

Treatment of Advanced Cancer—The Point for Disease-Directed Therapies

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Disclosures

No relevant conflict of interest



Introduction

- **Cancer Statistics** (SEER data 2009 from NCI website)
 - Median age at diagnosis: 66 years
 - Median age at death: 73 years
 - Age-adjusted incidence rate: 462.9 per 100,000 per year
 - Age-adjusted death rate: 186.9 per 100,000 per year

Introduction

- Advanced Cancer (NCI website)—Cancer that has spread to other places in the body and usually cannot be cured or controlled with treatment
- "I know that just because I have stage-4 cancer doesn't mean I'm going to die tomorrow. My friend has lived a long time with her advanced cancer" (Li, a patient with cancer)

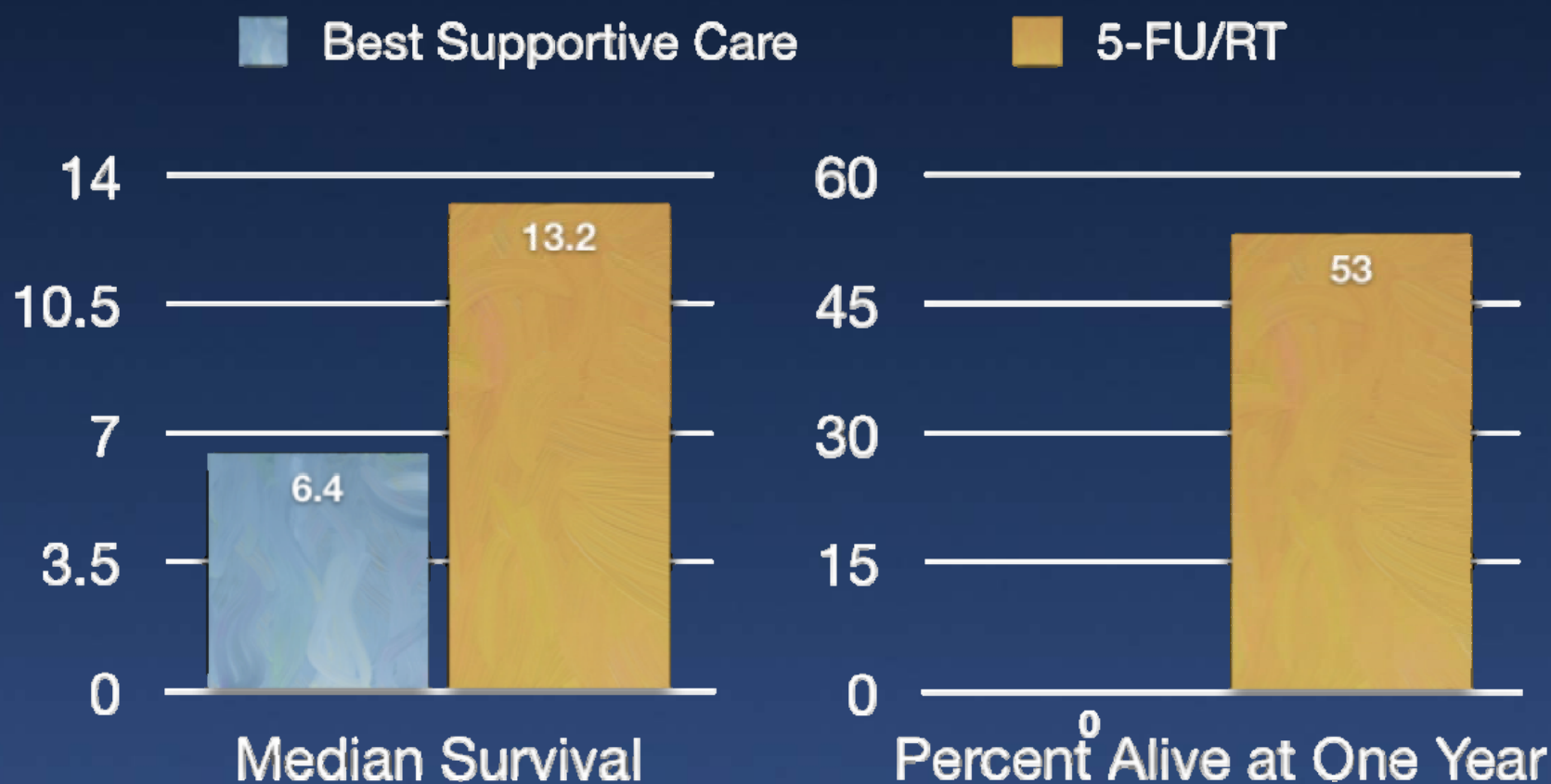
