Muscle Loss and Aging: Even Arnold has Sarcopenia

Olga Kotelko 1.5m
Women’s high school 6.9m
Women’s world 7.5m
Publications on Sarcopenia in PubMed (1993 to 2015)
Sarcopenia
Loss of muscle mass; not due to cachexia or PVD

Kratopenia
(Thinamopenia)
Loss of force
ie strength

Dynapenia
Loss of power;
Force X velocity

Fatigue
Resistance
Aerobic
Illness
Loss of Weight

Frailty

Disability

Loss of ADLs

Clean and jerk
world weightlifting records

<30 35 40 45 50 55 60 65 70 75 80 80+
0 50 100 150 200 250
Sarcopenia
Kratopenia (Thinamopeniae)
Dynapenia
Frailty
Disability

DEXA
Bioelectrical impedance
MRI/CT
MAMC/Calf Circumference
Ultrasound

Isometric (Dynamometry)
Isotonic

Walking speed (>1 m/sec)
Walking distance (6 min)
Stair climbing

CHS (Fried) Criteria
IANA Criteria
SOF Criteria

ADLs
Barthel Index
Functional Index Measure
REPORT

Sarcopenia: European consensus on definition and diagnosis

Report of the European Working Group on Sarcopenia in Older People

Alfonso J. Cruz-Jentoft, Jean Pierre Baeyens, Jürgen M. Bauer, Yves Boirie, Tommy Cederholm, Francesco Landi, Finbarr C. Martin, Jean-Pierre Michel, Yves Rolland, Stéphane M. Schneider, Eva Topinková, Maurits Vandewoude, Mauro Zamboni
## Comparison of Sarcopenia Definitions

(EWGSOP = European Working Group of Sarcopenia in Older Persons; SCWD = Sarcopenia Cachexia and Wasting Diseases; IANA = International Association of Nutrition and Aging)

<table>
<thead>
<tr>
<th>Definition</th>
<th>Function</th>
<th>Muscle Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIG: Cachexia-Anorexia in Chronic Wasting Disease [3]</td>
<td>Gait Speed &lt;0.8m/s, OR other physical Performance test</td>
<td>Low muscle mass (2SD)</td>
</tr>
<tr>
<td>EWGSOP [4]</td>
<td>Gait speed &lt;0.8m/s, Grip strength 40kg males 30kg females</td>
<td>Low muscle mass (not defined)</td>
</tr>
<tr>
<td>IWGS Sarcopenia Task Force [5]</td>
<td>Gait speed &lt;1.0m/s, Grip strength</td>
<td>Low appendicular lean mass (&lt;7.23kg/m² in men; 5.67 in women)</td>
</tr>
<tr>
<td>Sarcopenia with Limited Mobility (SCWD) [6]</td>
<td>6 min walk &lt;400 m, OR gait speed &lt;1.0m/s</td>
<td>Low appendicular lean mass/height²</td>
</tr>
<tr>
<td>Asian Working Group for Sarcopenia [7]</td>
<td>Gait speed &lt;0.8m/s, Grip strength 26kg males 18kg females</td>
<td>Low appendicular lean mass/height²</td>
</tr>
<tr>
<td>Foundation National Institute of Health [8]</td>
<td>Gait speed &lt;0.8m/s, Grip strength 26kg males 16kg females</td>
<td>Appendicular lean mass/BMI</td>
</tr>
</tbody>
</table>
In the New Mexico Aging Process Study we found *obese sarcopenia* to be longitudinally the best predictor of future disability and mortality.
Similarities and comparisons between the sarcopenia field and that of osteoporosis have always been and continue to be inescapable. A younger term and a younger field of clinical investigation, sarcopenia seems to parallel the development of osteoporosis. Not unlike the case of sarcopenia, a working definition of osteoporosis was not universally reached for decades. Looking back and learning from where the osteoporosis field started and where it is now, one cannot be but optimistic that the emerging sarcopenia field will follow a similar course.
WHO Fracture Risk Assessment (FRAX)
www.shef.ac.uk/FRAX/

- Previous fracture
- Parent fractured hip
- Current smoking
- Glucocorticoids
- Secondary osteoporosis
- Alcohol >3 units/day
- Femoral neck BMD
FRAX Questions vs BMD

