More than Pain Management: Supportive Care of the the Patient with Cancer

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Definition of Palliative Care

Comprehensive, specialized care provided by an interdisciplinary team to patients and families living with a life-threatening or severe advanced illness expected to progress toward dying and where care is particularly focused on alleviating suffering and promoting quality of life. Major concerns are pain and symptom management, information sharing and advance care planning, psychosocial and spiritual support, and coordination of care.

Academy of Hospice & Palliative Medicine 2004

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Re-energize the Definition

- **Palliative care *not just for dying patients***
- **Elements of good palliative care and hospice care as part of standard care for cancer from the time of diagnosis and throughout the course of treatment**

Palliative Care Throughout the Trajectory of Cancer Illness

Modalities of Care

- Evidence-based role of palliative chemotherapy
- Role of palliative radiation therapy
- Role of palliative surgery
- Ask the Question and Follow-up: *"How Are You?"*
- Manage Pain
- Recognize & Treat Fatigue
- Maintain Nutrition to Reduce Morbidity & Mortality
- Enhance Patient & Family Adjustment
- Goals of Care & Advance Planning

Palliative Chemotherapy

• **Pancreatic** (gemcitabine)	• ↑ Survival
• **Colon** (irinotecan)	• ↑ Survival & ↑ QoL
• **Breast** (navelbine, hormonals)	• Symptom reduction, ↑ QoL
• **Lung** (docetaxel)	• ↓ tx. of tumor-related conditions, ↑ QoL
• **Prostate** (prednisone + taxane)	• ↑ function; ↓ pain
• **Ovarian** (taxanes)	• ↑ QoL

Blum, manuscript in preparation

Palliative Radiation Therapy

- **Symptom Relief Radiation Therapy**
  - **Bone metastases**
    - **External beam RT**
    - **Infusion Strontium-99 (done at *Nuclear Medicine center*)**
  - **Recurrences that obstruct respiration, swallowing**
  - **"band-like" pain from pancreatic cancer**
  - **Superior vena cava syndrome**
  - **Reduce smell of fungating wounds (surface RT)**
- ***"Quad shot" bid* treatment x 2 days; reevaluate two weeks after; can repeat**

Palliative Surgery

- Attitudinal shift
  - Professional
  - Patients & families
- *Minimally invasive* procedures makes surgical intervention more attractive and useful
  - CALGB studies:
    - Bedside chest tube vs. Ambulatory *Pleurex* ® catheter for pleural effusions;
    - VATS thoracoscopic drainage of malignant pleural effusions: accepted for publication in *Chest* (↑ drainage; ↑ QoL; ↑ infectious complications; = survival Fleishman Proc ASCO 2004:1458, Dressler, C Chest. 2005 Mar;127(3):909-15)
- Bowel obstruction, ascites also amenable to minimally invasive approach

Adapted from Boolbol 2004

"How Are You?" [1]

- Based upon NCCN *Distress Thermometer*
- Qualitative and qualitative measure distributed at *pivotal visits* based upon modality of care or survivorship
- *Do ask! Do Tell!*: What are you needs?
- Most common responses: Pain, Fatigue, Worry, Sadness, Dry Skin/Sleep Blum Fleishman Proc ASCO 2002:2836
- Best serves the patients who suffer silently
- Validated against standardized measures (Jacobsen, et al Cancer. 2005 Apr 1;103(7):1494-502)

Distress Thermometer

[name label]

Continuum Cancer Centers

Continuum Cancer Centers of New York

We are interested in learning how your illness has affected you and your family.

FIRST:
Please circle the number (0-10) that best describes *how much distress* you have been experiencing in the past week including today.

THEN: Please indicate WHICH of the following is a cause of distress. A staff member may call you to follow-up. At what telephone number would you like to be called?_____

Practical
- ☐ Housing
- ☐ Insurance
- ☐ Work/school
- ☐ Transportation
- ☐ Child care

Family
- ☐ Dealing with partner
- ☐ Dealing with children

Emotional
- ☐ Worry
- ☐ Fears
- ☐ Sadness
- ☐ Depression
- ☐ Nervousness

Spiritual/Religious
- ☐ Relating to God
- ☐ Loss of faith

Physical
- ☐ Pain
- ☐ Nausea
- ☐ Fatigue [RN/MD: Hg:___ Hct:___]
- ☐ Sleep
- ☐ Getting around
- ☐ Bathing/dressing
- ☐ Breathing
- ☐ Mouth sores
- ☐ Eating
- ☐ Indigestion
- ☐ Constipation
- ☐ Diarrhea
- ☐ Changes in urination
- ☐ Fevers
- ☐ Skin dry/itchy
- ☐ Nose dry/congested
- ☐ Tingling in hands/feet
- ☐ Feeling swollen
- ☐ Sexual
- ☐ Appearance

Other: _____

DRAFT 01-07-02

"How Are You?" 2

- Collect at *pivotal* visit; varies by cancer, treatment modality, time course
- Multi-disciplinary Committee to respond; refer out for specialists as necessary
- Response by rating:
  - *0-3*: information/education, "wellness" programs
  - *4-6*: call back; telephone assessment or referral
  - *7-10*: same-day assessment before patient leaves

Recognize & Manage Fatigue

- Emerging role of cytokines
- Fatigue is more than anemia
- Multi-modal approach
  - Optimize physiologic parameters (e.g., thyroid)
  - Exercise (preventively)
  - Nutrition (preventively)
  - The Present: stimulants
  - The Future: monoclonal antibodies that reduce cytokines

Successful Trial: Fatigue & Cognitive Impairment After Chemotherapy

- Placebo-controlled randomized trial of *d*-methylphenidate (Focalin®) > 2months, s/p ≥4 cycles of chemotherapy
- 132 patients; 75% breast cancer
- Statistically significant improvement in fatigue, approached significance for ability to learn/retain new information (ice storms barrier to in-person follow-up)

Proc ASCO 2005:8000; San Antonio Breast Conf, 2005

Hypogonadism in Male Patients

- HIM study 2006: 38.7 in primary care practice, < 300 ng/dl
- NSCLC & dialysis: 43-63% decrease in plasma/free testosterone
- Hodgkin's Disease
- HIV/AIDS: replacement with testosterone, oxandrolone