Chemotherapy in NSCLC

- Three meta-analyses have all concluded that chemotherapy extends survival compared to best supportive care
- The most recent analyzed individual patient data from 2714 cases enrolled on 16 randomized trials (J Clin Oncol. 2008 Oct 1;26(28):4617-25. Epub 2008 Aug 4)
- Chemotherapy was associated with an improved survival at 12 months (29% versus 20%). The survival benefit was present independent of histology, performance status, and age

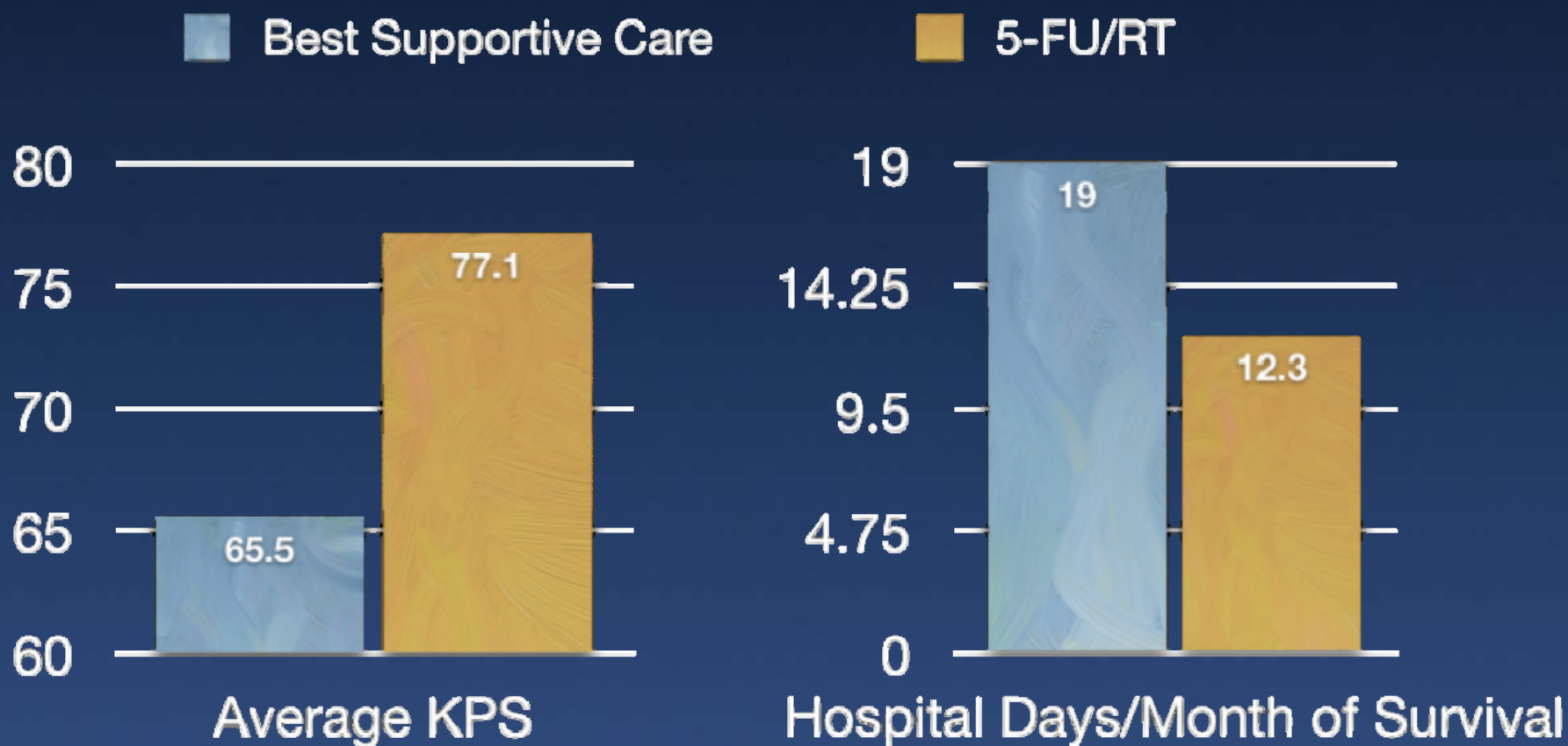
Locally Advanced Pancreatic Cancer

- RT/Chemotherapy vs Best Supportive Care (Shinchi H et al.; *Int J Radiat Oncol Biol Phys* 2002 May 1;53(1):146-50)
- Japanese trial of 31 patients randomly assigned to external beam RT plus infusion 5-fluorouracil or to best supportive care

