Review of Cancer Therapy

think about: chemotherapy (chemotx) is driven by a balance in patient's experience of toxicities. This guy was very concerned with helping us remember to consider the patient's toxicities (as any good physician should) when evaluating treatment

Gerry Blobe, M.D., Ph.D.

In general, I thought this was a pretty advanced lecture: if your patient had a particular type of cancer, how would you treat them? We didn't discuss mechanisms at all (I added in info after-the-fact), only treatment plans...real oncologist work. He mostly went through each case merely musing about treatment plans.

state of cancer tx: generally good, but metastatic cancer prognoses are still very poor

State of Cancer Therapy

- Able to cure 50% (75% for pediatric cancers)
- Able to cure ~90% of cancers which present early (Stage I/II)
  - surgery + adjuvant therapy (chemo/radiation)
- Able to cure a subset of other cancers with chemotherapy or combination therapy.
  - chemotherapy sensitive cancers
- Most cancers, once they have metastasized are incurable.
  - In these cases, the goal shifts to
    - prolonging survival
    - improve/maintain quality of life
  - Addition of targeted therapies and multi-modality therapy is changing this (i.e. metastatic colon cancer may be a curable disease)

Tx: surgery (for early detection and localized tumors)
radiation (also good for local therapy)

Treatment Options for Cancer

- Surgery
  - If detected early (symptoms, i.e. bladder cancer), effective screening method (i.e. colon cancer) or detected incidentally (i.e. gallbladder)
  - Treatment of choice for localized solid tumors (need good staging)
    - >90% 5 year survival
  - Side effects minimal (bleeding, infection, wound healing)
- Radiation
  - Acts by damaging DNA (cross-linking, DNA breaks)
  - Local therapy, can be focused (gamma knife)
  - Side effects are fatigue, N/V, local irritation

More Tx: chemotherapy--systemic, wide range of side effects (targeting BM, GI tract, hair, repro organs), wide variety of administrations
targeted agents--target pathway or protein, fewer side effects

Treatment Options for Cancer

- Chemotherapy
  - Act by interfering with basic DNA→RNA→ protein pathway (generic)
  - Systemic therapy with few "sanctuary" sites-CNS, testis
  - can be administered orally, topically, IV, IP-peritoneum, IT-thecal sac
  - Side effects target organs with high cell turnover
    - GI tract, BM, hair, reproductive organs
  - Mechanisms usually converge to result in cell cycle arrest and apoptosis
- Targeted Agents
  - Act by targeting a specific pathway or protein
  - Systemic therapy
  - Side effects are agent/pathway specific, generally milder than chemo

More Tx: why not combine them?
1) effective as single agents
2) different mechanisms of action
3) non-overlapping toxicity
4) intensive/intermittent schedule
5) multiple cycles

Combination therapy

- Combination therapy used when 1 agent ineffective
  - use agents which are effective as single agents
  - different mechanisms of action (hope for synergy)
  - non-overlapping dose-limiting toxicity
  - intensive, but intermittent scheduling to allow time for recovery
  - Give multiple cycles

commom combo therapy: carboplatin + Paclitaxel = SYNERGY

what are model aspects for combo therapy?

Combination Therapy: Example

Agent	Toxicity	MOA	Resistance
Carboplatin	BM	DNA Cross-linking	Repair of damage
	Renal		Reduced uptake
			Increased GSH
Paclitaxel	BM	Microtubule stabilizer	Cell exprot (MDR)
	Neurotoxic		Structural alterations in tubulin
	Edema		
	Allergic Rxn		

Uses: NSC Lung, breast, ovarian , endometrial, bladder, H&N

Give paclitaxel, then platin (reduced myelosuppression)-order matters

efficacy is the same for any order of administration, but the toxicity is what drives the administration

Neo-adjuvant: chemotx before surgery>>less invasive surgery
Adjuvant: surgery before chemotx>>prevention of relapse (increases cure rate)

Chemotherapy: Different Roles

- Neo-adjuvant chemotherapy (anal, breast, esophageal, laryngeal, NSC Lung, pancreatic)
  - use of chemotherapy (with or without irradiation) prior to potentially curative or palliative surgery
  - Used to allow less invasive, less debilitating surgery (preserve larynx, or anal sphincter), better delivery and perhaps better local control

