Muscle weakness: Drug treatment
Martine Extermann

Disclosure
- I am the local PI for studies GTX 504 and 505 and a consultant for GTx.

Appetite stimulants
- Megestrol acetate
  - Weight gain but no LBM gain
- Ghrelin
  - ↑ appetite in cancer patients and others
  - ↑ LBM, HGS, peak VO2 in CHF patients
- Ghrelin mimetics (e.g. anamorelin, RC-1291)
  - Randomized pilot: ↑ LBM (↑ IGF-1)

Beta-adrenergic receptor stimulation
- MT 102
  - β-blocker with intrinsic activity; antagonist 5-HT1a receptor
  - ↑ in rats, ↑ LBM, weight, and functional activity
  - Randomized phase II study (2 doses vs placebo), ongoing.

Immunomodulators
- Thalidomide
- Celecoxib
- ALD-518 (anti IL-6 antibody)
- AVR-118 (anti-IL-8 and MCP-1 antibody)

Change in bone free arm muscle area (AMA) in pancreatic cancer patients randomised to either thalidomide (n=17, week 4; n=12, week 8) or placebo (n=16, week 4; n=8, week 8).


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Nutritional supplements

- L-carnitine
  - Pancreatic cancer: ↑ BMI (cell mass, fat) (Kraft 12)
- Vitamin D
  - Multiple geriatric studies: ↑ muscle strength
  - Prostate cancer: ↑ muscle strength (Van Veldhuizen 00)
- Fatty acids
  - Eicosapentenoic acid: 5 studies, effectiveness?

Thalidomide combined with MA and supplements

- Randomized study: combo better than MA, eicosapentenoic acid, L-carnitine, thalidomide alone
- Lean body mass, resting energy exp., active energy exp., fatigue, IL-6, appetite, Glasgow prognostic score all improved.


EPO

- Darbopoietin
  - 221 CRC patients, peri-op treatment
  - ↑ post-op work capacity and Hb
  - No effect on fatigue, postural sway, QOL, and muscle strength

Norager et al., Oncology 2006

Anabolic steroids

- Testosterone
- Nandrolone
- Oxandrolone

- Proven, but very little cancer literature

Selective androgen receptors modulators

- Enobosarm (a.k.a. ostarine)
  - In phase III trials in NSCLC
- LGD-4033
  - Early study shows increase in lean body mass in young men without PSA changes (Basaria 2012)
  - Several molecules in preclinical development

Ostarine increased lean body mass and improved physical function in three efficacy clinical trials

Phase II cancer cachexia trial:
- 159 subjects with cancer cachexia, 4 months tx

Phase II sarcopenia trial:
- 120 elderly men and postmenopausal women, 3 months tx

Phase Ib sarcopenia trial:
- 88 postmenopausal women, 3 months tx

Placebo Ostarine 3mg

Stair climb
- Placebo Ostarine 3mg
- Placebo Ostarine 3mg
- Placebo Ostarine 3mg

Bilateral leg press
- Placebo Ostarine 3mg
- Placebo Ostarine 3mg
- Placebo Ostarine 3mg

courtesy: S. Dodson
Conclusions

- Several agents have at least a marginal effect on LBM
- Most studies are small
- A consistent effect on strength remains to be confirmed in cancer patients.
- Given the limits of physical exercise in the elderly, pharmacologic interventions are a great opportunity.