Leslie et al, Osteoporosis Int
Participants with a total score higher than 4 were classified as having sarcopenia.
<table>
<thead>
<tr>
<th>6-Year Outcomes</th>
<th>Males and Females</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds Ratio (95% CI)</td>
</tr>
<tr>
<td>Incident ADLs $\geq 1^*$</td>
<td>4.46 (2.68-7.42)</td>
</tr>
<tr>
<td>Incident IADLs $\geq 1^*$</td>
<td>2.52 (1.56-4.07)</td>
</tr>
<tr>
<td>Hospitalized overnight past year**</td>
<td>2.43 (1.46-4.05)</td>
</tr>
<tr>
<td>Gait Speed $&lt; 0.8$ m/s**</td>
<td>2.46 (1.13-5.34)</td>
</tr>
<tr>
<td>Mortality*</td>
<td>1.87 (1.17-2.98)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Males and Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>SARC-F Scores $\geq 4$</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Yes (n=93)</th>
<th>No (n=483)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chair stands**</td>
<td>16.00±7.1</td>
<td>11.76±5.1</td>
<td>.004</td>
</tr>
<tr>
<td>Grip strength**</td>
<td>28.11±12.0</td>
<td>31.53±11.2</td>
<td>.549</td>
</tr>
</tbody>
</table>
SARC-F in Baltimore Longitudinal Study 60+ years

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gait Speed &lt;0.8 m/s</td>
<td>9.41(2.51-35.27)</td>
<td>0.001</td>
</tr>
<tr>
<td>Mortality</td>
<td>3.07(1.60-5.73)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Bar chart showing comparisons of ADLs, IADLs, and Grip Strength between SARC-F <4 and SARC-F >4.
Odds Ratio for 4 year outcomes associated with different sarcopenia definitions

Woo et al: Hong Kong Data

- Males
- Females
Frailty and Caenorhabditis Elegans

• Body movement declines with age
• This is related to muscle deterioration (sarcopenia)
• Muscle deterioration correlates with behavior deficits (frailty)
• These changes are correlated with life span and delayed by mutations in daf-2
Allelic Variations Associated with Strength and Body Mass

- Myostatin (GDF8, K133R)
- CNTF and its receptor
- Vitamin D receptor (VDR Bsm1)
- Angiotensin Converting Enzyme
- Androgen receptor gene (CAG-repeats)
- Cyclin dependent kinase inhibitor 1A
- MYOD1
Sarcopenia originates at birth.

Sayer et al. J Gerontol A 59:930, 2004

730 men, 673 women
Known weight at birth and one year

Grip strength correlates with birth weight, not infant growth.
BIOCHEMISTRY OF SARCOPENIA

GH/Testosterone/Creatine

IGF-1

MGF

PI3K

AKT

GLUCORTICOIDS

AMINO ACIDS

MTOR

S6K1

PROTEINS

HYPERTROPHY

CYTOKINES

TNFRI

IKK

IkappaBalpha

NFkappaB

FADD

Capsase 8

DNA fragmentation

APOPTOSIS

STEM CELL

Capsase 3

Diabetes

ACTOMYSIN

ACTIN/ MYOSIN

PO4

FOXO

+ PO4

Atrogin I

(MAFbX)

MURF I

Ubiquitin

Proteasome

Protein degradation

ATROPHY

Cachexia

Inducing Factor

Rejuvenation of aged progenitor cells by exposure to a young systemic environment

Irina M. Conboy¹ ², Michael J. Conboy ³, Amy J. Wagers ², Eric R. Girma ⁴, Irving L. Weissman ⁵ & Thomas A. Rando ¹ ²

Original Article


Antiproteolytic effects of plasma from hibernating bears: A new approach for muscle wasting therapy?

Gemma Fuster¹, Silvia Busquets ², Vanessa Almendro, Francisco J. López-Soriano, Josep M. Argilés

Cancer Research Group, Departament de Bioquímica i Biologia Molecular, Facultat de Biologia, Universitat de Barcelona, Diagonal 645, 08028 Barcelona, Spain

Received 19 January 2007; accepted 2 July 2007
Parabiosis Rejuvenates Old Mice

Muscle
Old muscle shows fiber size heterogeneity
And fiber grouping

Increase in muscles with MYOSIN HEAVY CHAIN
with aging and denervation
The Motor Unit Number Index (MUNIX) in sarcopenic patients

MOTORNEURONS and AGING

25-30% reduction in motorneurons

Small motorneurons sprout and innervate type II with eventual loss of type II fibers

Elevated levels of a C-terminal agrin fragment identifies a new subset of sarcopenia patients
INCREASED LEPTIN
DECREASED CALORIE AND PROTEIN INTAKE
DECREASED PHYSICAL ACTIVITY