BI Cancer Center Pilot Study

- convenience sample (in- and out-patients)
- male patients
- excluded:
  - prostate, testicular or [male breast] cancers
  - known hypogonadism
  - HIV/AIDS
  - testosterone/DHEA supplementation within 90 days

Pilot Results [1]

- N=40
- age: 24-82 years
  - 13 <50 years old
  - 26 >50 years old

Pilot Results 2

- total testosterone < 300 ng/dl established as *usual* cut-off score
- 18/40 (45%): total testosterone < 300 ng/dl
- 10/18 (56%): aerodigestive cancers
  - 6: head and neck
  - 3 lung
  - 4 lymphoma
  - 1 gastric
  - 1 rectal
  - 1 bladder
  - 1 CLL

Current Open Study

- Confirm initial pilot results with larger trial
- Better represent genetic diversity of US male population
- Sites:
  - BI
  - SLR
  - University of Iowa Cancer Center
  - Ohio State University
  - Christiana Care Newark, Delaware

Nutrition: Weight Loss [1]

- Weight loss in cancer is a harbinger of poor prognosis
- Mechanical, metabolic or practical causes; trace the path of food through the body
- Particularly vulnerable: lung, pancreatic, head and neck, colorectal
- Three stage process:
  - Type and amount of calories via accessible portal: Intake
  - Retention of Calories
  - Energy Expenditure
- Optimal intervention targets all three stages

Nutrition: Weight Loss 2

Intake

- Route
  - Oral
  - Parenteral
    - Feeding tubes: gastrostomy, jejunostomy
    - Intravenous: central, peripheral
- Quality/type of calories
  - "Dense"
  - Pre-digested
- Pharmacologic Approaches
- Nutritional Counseling

Pharmacological Approach to Cancer Cachexia [1]

DRUG	COMMENT
glucocorticoids	↓ nausea; improvement of appetite; little effect on LBM; signif. side effects; increased muscle catabolism
progestational agents	CALGB study 600-800 mg/day; little effect on LBM; thrombotic risk
cyproheptadine and other anti-5-HT drugs	effect on appetite and nausea; short-term effect; very sedating; minimal weight gain
prokinetic agents	metoclopramide may relieve fullness and early satiety; short-time effect
cannabinoids	dronabinol effective in preventing chemotherapy-related emesis; “munchies”, euphoria (“high”)

Pharmacological Approach to Cancer Cachexia 2

DRUG	COMMENT
5'-Deoxy-5'-fluorouridine	Attenuates cachexia in mice; no clinical sudies available
Melatonin Mahmoud Am J Hospice Pall Care 22(4):295-309 Jul-Aug 2005	Decreases IL-6; may attenuate weight loss and improve anorexia; high doses needed; antioxidant ?; trials needed
Thalidomide	Inhibits TNF anf IL-6; attenuates weight loss; neuropathy, myelosuppression, rash, somnolence
β-2 agonists	Suppress hyperactivation of muscle proteolysis in exp. cachexia; no clinical trials; possible side effects
NSAIDs	Inhibit prostaglandin synthesis; may reduce weight loss in animals
Olanzipine	Stigma; sedation trade-off

Pharmacological Approach to Cancer Cachexia [3]

failed attempt:

hydrazine sulfate

- **"rocket fuel" petroleum by-product**
- **thought to be a cytotoxic agent in 1950's in Russia**
- **Thought to increase appetite and weight**
- **three US studies in NCI clinical trial groups (CALGB & NCCTG)**
- **NSCLC (IIIB-IV) & colon cancer**
- **<u>NO</u> survival advantage or weight gain; minimally worsened quality of life (nausea, neuropathy)**
- **allegations of poor study design**

Kosty MP, Fleishman SB, et al (CALGB 8931).; LoPrinzi, C et al (NCCTG) Jl Clin Oncol 13:12(6):1113-20, June, 1994.

More Powerful Than an Rx

- Omega-3 fatty acids (eicosapentanoic acid, EPA) marketed as food supplement
- Essential amino acid mix:
  - arginine
  - glycine
  - β hydroxybutyrate
- Carnitine: nutraceutical for fatigue

Cruciani et al Ann N Y Acad Sci. 2004 Nov;1033:168-76

EPA: eicosapentaenoic acid

- an omega-3 fatty acid
- downregulates inflammatory response associated with cancer-induced weight loss through membrane, receptor and enzymatic functions
- found in deep-sea oily fish (salmon, mackerel, tuna, sardines)
- typical Western dietary intake: approximately 0.1 g/day