- Adjuvant chemotherapy (breast, colon, NSC lung, gastric)
  - use of chemotherapy following eradication of primary tumor by surgery or irradiation
  - prevention of relapse due to micrometastases, increases cure rate
  - For colon cancer, this decreases risk of recurrence by ~1/3

often there are both of these aspects in real treatment plans: chemo, then surg, then more chemo

Chemotherapy: Different Roles

- Curative chemotherapy
  - use of chemotherapy to cure the individual (Testicular cancer, choriocarcinoma, HD, NHL, AML, ALL, childhood cancers, breast cancer, colon cancer?)
  - Usually very sensitive tumors (rapidly dividing)
- Palliative chemotherapy
  - use of chemotherapy to extend life and improve quality of life
  - Most common use (breast, colon, ovarian, pancreatic, lung)

Toxicity--Nausea/Vomiting and pretty much always bone marrow; remember hair, GI tract, and repro organs

Chemotherapy-Toxicity

- All cause N/V-action on both CNS and small intestine

remember Nadler's lecture for review these mechanisms act by 5-HT3, D2, NK1

- Most common-BM, mucositis, alopecia also reproductive organs

rapidly dividing cells

- Almost all cause BM suppression, only a few that don't/mild (bleomycin, cisplatin, methotrexate and vincristine)

we evaluate one's candidacy for chemotx by PERFORMANCE STATUS--this means evaluating one's cancer in the midst of many other (potentially debilitating) co-morbidities

pop quiz: name the NSC lung cancers

NSC Lung Cancer: Case Presentation

non-small cell

- 72 yo retired railroad worker with h/o HTN and COPD, with 80 pack year history of tobacco use presents with a worsening cough and SOB, patient is able to care for himself and keeps a garden

always take note of co-morbidities

- CXR reveals 5 cm mass in RUL with bilateral mediastinal LAN

lymphadenopathy

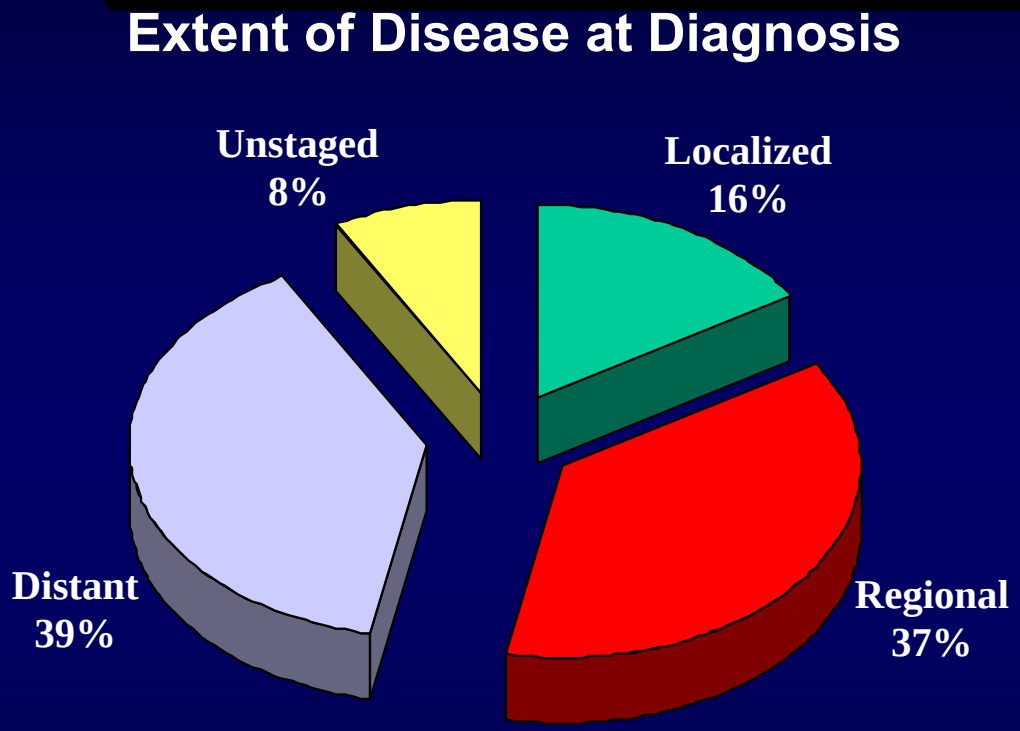
chest abdomen pelvis

- Initial work-up includes CBC and CT C/A/P reveals widely metastatic disease, with metastases to liver and bone
- What is his prognosis and what treatment should he receive?

