Downregulates tumor necrosis factor (TNF)
- Influences corneal restoration
- Neuroregeneration, esp. from TBI
- Upregulates Growth Hormone receptors.
BPC-157

- Muscle Tissue Responds > Tendon
- Due to vascular affinity of BPC 157

- Leukotriene B4
- Lipid mediators
  - Produced during inflammation.
- Thromboxane B
  - Vasoconstrictor/Hypertensive Agent
- Myeloperoxidase
  - Proatherogenic enzyme
BPC 157 and Growth Factor Production

- Insulin derived growth factor
- Platelet-derived growth factor
- Transforming Growth Factor- Beta
- Basic fibroblast growth factor
- Vascular endothelial growth factor
- Growth Hormone (HGH)

  - HGH promotes cell regeneration and proliferation
  - HGH growth hormone increases collagen secretion.
BPC 157 and Ligament Repair

- **MCL Tear**
  - Promotes microscopic regeneration
  - Functional recovery after injury
  - Stimulates granulation tissue collagen I production
  - Increases fibrin matrix repair mechanism.
  - The recovered ligamentous tissue is thicker and sturdier than before the injury.
• **Corticosteroids long term block nitric oxide collagen synthesis** =
  • Atrophy of the treated joint, muscle, or tendon.

• **BPC Blocks Long Term Effects of Corticosteroid Injections**

• **BPC-157 protects endothelium and the formation of scar tissue**
BPC 157 and The GI Tract

- Revives, repairs and rejuvenates the GI tract.
- Provides considerably more healing than:
  - H2-blockers (ranitidine)
  - Proton pump inhibitors (omeprazole)
  - Gastric coating agents (sucralfate) (8)
Useful adjunct in:
- Inflammatory bowel disease/irritable bowel syndrome
- Ulcerative colitis
- Leaky gut syndrome
- Diverticulitis
- Gastric reflux
- Crohn's disease
- Persistent gastric ulcers

BPC 157 and The GI Tract
**BPC 157 and Inflammation**

- Prevents and reverses:
  - Mitochondrial damage
  - Inflammatory aspects of rheumatoid arthritis
  - Inflammatory aspects of Lupus and Hashimoto’s
  - Heals wounds in corneal epithelium.
BPC 157 and Anxiety/Depression

- Increases serotonin to a higher degree than SSRI
- Effective against both acute and chronic anxiety.
BPC 157 and Anxiety/Depression

• Increases serotonin to a higher degree than SSRI

• Effective against both acute and chronic anxiety.
Improves heart failure
Stabilizes both high and low blood pressure
Eliminates hyperkalemia\(^{(25)}\)
Prevents and reverses arrhythmias
  - A-Fib, A-V Block, Ventricular tach,
  - Premature atrial contractions
  - Premature ventricular contractions

\(\text{BPC 157 and Cardiovascular S/S} \ (14-17)\)
BPC 157 adds diversity to your rx. Tool chest

- Reduces and reverses *urinary stress incontinence*
- Protects the liver in the face of *alcohol-induced cirrhosis*
- *Cytoprotective* from NSAID administration, mold, C. difficile, and neurotoxins. (18-21)
- Prevents *hepatic encephalopathy*
- Interacts with dopamine, serotonin, opioid, and *GABA neurotransmitters*
- Prevents *glutathione depletion*. (22)
- Mitigates neuronal damage, improves early outcomes, and delays mortality in 1st 24 hours *post TBI*. (23-24)
BPC 157 adds diversity to your rx. Tool chest

• **Attenuates:** (25)
  – Behavioral agitation
  – Muscle twitches
  – Restless leg syndrome, leg contractures,
  – Edema
  – Atrophic muscles.

• **Enhances:** (26-28)
  – GH (increases GH receptors)
  – Outperforms acyclovir in the treatment of HSV infection,
  – Normalizes esophageal and pyloric sphincter control.
Multiple Sclerosis \(^{(29)}\)
- Decreased nerve damage in the corpus callosum, the laterodorsal thalamus, and anterior horn motor neurons.