EPA Clinical Studies

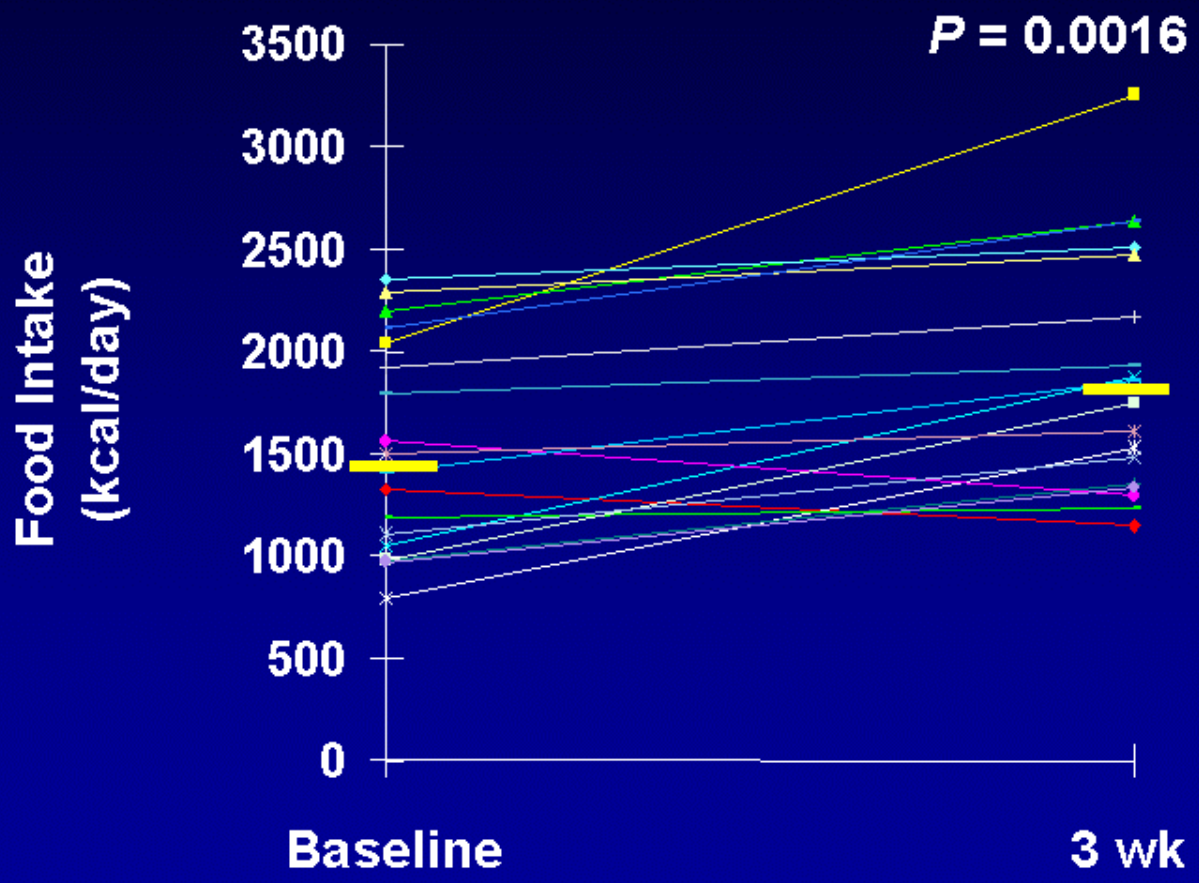
Study	Design	Results
Wigmore et al: *Nutrition* **1996;12:27.**	**Pancreatic cancer, 2.2 g EPA,12 weeks; 2.9 kg/mo wt loss prior to supplementation**	**Weight stabilization**
Wigmore et al: *Nutr Cancer* **2000;36:177.**	**Pancreatic cancer, 6 g EPA/day,12 weeks; 2.0 kg/mo wt loss prior to supplementation**	**Weight stabilization**
Bruera et al: *J Clin Oncol* **2003;21:129.**	**Mixed tumor types, 1.8 g EPA/day, 2 weeks; >5% wt loss prior to supplementation**	**Weight stabilization**

Pilot Study: EPA in Unresectable Pancreatic Cancer

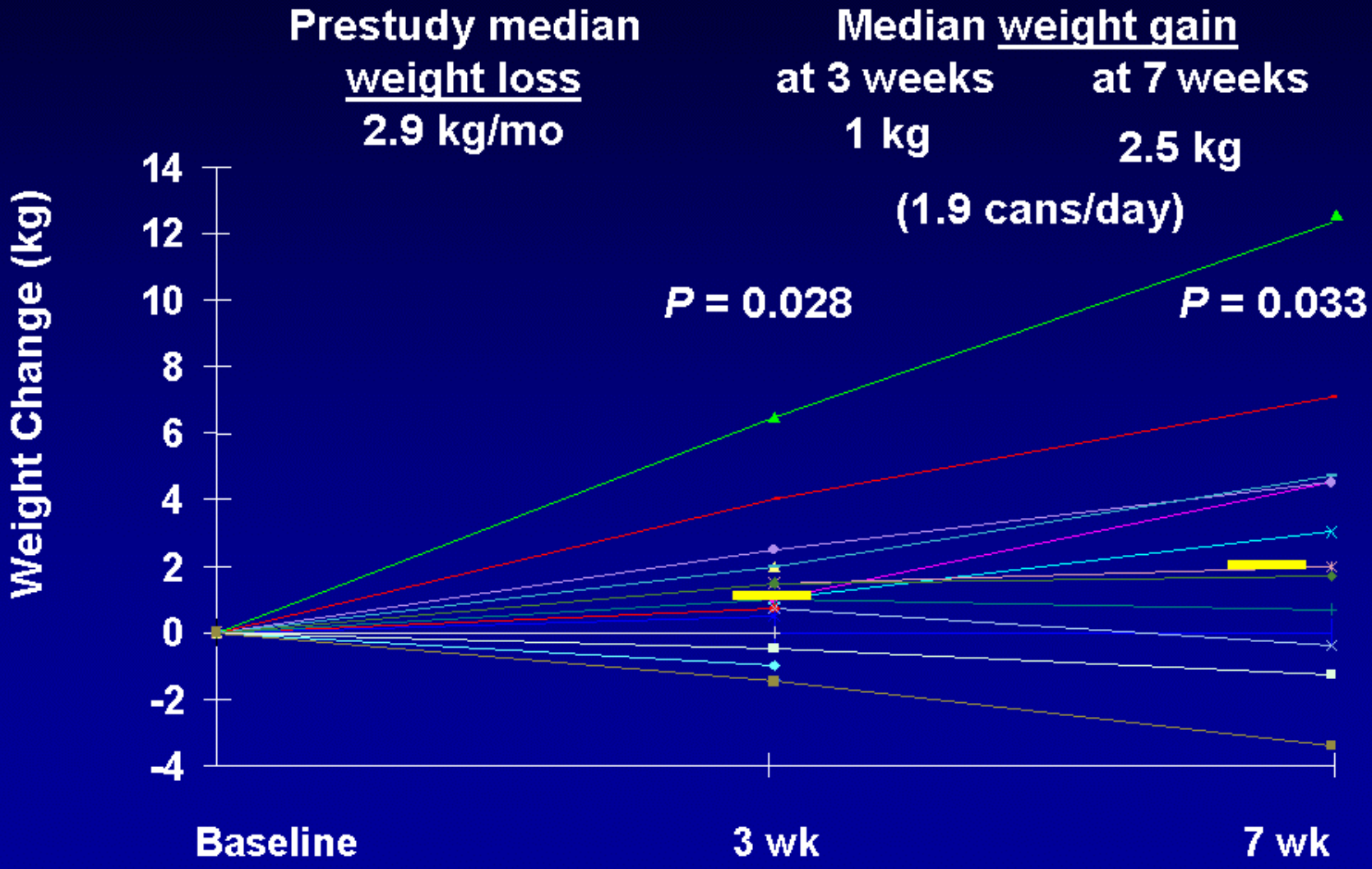
- Ensure Plus-type product enriched with EPA
- N=20; mean age 62 (51-75)
- >4w after chemotx (5-FU, RT)
- Measured weight, resting energy expenditure, body composition, performance status, QoL
- Used BIA (bioimpedance analysis, D_30 ("heavy water") to verify weight gain is lean body mass (muscle) rather than fluid or fat
- grip strength, Karnofsky status, EORTC