VISCENTAL OBESITY
INCREASED FAT INFILTRATION

INCREASED ADIPOGENETIN

INCREASED CALORIE AND PROTEIN INTAKE
DECREASED PHYSICAL ACTIVITY

INSULIN RESISTANCE

HYPERTRIGLYCERIDEMIA

DECREASED PHOTIN D DEFICIENCY
DECREASED GROWTH HORMONE AND GHERELIN

VITAMIN D DEFICIENCY
DECREASED CNTF
DECREASED GROWTH HORMONE AND GHERELIN

DECREASED MGF
DECREASED IGF-1EA

DECREASED ANABOLIC HORMONES
TESTOSTERONE
DHEA

DECREASED IGF-2
CNTF

GENETIC
Myostatin
ActivinIIIR
Notch I
IGF-2
CNTF

MITOCHONDRIAL ABNORMALITIES

CYTOKINE EXCESS
egTNFα
IL-6

DECREASED MOTOR UNITS

ATHEROSCLEROSIS

HYPOGAMMA LIPOIDOSIS
Patients With Type 2 Diabetes Show a Greater Decline in Muscle Mass, Muscle Strength, and Functional Capacity With Aging

Participants with diabetes mellitus had significantly slower gait speed ($0.96 \pm 0.02 \text{ vs } 1.08 \pm 0.01 \text{ m/s}; P < .001$)
Fig. 1 Normalized maximal isometric muscle strength of the plantar flexors (MaxPlant), dorsal flexors (MaxDors), knee extensors (MaxExt) and knee flexors (MaxFlex) (P-value: main effect of the analysis of variance between the three groups. Post hoc analy... T. Herman IJzerman, Nicolaas C. Schaper, Tom. Melai, Kenneth Meijer, Paul J.B. Willems, Hans H.C.M. Savelberg

Lower extremity muscle strength is reduced in people with type 2 diabetes, with and without polyneuropathy, and is associated with impaired mobility and reduced quality of life

Diabetes Research and Clinical Practice, Volume 95, Issue 3, 2012, 345 - 351
Sarcopenia and Diabetes
African Americans 50 - 65 years

Diabetics who were SARC-F positive had a high risk of future ADL and IADL deficits
6 Minute Walk Distance

All greater than p<0.001

- Diabetes: 415.27
- No Diabetes: 473.85
### Frailty (FRAIL) and Sarcopenia (SARC-F) in Diabetic Outpatients

#### Prevalence by Age Group

<table>
<thead>
<tr>
<th></th>
<th>50-59 (n=59)</th>
<th>60-69 (n=82)</th>
<th>70+ (n=57)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frailty (FRAIL; 0-5), %</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Healthy (0)</td>
<td>42.4</td>
<td>28.0</td>
<td>28.1</td>
</tr>
<tr>
<td>Pre-Frail (1-2)</td>
<td>39.0</td>
<td>40.2</td>
<td>36.8</td>
</tr>
<tr>
<td>Frail (3-5)</td>
<td>18.6</td>
<td>31.7</td>
<td>35.1</td>
</tr>
<tr>
<td><strong>Sarcopenia (SARC-F; 0-10), %</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No (0-3)</td>
<td>78.0</td>
<td>75.6</td>
<td>56.1</td>
</tr>
<tr>
<td>Yes (4-10)</td>
<td>22.0</td>
<td>24.4</td>
<td>43.9</td>
</tr>
<tr>
<td><strong>Cognitive Dysfunction (RCS; 0-10), %</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No (8-10)</td>
<td>78.9</td>
<td>77.8</td>
<td>61.8</td>
</tr>
<tr>
<td>Yes (≤ 7)</td>
<td>21.1</td>
<td>22.2</td>
<td>38.2</td>
</tr>
</tbody>
</table>
Sarcopenia Outcomes
SLU Endocrine Clinic
Adjusted for Age, Gender, Education and HgBA1C

**ODDS RATIO**

- Hospital Utilization  \[3.735 \ (1.649 - 8.458)\]  
  \[P<0.002\]

- New Disability  \[4.237(1.764-10.181)\]  
  \[P<0.001\]
Treatment for SARCOPENIA is RESISTANCE EXERCISE
Bed Rest

Bed Rest leads to 3x rate of muscle loss in 1/3 time.

Young (30 days)

Old (10 Days)

Old 3 day_hosp

Increased protein intake stops muscle loss and decreases strength loss.