Wound healing in alkali chemical burns (Topical). \(^{(30)}\)

Corneal abrasions responded 2 pg/ml, 2 ng/ml, 2ug/ml strength. \(^{(31)}\)
- 2 drops were administered drops every 8 hours for 40 hours.
Safety of BPC 157

- No lethal dose (LD1) to kill 1% of the population could be found. (32)
- By contrast, the lethal dose 50 (i.e., the dose needed to kill 50% of a given population) was:
  - 6 liters for water
  - 175 shots of espresso
  - 13 shots of 40% proof alcohol.
### Summary of Potential Therapeutic Uses (34)

<table>
<thead>
<tr>
<th>Potential Uses</th>
<th>Potential Uses</th>
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<tbody>
<tr>
<td>• Lyme disease/HIV (especially in conjunction with TA1)</td>
<td>• Mold and toxin exposure</td>
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<tr>
<td>• Chronic viral or intracellular infections</td>
<td>• Neurodegenerative disease</td>
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<tr>
<td>• CFS/Fibromyalgia</td>
<td>• Muscle/tendon/Bone repair</td>
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<tr>
<td>• Autoimmune disease (asthma, lupus, etc..)</td>
<td>• Pain Syndromes</td>
</tr>
<tr>
<td>• Inflammatory conditions (markers: CRP, C4a, ESR)</td>
<td>• Eye inflammation and dry eye (with TB4 and stem cell eye drops)</td>
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<tr>
<td>• CVD</td>
<td>• Mitochondrial dysfunction</td>
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<tr>
<td>• Post-surgical</td>
<td>• Depression anxiety</td>
</tr>
<tr>
<td>• Diabetes</td>
<td>• Heart disease/dysfunction</td>
</tr>
<tr>
<td>• Aging</td>
<td>• Given with stem cells (with TB4)</td>
</tr>
<tr>
<td>• Allergies/MCAS</td>
<td>• Urinary incontinence</td>
</tr>
<tr>
<td>• Chemical sensitivity</td>
<td>• Hyper and hypercoagulability</td>
</tr>
<tr>
<td>• GI ulcers/inflammation</td>
<td>• HTN and hypotension</td>
</tr>
<tr>
<td>• Inflammatory bowel disease</td>
<td>• Adjunct to growth hormone replacement (increases GH receptors)</td>
</tr>
<tr>
<td>• Leaky Gut</td>
<td>• Viral infections</td>
</tr>
<tr>
<td>• H-pylori and GERD</td>
<td>• Hypothyroidism/thyroid resistance</td>
</tr>
<tr>
<td>• Periodontitis</td>
<td>• Boosts mitochondrial function</td>
</tr>
<tr>
<td>• Prevent/treat heart arrhythmias</td>
<td>TBI</td>
</tr>
</tbody>
</table>

TBI
BPC 157 Dosing

• **Dosing:**
  – (Packaged in 2000 mcg/ml 5 ml vials.)
  – Oral Capsules 500 mcg

• Orally: 500 mcg troche/capsule for GERD.

• SQ: 800-1000 mcg SQ2x/d x 4-7 days for an acute injury.


• Or

  0.15 ml sq daily

• IV: 2.5 ml (3 mg) with 5 ccs normal saline over 24 minutes for pain.