Br J Ca 81:86 1999 J Nutr 129(6):1120-25 1999 Clin Sci 98:389-99 2000

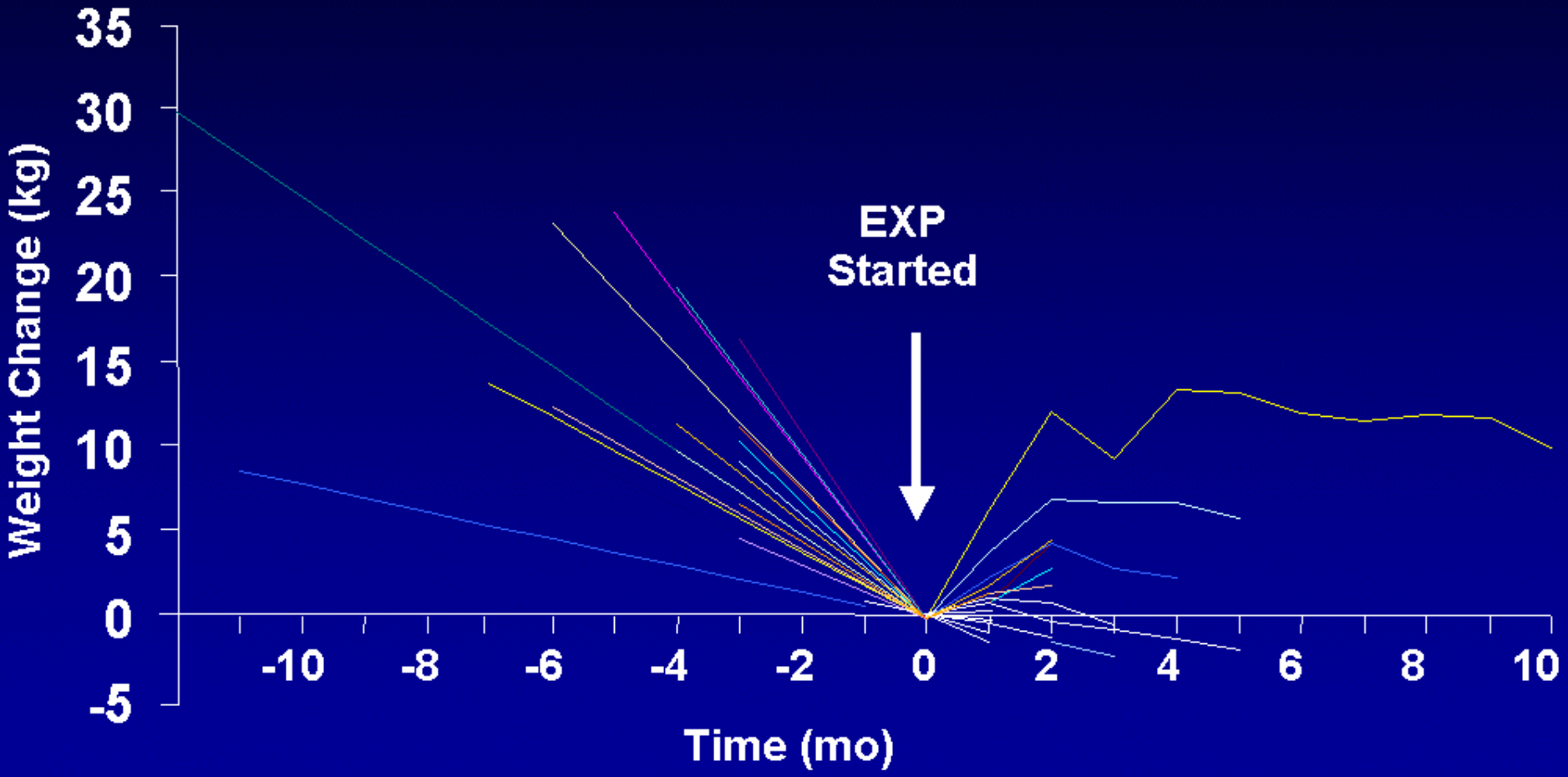
Dietary Intake (n=18)