Locally Advanced Pancreatic Cancer



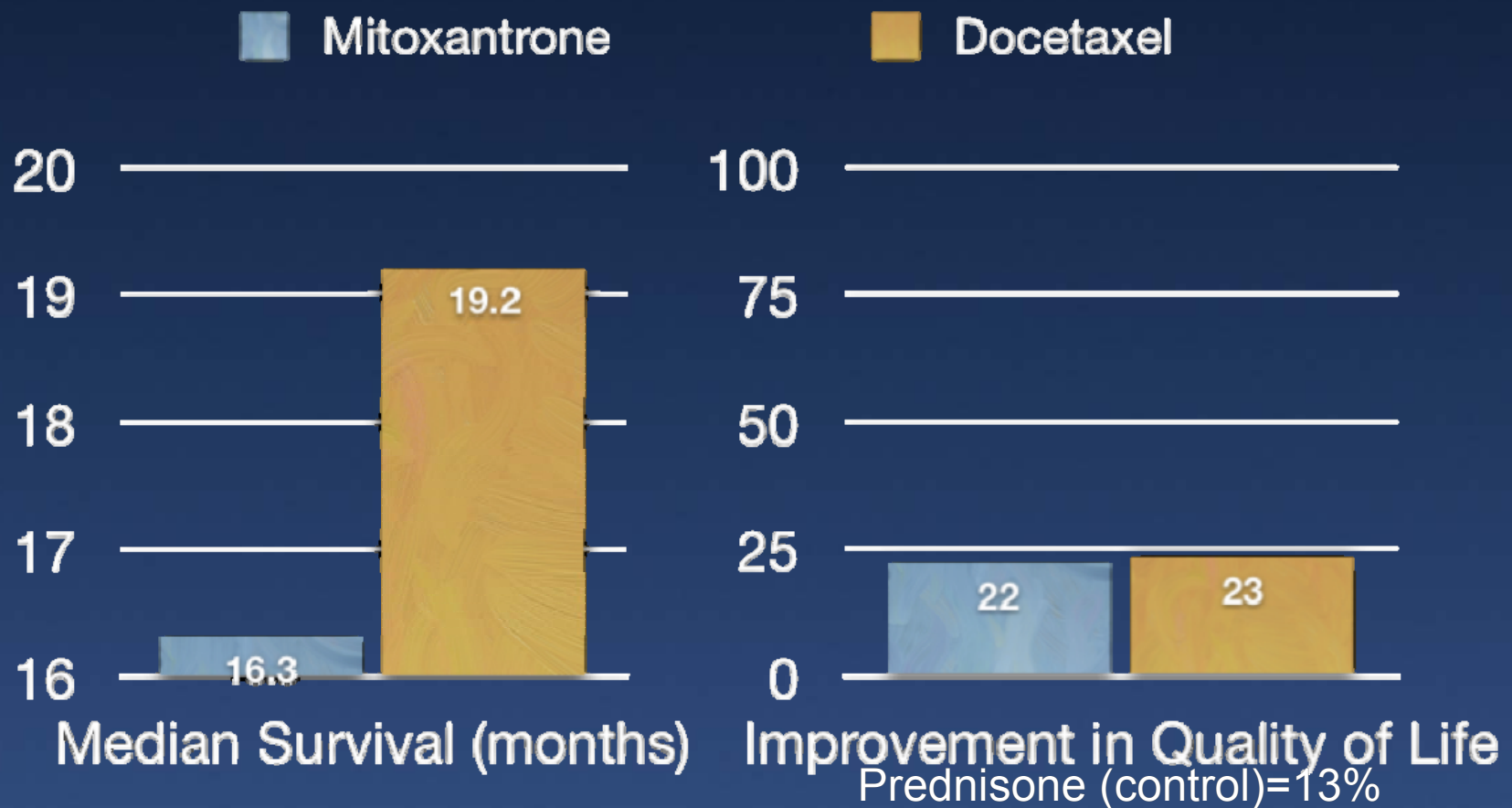
Locally Advanced Pancreatic Cancer



Hormone Refractory Prostate Cancer

- **TAX-327 Trial** (Tannock IF; et al.; *N Engl J Med* 2004 Oct 7;351(15):1502-12, Berthold DR; et al.; *J Clin Oncol.* 2008 Jan 10;26(2):242-5)
 - 1006 men with hormone-refractory prostate cancer given prednisone as a control arm and two treatment arms with patients randomized to prednisone plus either mitoxantrone (Novantrone[®]) or docetaxel (Taxotere[®])