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References


2. L. BRCIC1, I. BRCIC2, M. STARESINIC3, T. NOVINSCAK3, P. SIKIRIC3, S. SEIWERTH1, MODULATORY EFFECT OF GASTRIC PENTADECAPETIDE BPC 157 ON ANGIOGENESIS IN MUSCLE AND TENDON HEALING 1Institute of Pathology, University of Zagreb Medical School, Zagreb, Croatia; 2. Clinical Department of Pathology and Cytology, University Hospital Center Zagreb, Zagreb, Croatia; 3. Department of Pharmacology, University of Zagreb Medical School, Zagreb, Croatia


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29. KLICEK R. ET AL. JOURNAL OF PHYSIOLOGY AND PHARMACOLOGY 2013, 64, 5, 597-612
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34. Huang T., et al. DRUG DESIGN, DEVELOPMENT, AND THERAPY 2015:9 2485–2499
35. Holtorf, K. A4M: International Peptide Society Certification Course. Las Vegas Nevada, December 12-16, 2018
Thymosin Alpha 1
Hepatitis B & C
HIV/AIDS
Cancer – non-small cell lung (NSCLC), hepatocellular, malignant melanoma
Chemotherapy adjunct - Reduces hematologic side effects with:
  - Cyclophosphamide
  - 5-fluorouracil (5FU)
  - Dacarbazine
  - Isocyanide
Chronic inflammatory conditions including autoimmunity
Cystic fibrosis
Lyme disease
Thymosin Alpha 1 - Indications (5)

- Anything Requiring an Immune Response
  - Steroid-induced apoptosis of thymocytes
  - Depressed response to vaccinations; adjunct to the flu vaccine
  - Geriatric immune support
  - DiGeorge’s syndrome
  - Sepsis
  - Influenza preventive
Thymosin Alpha 1-Mechanism of Action

Improves anti-inflammatory cytokines IL-1 beta, IFN-γ, IL-2, IL-3, IL-6, IL-10. \(^{8-9}\)

CD3+, CD4+ and CD8+, antioxidant activity by specifically improving intracellular glutathione.
Prolonged mean lifespan by 28% and exhibited a 2.8-fold reduction in all cancers. (18)

Nonresectable non-small cell lung cancer demonstrated a statistically significant improvement in relapse-free survival (P=0.04) when TA1 was administered for up to 1 year following radiation therapy.

Overall survival (P=0.009) correlated with T cell restoration to pretreatment levels. (19)
➢ Women have significantly lower intrinsic TA1 than men (P < 0.0001)

➢ Autoimmune patients are significantly lower in TA1 levels than healthy controls. (P < 0.0001)

➢ Patients on disease-modifying, anti-rheumatic drugs (DMARD) exhibit significantly higher TA1 than autoimmune patients not on DMARDs. The DMARDs crowd remains lower than healthy controls, however.

➢ TA1 levels are significantly lower in patients with severe infections and cancer.
Thymosin Alpha 1-Side Effects

- Redness and pain at the injection site.
- Generalized erythema, transient muscle atrophy, polyarthralgia, and rash.
- A transient increase in ALT, up to twice baseline.
- Current recommendations include continuing therapy unless frank signs of liver failure occur.
Thymalfasin (Brand Name - Zadaxin)

Proprietary thymosin alpha 1 product

Developed by the Shanghai-based SciClone Pharmaceuticals Holding Company.

Approved in 30 countries for hepatitis B and C and as a cancer chemotherapy adjunct. (22)

Indicated for: (23-24)


Dose:
- 1.6 mg, injected SubQ, 2 times weekly for 6-12 months
- Patients weighing < 40 kg, dosage adjusted to 40 mcg/kg, 2 times weekly.
Thymosin Alpha 1-Dose

Dosage

1.5 mg subcutaneous (SQ) every third day

RX:

- Viral Infection - 2 weeks
- HIV/Cancer/Hepatitis/Complicated immune suppression/over-activation - 3 mo.

Has a 2-hour Half-Life
REFERENCES


REFERENCES


REFERENCES


20. International Peptide Society, Thymosin Alpha 1 Monograph, 2018, Cincinnati, OH, 2018; 8


But wait!