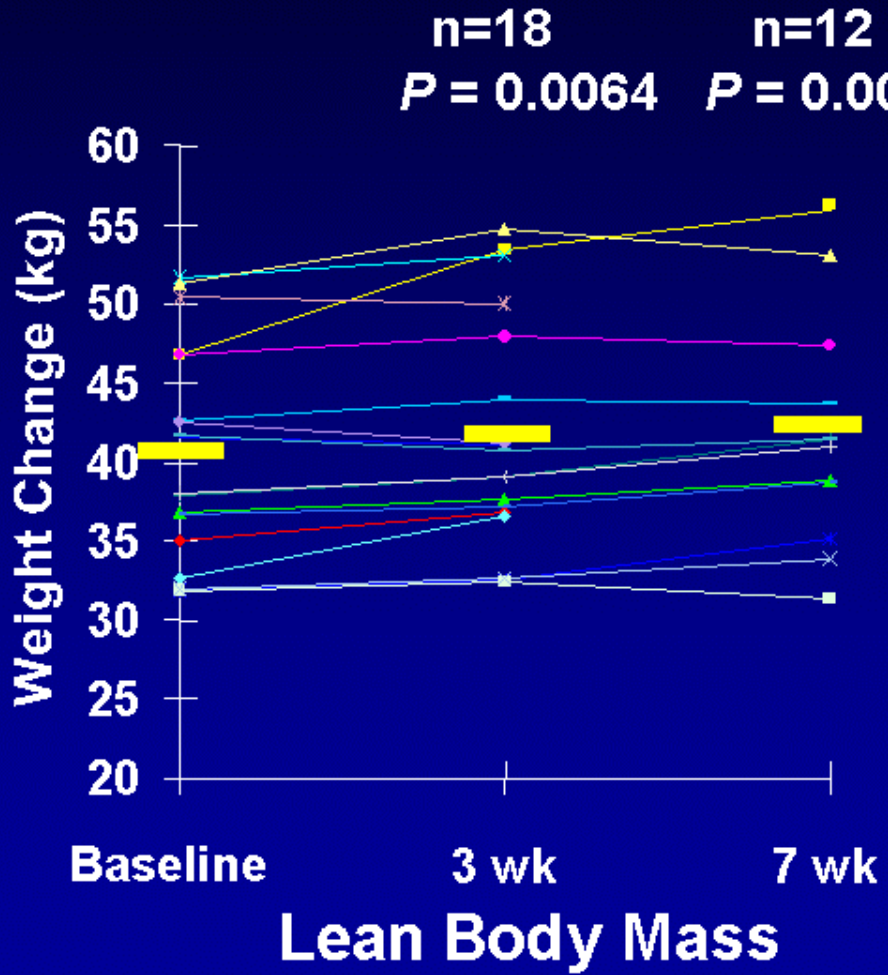
Weight Change

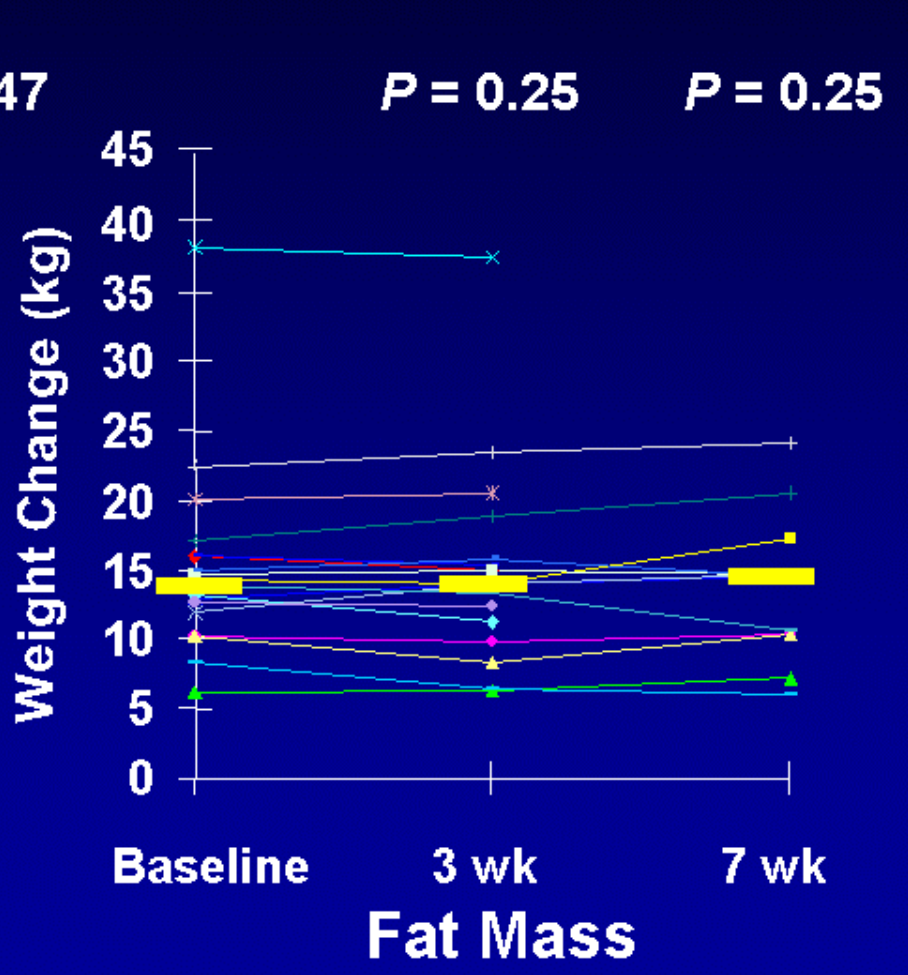


Effect of EXP on Weight Change in Patients With Unresectable Pancreatic Cancer

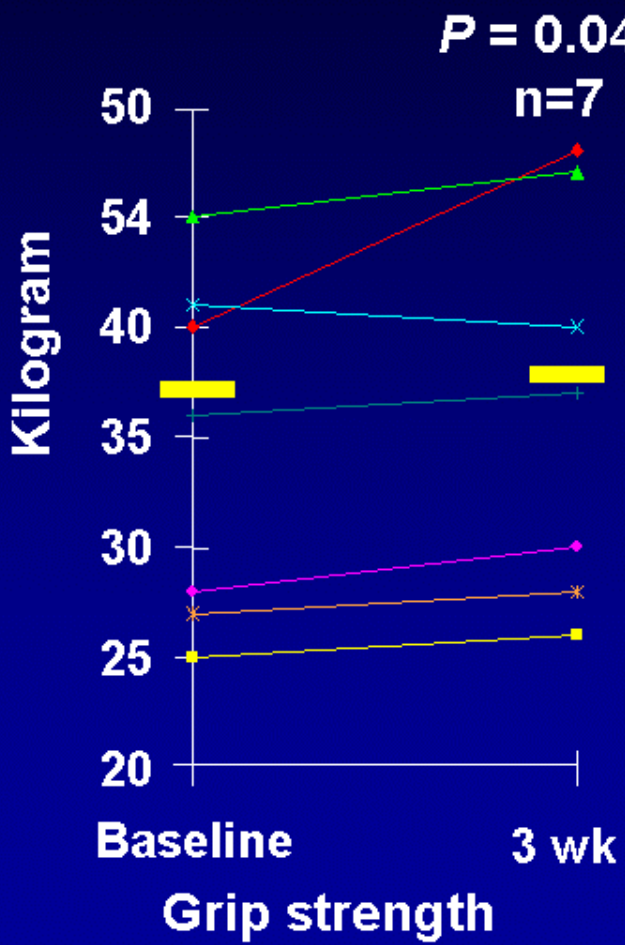


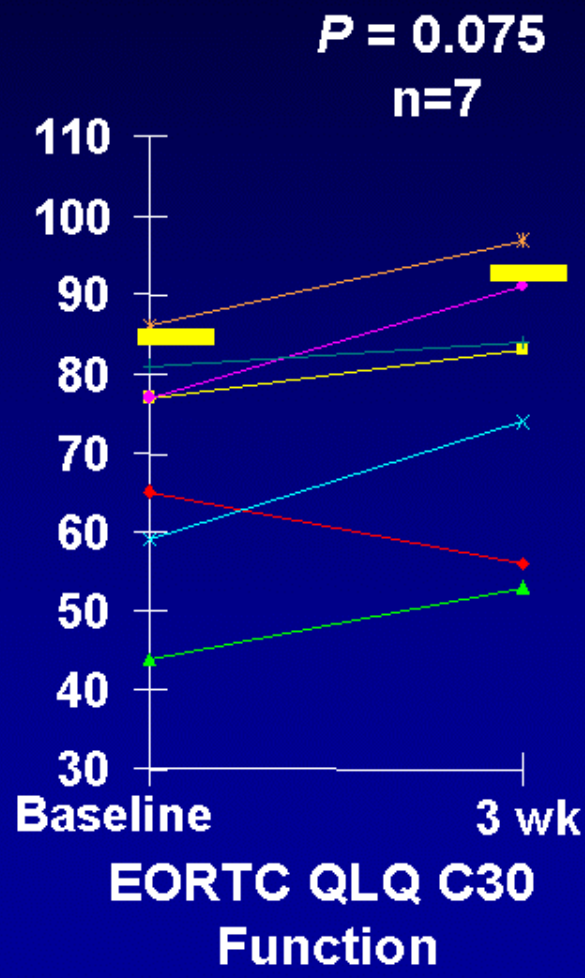
Body Composition



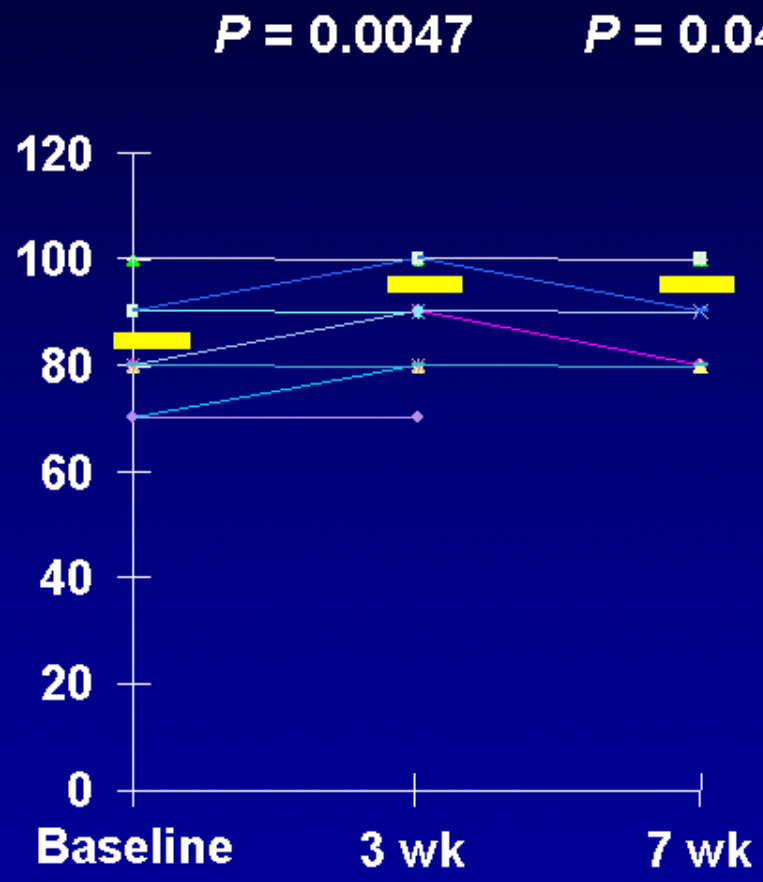


Functional Status

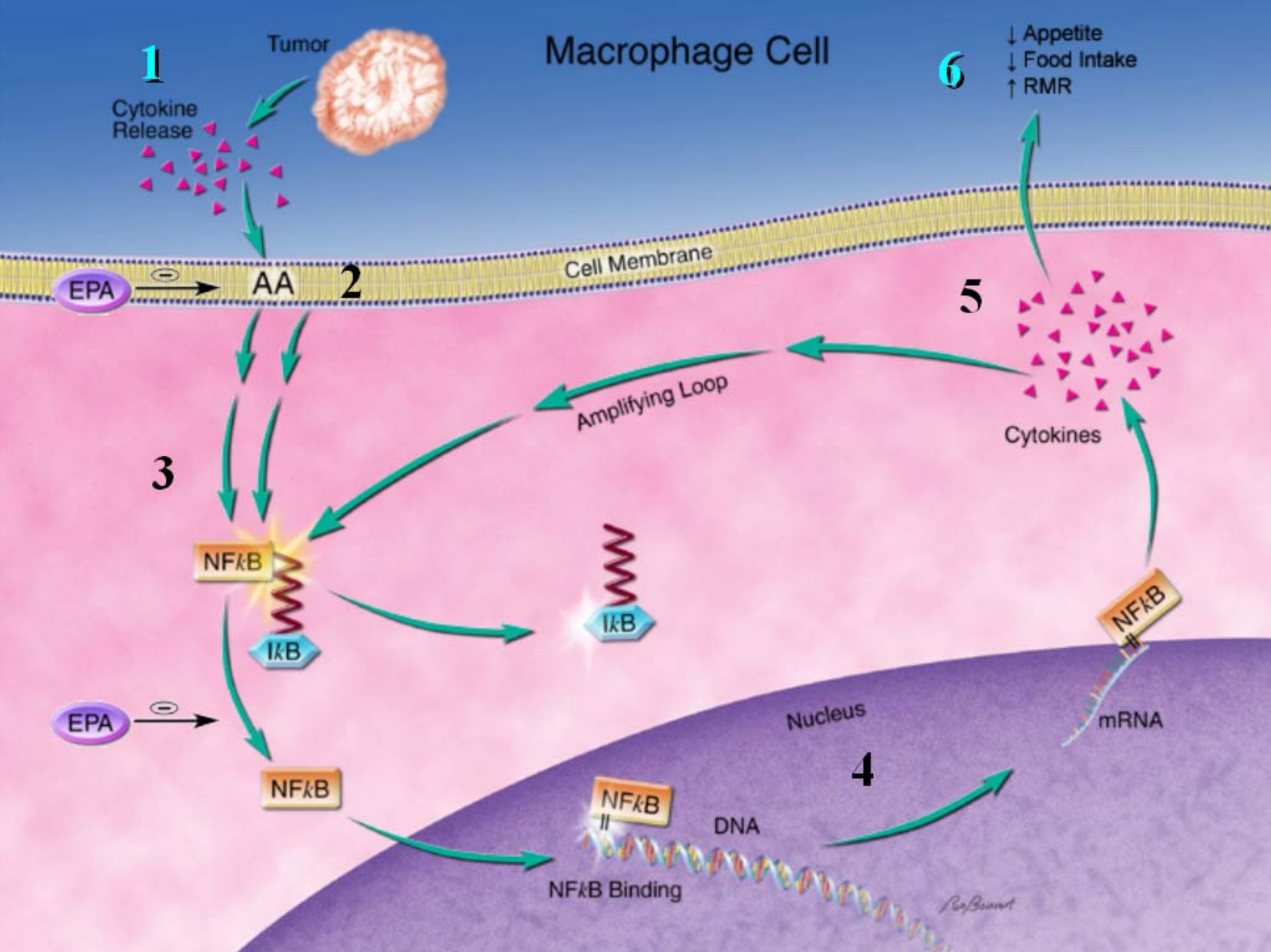


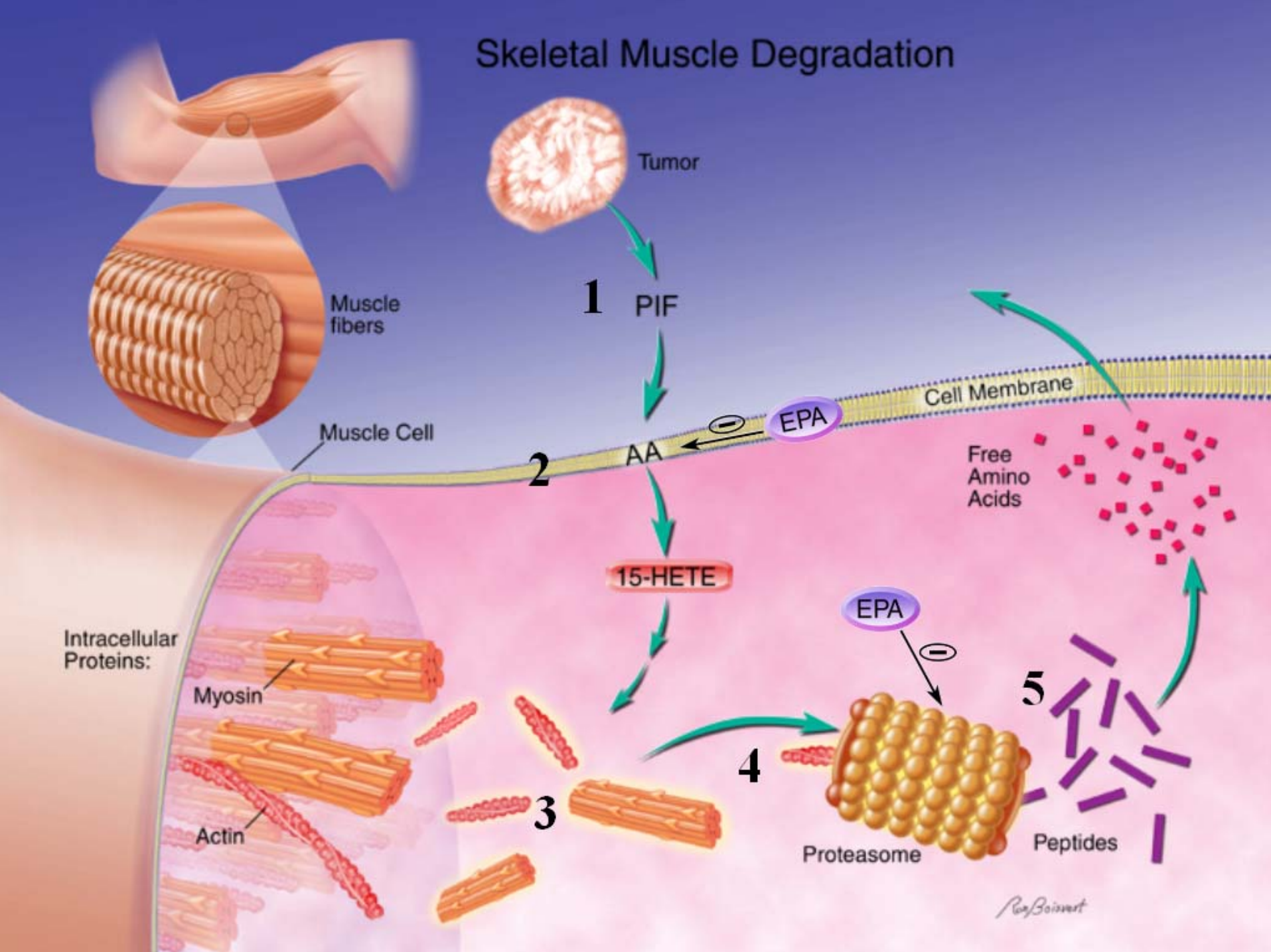


Performance



Karnofsky Performance Status


Macrophage Cell
1
Tumor
Cytokine Release
6
↓ Appetite
↓ Food Intake
↑ RMR
Cell Membrane
EPA
AA
2
5
Cytokines
Amplifying Loop
3
NFkB
IkB
IkB
EPA
NFkB
Nucleus
4
NFkB
DNA
NFkB Binding
NFkB
mRNA


Skeletal Muscle Degradation
Tumor
1
PIF
Muscle fibers
Muscle Cell
Cell Membrane
EPA
2
AA
Free Amino Acids
15-HETE
EPA
Intracellular Proteins:
Myosin
Actin
3
4
5
Proteasome
Peptides

Nutrition: Weight Loss 3

Retention:

Appetite stimulants generally encourage fat and fluid retention, not *lean body mass*

- **Anabolic steroids (oxandrolone, Oxandrin ®)**
  - **– *Onco-genic* potential??**