Hormone Refractory Prostate Cancer



Hormone Refractory Prostate Cancer

- TAX-327 Trial (Berthold DR; et al.; *J Clin Oncol.* 2008 Jan 10;26(2):242-5)
 - Based on this trial, the American Society of Clinical Oncology recommends that docetaxel plus prednisone become the standard of care for men with hormone-refractory prostate cancer

Advanced Breast Cancer

- Difficult population to address...
 - Very heterogeneous
 - Composed of hormone-sensitive and hormone-refractory disease, as well as hormone-insensitive disease
 - *Her-2* positive vs *Her-2* negative

Advanced Breast Cancer

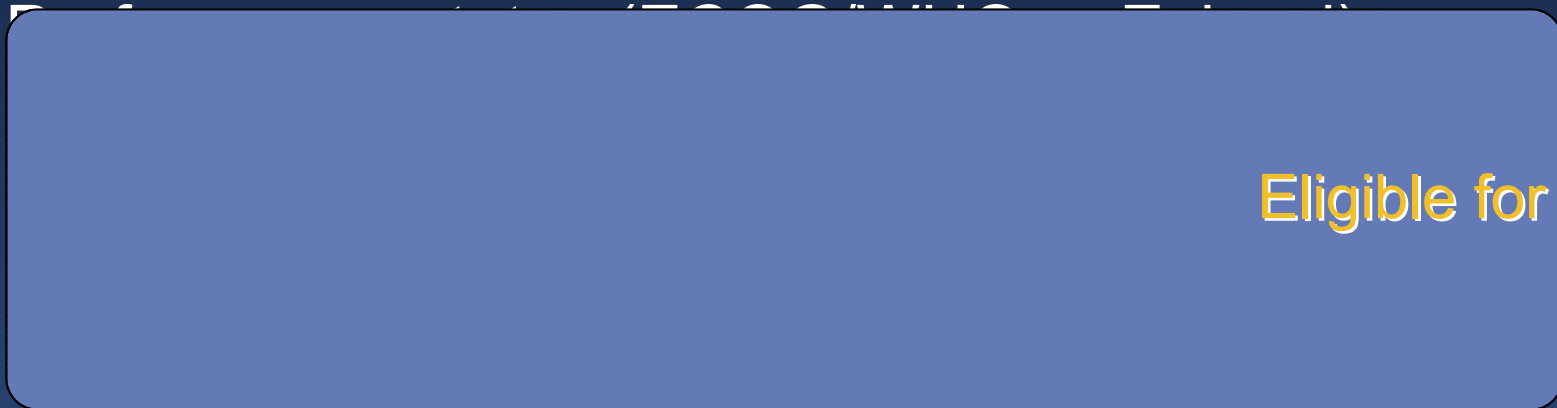
- No prospective trials evaluating disease-directed therapies vs best supportive care
- Mean survival for metastatic breast cancer ~24 months (range of a few months to a few years)
- Meta-analyses have demonstrated improved overall survival with treatment

Advanced Breast Cancer

- Quality of Life
 - The major focus of treatment is palliation of symptoms
 - Several studies demonstrate improved quality of life for patients receiving disease-directed therapies

Why Performance Status Matters...