[Image: Star Trek character with a surprised expression]
PT 141-BREMELANOTIDE

A “Little Blue Pill Alternative”
Peptides - Bremelanotide PT-141

- Acts at the CNS level, binding to melanocortin receptors in the hypothalamus
- Found to induce erection in 80% of males who did not respond to PDE5 inhibitor drugs
- Heightens Libido
- Side Effects: Flushing, Nausea (may be severe in 10%), Spontaneous Penile Erection

Safety and Efficacy of Bremelanotide for HSDD in Women: RECONNECT Study Open-Label Extension Phase Results
Anita Clayton, 1 Sheryl Kingsberg, 2 James Simon, 3 Robert Jordan, 4 and Johna Lucas 4 1 University of Virginia, Charlottesville, VA; 2 University Hospitals Cleveland Medical Center, Cleveland, OH; 3 George Washington University and Women’s Health & Research Consultants, Washington, DC; 4 Palatin Technologies, Inc., Cranbury, NJ
PT-141 Failed Sildenafil Study

- Study of failure of Sildenafil; Rx PT 141
- Randomized Double Blind Placebo controlled study
- N = 342 married men

- 10 mg PT-141 as an intranasal spray
  - 45 minutes to 2 hours prior to sexual stimulation

- Minimum 16 doses/Attempts

- PT-141 Patients had greater intercourse satisfaction (p=.03)

- Side Effects: Nausea, flushing, headache

Peptides - Bremelanotide PT-141

Treatment for female sexual dysfunction
- Premenopausal women diagnosed with female sexual arousal disorder (FSAD), hypoactive sexual desire disorder (HSDD) or both were enrolled in the multi-centered, randomized, placebo-controlled, parallel-group dose-ranging trial.
- Patients were treated for 16 weeks and randomized to one of four double-blind treatment groups receiving placebo or subcutaneous (SC) bremelanotide doses of 0.75mg, 1.25mg or 1.75mg.
- Responder analyses showed bremelanotide had a statistically significant increase in the percentage of women whose total score on the Female Sexual Function Index (FSFI) improved: 69% for 1.75mg v. 46% for placebo (p<0.05).
- A significantly higher percentage of women on bremelanotide v. placebo achieved at least one satisfying sexual event (SSE): 55% for 1.75mg v. 37% for placebo (p<0.05).
- As-needed administration of bremelanotide 1.75mg v. placebo also demonstrated episodic increases in levels of desire (0.4 v. 0.0, respectively) and in the women’s satisfaction with their levels of desire (0.6 v. 0.1, respectively).
- 50% increase in (Satisfying Sexual Events (SSEs) versus a 12% increase with placebo.
Peptides - Bremelanotide PT-141

Men: 0.1 ml SQ PRN

Do not use with PDE5i (proceed with caution- priapism risk)

Women: 0.2 ml SQ PRN

2ml Vial

Maximum 3 times per week

Variable timing to onset of action
First dose predicts

Effects can last hours

SE: Nausea / GI upset, flushing
PT-141 Dosing

- PT 141 – 1000 mcg/ml
- 2 ml vial
- 1.75 mg sq prn
- 45 minutes before event
- Not > 1 dose/24 hours
- Not > 8 doses /month

- Libido can increase after 2-6 hours
- Recommend trying it 12 hours before the event
- Careful mixing it with PDE 5 inhibitor- 12 hour erections can occur

- June 28, 2019
  - Now FDA Approved!
FDA Approved: Vylessi

- Premenopausal female sexual dysfunction
- No indication for men or post-menopausal women
- Not indicated for sexual performance issues
- Contraindicated:
  - Uncontrolled HBP, CVD
- Caution:
  - <1% incidence of focal hyperpigmentation
  - Nausea on second dose. 13% discontinuation rate

www.thepharmaletter.com/article/amag-pharma-closes-deal-for-northamerica-rights-to-rekynda
The American Osteopathic Society of Rheumatic Diseases

OMED October 25-28, 2019 Baltimore Maryland

Congress of Medical Excellence 2.0
February 28, 29, March 1, 2020
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