  - **– Use with testosterone in male HIV/AIDS pts. ?**

Androgenic Agents

oxandrolone **(synthetic testosterone derivative)**

- **10 mg bid; increased weight, lean tissue, performance status and QoL (103 pts;)**

VonRoenn JH, Tchekmedyian S Intl Symposium Supp Care in Cancer June, 2002

- **10 mg bid; significant increase in LBM and weight; acceptable safety profile (131 pts)**

VonRoenn JH, Tchekmedyian S Proc ASCO May, 2003 Abstract # 3013

- **20 mg x 4 mo; aero-digestive cancers; increased or stabilized weight**

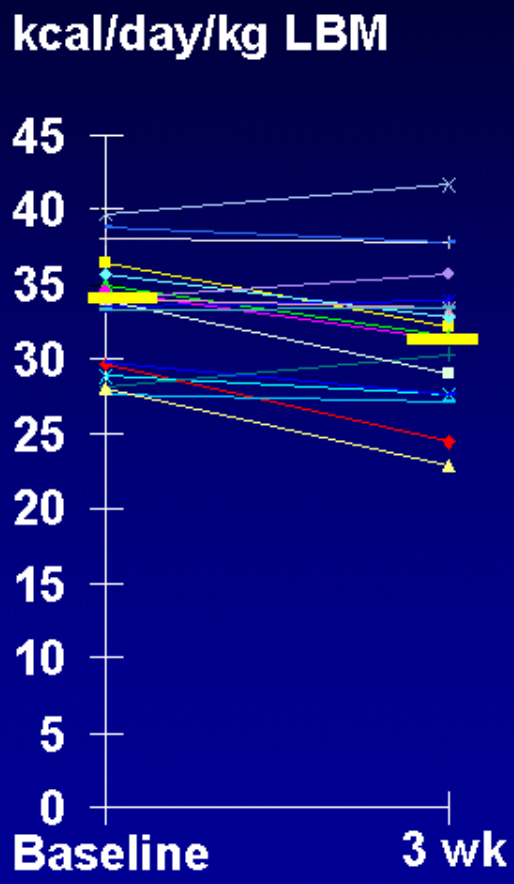
Tchekmedyian S, Thropay J, et al. Proc ASTRO 2002 Abstract #2176

Nutrition: Weight Loss 4

Energy Expenditure

- **Exercise**
- **Restorative sleep**
- **Energy conservation**
  - **"Budget" energy use**
  - **Reduce *Resting Energy Expenditure***

REE



P = 0.018

REE/kg LBM

Barber et al: *Clin Sci* 2000;98:389.

Goal of Cancer-Specific Nutritional Intervention

- to provide calories and protein together with metabolically active nutritional substrate