he has metastatic lung cancer

poor screening technology to catch lung cancer in general--we catch it too late

Most NSCLC Is Diagnosed at Advanced Stages



- 55% of patients present with stage IIIB or stage IV disease

most cancers are diagnosed in advanced stage

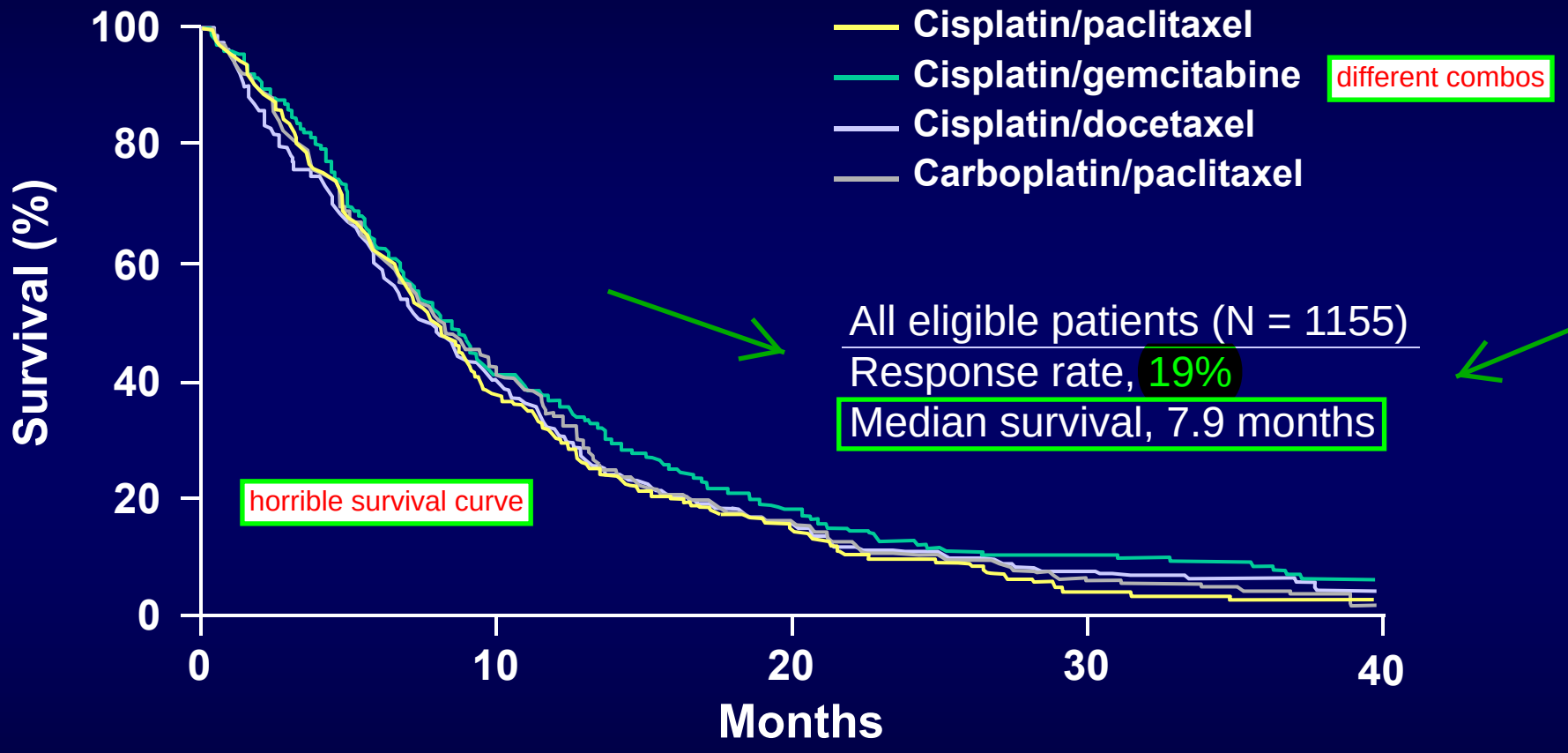
Stage III = spread to LNs
Stage IV = spread to other organs

- ~5–6 months median survival for untreated stage IIIB/IV NSCLC
- ~15% 5-year survival rate with standard therapy

Pop Quiz:
common chemotx toxicities:

lung cancer

ECOG 1594:
Alternative Doublets, Similar Outcomes



Schiller et al. *N Engl J Med*. 2002;346:92.