Hospitalization accelerates muscle loss.

1.25 protein/kg/day
Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial

Schweickert WD, et al. Lancet 2009;373:1874-
Effects of High-Intensity Progressive Resistance Training and Targeted Multidisciplinary Treatment of Frailty on Mortality and Nursing Home Admissions after Hip Fracture: A Randomized Controlled Trial
Singh et al JAMDA, Jan 2012

- Comprehensive Geriatric Assessment and 12 months resistance training twice weekly

- Mortality OR 0.19 (0.04 – 0.91)
- Nursing Home OR 0.16 (0.04 – 0.64)
- ADL’s p <0.02
- Assistive Device p<0.01
From: Effect of Structured Physical Activity on Prevention of Major Mobility Disability in Older Adults: The LIFE Study Randomized Clinical Trial


1635 sedentary men and women aged 70 to 89 years who had physical limitations
Physical performance

![Graph showing SPPB (points) over time for Placebo and Protein groups.](image)

<table>
<thead>
<tr>
<th>P-value</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>0.050</td>
</tr>
<tr>
<td>Time</td>
<td>0.003</td>
</tr>
<tr>
<td>Treatment x Time</td>
<td>0.019</td>
</tr>
</tbody>
</table>

Tieland et al., JAMDA 2012
Effects of Exercise and Amino Acid Supplementation on Body Composition and Physical Function in Community-Dwelling Elderly Japanese Sarcopenic Women: A Randomized Controlled Trial
From: **Effect of Structured Physical Activity on Prevention of Major Mobility Disability in Older Adults: The LIFE Study Randomized Clinical Trial**


1635 sedentary men and women aged 70 to 89 years who had physical limitations
PROVIDE (PROTEIN) STUDY CENTRES ACROSS EUROPE
• PROT-AGE recommendations for dietary protein intake in healthy older adults
  • To maintain and regain muscle, older people need more dietary protein than do younger people; older people should consume an average daily intake in the range of 1.0 to 1.2 g/kg BW/d.
  • The per-meal anabolic threshold of dietary protein/amino acid intake is higher in older individuals (ie, 25 to 30 g protein per meal, containing about 2.5 to 2.8 g leucine) in comparison with young adults.
  • Protein source, timing of intake, and amino acid supplementation may be considered when making recommendations for dietary protein intake by older adults.
  • More research studies with better methodologies are desired to fine tune protein needs in older adults.
FSH

LH

Testosterone
Factor Analysis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sarcopenia</th>
<th>New Mexico Aging Process Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle Mass</td>
<td>0.30</td>
<td>0.45</td>
</tr>
<tr>
<td>Muscle Strength</td>
<td>0.45</td>
<td>0.06</td>
</tr>
<tr>
<td>Age</td>
<td>0.25</td>
<td>0.34</td>
</tr>
<tr>
<td>Energy Intake</td>
<td>0.34</td>
<td>0.35</td>
</tr>
<tr>
<td>Physical Activity</td>
<td>0.27</td>
<td>0.23</td>
</tr>
<tr>
<td>IGF-1</td>
<td>0.45</td>
<td>0.27</td>
</tr>
<tr>
<td>FTI</td>
<td>0.27</td>
<td>0.23</td>
</tr>
</tbody>
</table>

Australia Andriol Study

12 Months
n=76

60+ Years
Borderline Hypogonadal
Andriol 80mg BID

Lean Body Mass
P<0.0001
Androgens

May be of particular benefit for the treatment of “sarcopenic obesity”

% Change in Lean Body Mass

% Change in Fat Mass

* P < 0.0001

* P < 0.002
Testosterone Dose Response
Bhasin et al JCEM 90:678-688
2005

Change in Fat Free Mass (kg)

Change in Fat Mass (kg)

Changes in Skeletal Muscle Mass (kg)

Change in Leg Press strength 1RM (kg)

T.E. Dose (mg wk)

Youn Old
**Fat cell lineage**
- Pre-adipocyte
- Progenitor cell
- Mature adipocyte
  - LPL
  - PPARy
  - C/EBPα

**Muscle cell lineage**
- Satellite cell
- Myoblast
- Myotube
  - MyoD
  - Desmin
  - MHC

**TESTOSTERONE**
- Increased Notch
- No change in Numb
- Inc. PCNA

**Muscle protein synthesis**

**Muscle protein turnover**

**ubiquitin-proteasome pathway**
THE MECHANISM BY WHICH TESTOSTERONE INCREASES SATELLITE CELLS AND DECREASES ADIPOGENESIS