- to provide safe and effective tool to help prevent weight loss
- promote a gain in lean body mass and improve outcomes in patients with cancer-induced weight loss

Nutritional Therapy/Screening

- noninvasive
- minimal time investment/pt
- able to be implemented in ambulatory, inpatient, extended care setting or at home
- patient and family participation
- part of routine care
- nutrition team: Physician, Nurse, Nutritionist, Oncology Social Worker, Chaplain

Why is Early Specialized Nutrition Intervention Important?

to impact on:

- **prevention of muscle weight loss**
- **response to treatment**
- **quality of life**
- **survival**

Psychosocial Care as More than an Support Groups…

- **Provide best total care for the patient**
- **Integrate medical, non-medical care, and practical care**
- **Reduce the burden of disease/treatment on the *Activities of Daily Living***
- **Counseling in context of activities: *Wellness Programs* provide same service, less stigma**
  - **Yoga, Reiki, Massage, Meditation, Cognitive Rehabilitation workshops, educational forums, cooking classes free and open to the public**
- **Pastoral Care: spiritual counseling; training**

Goals of Care & Advance Planning

- Approached differently in different cultures
- Cure → control → care *or* cure → control → care
  care → → → → → care
- "North American" trends
  - Shared-decision making between patient and provider
  - Physician cannot make decisions regarding resuscitation, "artificial nutrition" or hydration without open discussion and consensus with patient or appointed surrogate (a Health Care *Agent* in some locales)
- Optimally, written document providing "clear and convincing evidence" of choice of spokesperson or treatment goals; *Health Care Proxy*

The Bottom Line

- Live
- Live well
- Live without symptoms of cancer
- Live without toxicity of treatment

What We *Can* Do

- Skilled Care
- Kind Treatment
- Honest without being brutal
- Participation in Decision-Making
- Never lose hope; even if hope is for a comfortable death
- Know when to say, “enough”
- Generate and sustain trust