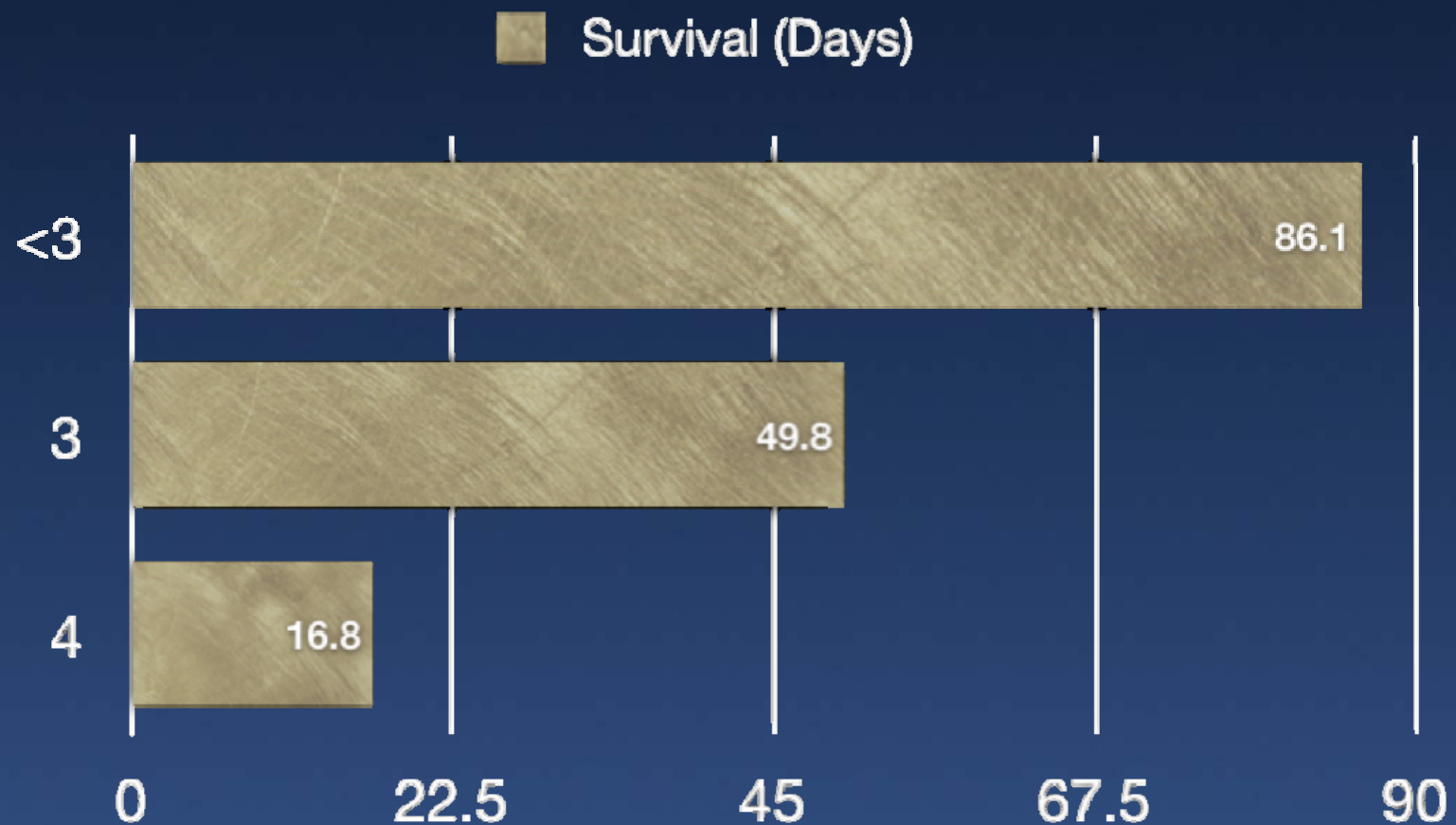
- Most prospective clinical trials include relatively fit patients



Eligible for trials

- 2 = Resting/reclining \leq 50% of a 24^h day
- 3 = Resting/reclining $>$ 50% of a 24^h day
- 4 = Bedfast

Performance Status as Predictor of Survival



Data from 1592 patients in Physician's Hospice Study (PS modified by presenter)

Treatment of The Poor Performance Status Patient

- Recommendations...
 - In patients who are otherwise healthy for age with good performance status, the first regimen can be multiagent therapy
 - In patients with concomitant health problems, or who have a poor performance status (ECOG PS 2-3), the first regimen should be a single agent
 - In patients with poor performance status (some ECOG 3 and all ECOG 4), no cytotoxic therapy should be considered
 - Age alone should not be the sole criteria for excluding chemotherapy
 - In cases where chemotherapy is inadvisable, other therapies can be considered

In Summary...

- Disease-directed therapies can be palliative in nature
- The goal should be lessening of suffering, following the medical “Golden Rule” of *primum non nocere* (first do no harm to the patient)
- Not every patient will benefit from disease-directed treatment!