**6PPARγ**

**c1a**

**6 ADIPOGENESIS**

**6 MYOSTATION**

**5 β Catenin**

**GSK3b**

**Smad4**

**Wnt**

**6 Wnt 6**

**5 MYOGENESIS**

**5 s-myc**

**6 Cdlc 7**

**6 Cyclin 1**

**6 Cyclin cr kinase**

**5 Myosin**

**Heavy pp6**

**5 Myosin 15B**

**5 Myosin 1xα**

**5 CELL CYCLING**

**5 MYOGENESIS**
Testosterone IM and Physical Performance
Page et al, JCEM 90:1502, 2005

- Age 75, 36 months
- T(n=24), T+F (n=24), Placebo (n=22)
- Improved TFP (chair rising, walking, stair climbing, opening/closing door)
- Improved LBM and handgrip strength
Physical Function Trial Outcomes.

<table>
<thead>
<tr>
<th>Table 2. Physical Function Trial Outcomes.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohort and Outcome</td>
</tr>
<tr>
<td>-------------------------------------------</td>
</tr>
<tr>
<td>Men enrolled in Physical Function Trial</td>
</tr>
<tr>
<td>Primary outcome: increase of ≥50 m in 6-min walk test — no/no total % (%)</td>
</tr>
<tr>
<td>Testosterone</td>
</tr>
<tr>
<td>Placebo</td>
</tr>
<tr>
<td>Secondary outcomes</td>
</tr>
<tr>
<td>6-Min walking distance — m</td>
</tr>
<tr>
<td>Testosterone</td>
</tr>
<tr>
<td>Placebo</td>
</tr>
<tr>
<td>Increase of ≥1/2 in PF-10 score — no/no total % (%)</td>
</tr>
<tr>
<td>Testosterone</td>
</tr>
<tr>
<td>Placebo</td>
</tr>
<tr>
<td>PF-10 score (%)</td>
</tr>
<tr>
<td>Testosterone</td>
</tr>
<tr>
<td>Placebo</td>
</tr>
</tbody>
</table>

All Testosterone Trials participants
Increase of ≥50 m in 6-min walk test — no/no total % (%)

| Testosterone                              | 392        | 40(35)         | 32(35) | 25(35) | 14(35) | 7.9(35) | 1.76 | (2.12 to 2.57) | 0.003 |
| Placebo                                   | 389        | 25(35)         | 35(35) | 37(35) | 41(35) | 41(35) | 0.08 | (0.02 to 0.14) | 0.007 |

6-Min walking distance — m

| Testosterone                              | 392        | 387.0±83.7     | 10.9±45.1 | 11.0±40.2 | 6.7±45.1 | 13.6±43.4 | 6.69 | (3.80 to 11.37) | 0.02 | (0.02 to 0.14) | 0.007 |
| Placebo                                   | 389        | 387.0±83.7     | 5.7±45.1 | 3.2±47.4 | 6.4±45.8 | 0.02 | (0.02 to 0.14) | 0.007 |

Increase of ≥1/2 in PF-10 score — no/no total % (%) |

| Testosterone                              | 309        | 115(89)        | 133(89) | 115(89) | 103(89) | 103(89) | 1.50 | (0.88 to 2.09) | 0.02 |
| Placebo                                   | 305        | 87(89)         | 103(89) | 89(89) | 82(89) | 0.02 | (0.06 to 0.24) | 0.002 |

PF-10 score (%)

| Testosterone                              | 309        | 71.3±20.2      | 5.6±14.7 | 6.1±16.7 | 5.3±18.5 | 4.3±16.9 | 3.06 | (1.18 to 4.94) | 0.18 | (0.06 to 0.24) | 0.002 |
| Placebo                                   | 305        | 69.7±21.2      | 3.9±12.2 | 3.4±16.2 | 2.3±17.9 | 1.3±16.9 | 0.02 | (0.06 to 0.24) | 0.002 |

*P* values in parentheses are means ±SD.

†The treatment effect for dichotomous outcomes is the odds ratio for achieving the outcome versus not achieving the outcome among men assigned to testosterone versus those assigned to placebo. For continuous outcomes, the treatment effect is the mean difference in the outcome among men assigned to testosterone versus those assigned to placebo. All analyses are adjusted for baseline total testosterone level (<200 or >200 ng per deciliter), age (>75 or >75 years), site, site participation in the main trial, use or non-use of antipsychotics, and use or non-use of phosphodiesterase type 5 inhibitors.

‡For continuous outcomes, the effect size is the treatment effect divided by the baseline standard deviation.

§The *P* value for the treatment effect was determined by using a logistic mixed model with a random effect for participant for dichotomous outcomes and a linear mixed model with a random effect for participant for continuous outcomes.

¶Scores on the physical function scale (PF-10) of the Medical Outcomes Study 36-item Short-Form Health Survey range from 0 to 100, with higher scores indicating better function.

The outcomes for all Testosterone Trials participants are exploratory outcomes.
Testosterone and Heart Failure
Caminiti et al, JACC 54:919;2009
STEROIDS ENHANCE PERFORMANCE
GTx SARM (Ostarine)
n=120, Mean age 64.8 yrs

Fat Free Mass (Dexa)

Stair Climb Power (Watts)
VITAMIN D AND FRAILTY

Longitudinal Fall in Vitamin D with Age

- Hypovitamin D is associated with declines in muscular strength and reported disability (Zamboni et al, J. Gerontol 57:m7, 2002)
- Low Vitamin D and high PTH are associated with sarcopenia (Visser et al, JCEM 88:5766, 2003)
- Low Vitamin D is an independent predictor of falls (Flicker et al, Jags 51:1533, 2003)

DBP-concentrations correlated with handgrip force \( (r = 0.16; P = 0.02) \)

Body mass index and absolute fat mass correlated with the DBP-concentrations
LESSONS FROM GH STUDIES

• GH increases nitrogen retention
• GH causes weight gain
• GH increases muscle mass
• GH possibly increases type II muscle fibers
• GH does not increase strength
• GH long term produces side effects
DOES MUSCLE mIGF-1 PLAY A ROLE IN SARCOPENIA?
GHRELIN

- Produced in stomach fundus
- Enhances food intake
- Muscle mass gain (?GH effect)
- Enhances memory
- ANAMORELIN (Phase 2): Over 12 weeks, lean body mass increased in 38 patients in the anamorelin group by a least-squares mean of 1.89 kg (95% CI 0.84 to 2.95) compared with a decrease of a least-squares mean of -0.20 kg (-1.23 to 0.83) for 36 patients in the placebo group (difference 2.09 kg)
- ROMANO 1 and 2: Increased lean mass and FAACT anorexia/Cachexia
Anamorelin for patients with cancer cachexia: an integrated analysis of two phase 2, randomised, placebo-controlled, double-blind trials.
Garcia JM¹, Boccia RV², Graham CD³, Yan Y⁴, Duus EM⁴, Allen S⁴, Friend J⁴.

- Over 12 weeks, lean body mass increased in 38 patients in the anamorelin group by a least-squares mean of 1.89 kg (95% CI 0.84 to 2.95) compared with a decrease of a least-squares mean of -0.20 kg (-1.23 to 0.83) for 36 patients in the placebo group (difference 2.09 kg [0.94-3.25]; p=0.0006)
MYOSTATIN DELETIONS

Peptobodies
Activin Receptors
GDF-8 and other negative regulators inhibit the growth of muscle tissue.

ACE-031 inhibits the negative regulators, and rebuilds muscle.
**Muscle Mass, Volume (DXA, MRI)**

- Total body lean mass (DXA) and thigh muscle volume (MRI) increased in higher dose groups and was sustained post-dosing.

**Bone Markers, Density**

- BSAP (a marker of bone formation) increased, sCTX (a marker of bone resorption) decreased, and lumbar spine BMD (DXA) increased.

**Fat Markers, Mass**

- Adiponectin increased, leptin decreased, and total body fat mass (DXA) decreased.
Treatment of sporadic inclusion body myositis with bimagrumab.
Amato, Anthony; Sivakumar, Kumaraswamy; Goyal, Namita; David, William; MD, PhD; Salajegheh, Mohammad; Praestgaard, Jens; Lach-Trifilieff, Estelle; Trendelenburg, Anne-Ulrike; Laurent, Didier; Glass, David; Roubenoff, Ronenn; MD, MHS; Tseng, Brian; MD, PhD; Greenberg, Steven

DOI: 10.1212/WNL.0000000000001070
Conclusions

• Diabetics are more likely to be sarcopenic than non-diabetics and this occurs at a younger age.

Diabetics loose muscle and muscle strength and have a high likelihood to have Sarcopenia

• SARC-F is a useful rapid screening tests in diabetics and older persons

• Testosterone is the primary hormone associated with sarcopenia