he just talked about different therapies in a general sort of way

Treatment Options for Advanced NSCLC

Unresectable stage III (dry*)

Chemotherapy with radiotherapy

Progression/recurrence

Stage IIIB (wet†) stage IV (metastatic)

First-Line[1]
Platinum-based doublet+/- bevacizumab
Nonplatinum-containing doublet
Single-agent chemotherapy (for elderly pts; poor PS<2)

Progression/recurrence

Second-Line[1-3]
Docetaxel
Pemetrexed
Erlotinib

Third-Line[1,2]
Erlotinib
Gefitinib‡

Speaker made note of EGFR mutations (typically found in non-smokers, females, Asians). We can use Erlotinib (pill, less toxicity than combo chemotx) to target such mutations

*"Dry" refers to the absence of pericardial or pleural effusion.
†"Wet" refers to the presence of pericardial and/or pleural effusion.
‡Gefitinib is currently indicated only for patients who are currently benefiting or have previously benefited from gefitinib therapy.[3]

1. Pfister et al. *J Clin Oncol*. 2004;22:330–353; 2. Tarceva® (erlotinib) prescribing information. South San Francisco, Calif: Genentech; 2005
3. US Food and Drug Administration. *Gefitinib (Marketed as Iressa) Information*. Available at: http://www.fda.gov/cder/drug/infopage/gefitinib/default.htm. Accessed August 28, 2006.

NSC Lung Cancer: Case Presentation

- Prognosis- chance of 5 year survival 15%

- Role for palliative therapy: Increases median overall survival
- Options include platin (cisplatin or carboplatin) with taxane (paclitaxel or docetaxel) or gemcitabine with targeted therapy against VEGF-bevacizumab for 6 months
  - Need to consider the patients prognosis from COPD
  - Need to consider histological subtype-if squamous cell-not a candidate for bevacizumab (increased risk of hemoptosis, pulmonary hemorrhage)

keep in mind co-morbidities (COPD, HTN)

bevacizumab precludes good wound healing...bleeding troubles during therapy

interesting limitation to bevacizumab....

Impact of Treatment on Metastatic NSCLCa

- Median Survival
  - BSC "best supportive care" 4.0 months
  - Single agent chemo 6.0 months
  - Doublet chemo 8.0 months
  - Doublet chemo+targeted (bevacizumab) 12.0 months

more treatment = longer survival

bevacizumab cannot be used in what type of lung cancer:

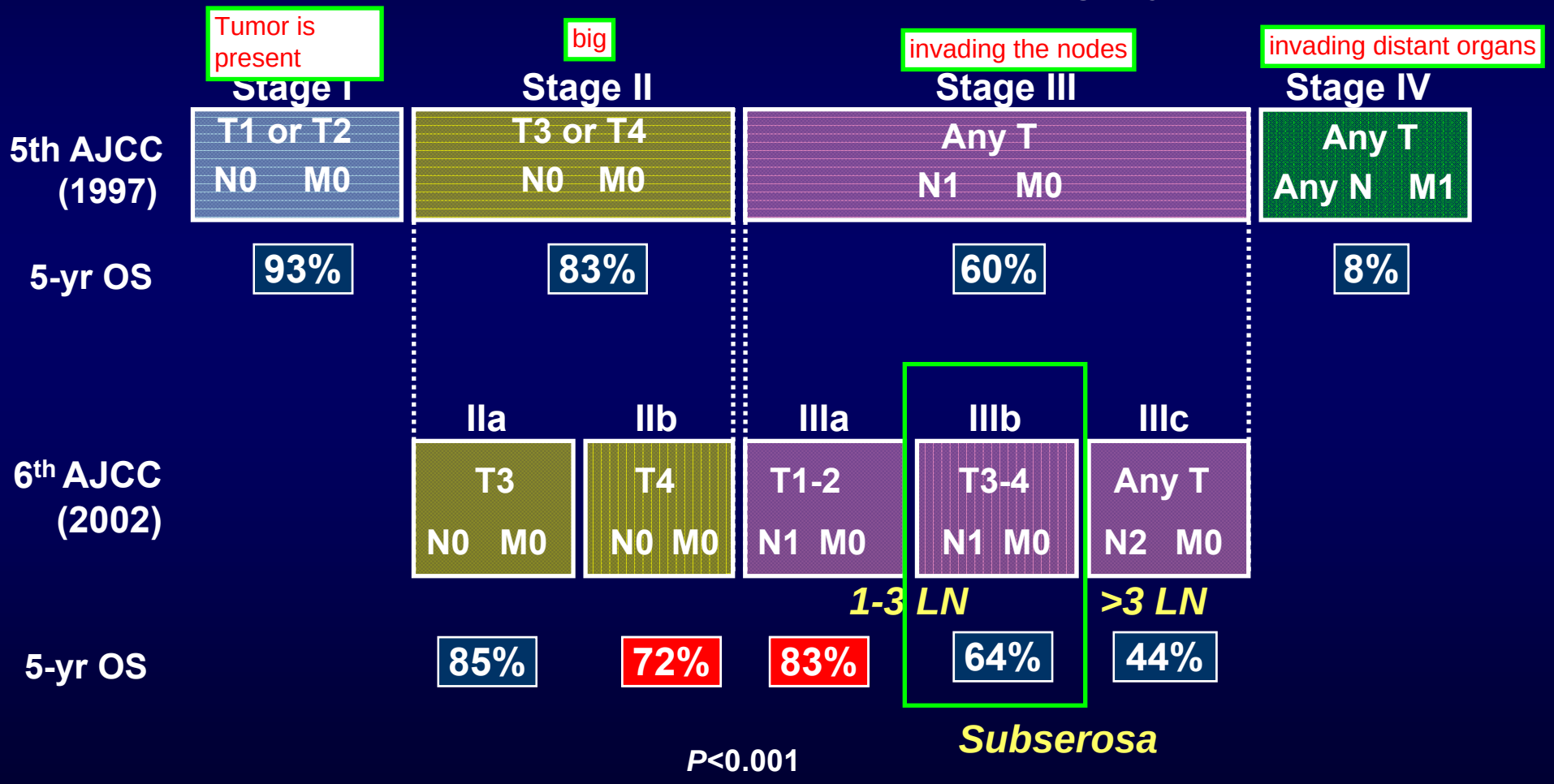
Colon Cancer: Case Presentation

- 70 yo retired banker with h/o DM, HTN, diagnosed with non-obstructing colon cancer (ascending colon) on a screening colonoscopy
- Initial work-up includes CBC, LFTs, CEA and CT C/A/P reveals no metastatic disease, CEA=5
- Undergoes hemicolectomy-pathology reveals Stage IIIB colon cancer (3/12 lymph nodes positive, tumor invades through the serosa)
- What is his prognosis and what treatment should he receive, if any?

5-year colon cancer survival by stage 5th and 6th edition AJCC system

Staging:
T=Tumor (1-4)
N=Nodes (0-2)
M=Metastases (0-1)

119,363 patients with colon cancer in the SEER[1] US registry (1991-2000)



1. Surveillance, Epidemiology, and End Results registry; 2 O' Connell et al, J Natl Cancer Inst 2004, 96: 1420-25

MOSAIC Trial: 6 year update

Disease Free Survival (%)	5-fluorouracil + leucovorin **5-FU/LV (n=1123)**	oxaliplatin + 5-FU + Leucovorin **FOLFOX-4 (n=1123)**	***P* Value**
Stage II	81.3%	85.1%	
Stage III	61%	69.7%	
Grade III Neuropathy (1mo)	0%	12.4%	
Neuropathy (1 yr f/u)	0%	1.1%	
Overall Survival			
Stage III (6 years)	68.3%	72.9%	<0.05
All patients (4 years)	70.4%	76.2%	0.008
All patients (3 years)	72.9%	78.2%	0.002

Colon Cancer: Case Presentation

- Prognosis- chance of 5 year survival 64% (if more than 3 nodes involved drops to 44%)

- Role for Adjuvant therapy: Increases chances of survival at 5 years, with ~ 25% relative reduction in mortality

remember when we talked about irinotecan, cetuximab, bevacizumab in our PIP session this week...?

- Options include oxaliplatin with infusional 5-FU (FOLFOX) for 6 months or capecitabine or bolus 5-FU
  - Need to consider the patients prognosis from diabetes, HTN
  - Need to consider whether any neuropathy will be exacerbated
- Interestingly, although targeted therapy (against VEGF-bevacizumab, EGFR-cetuximab) have role in metastatic diease, no effect in adjuvant setting, Why? hmmm...unknown

another colon cancer case

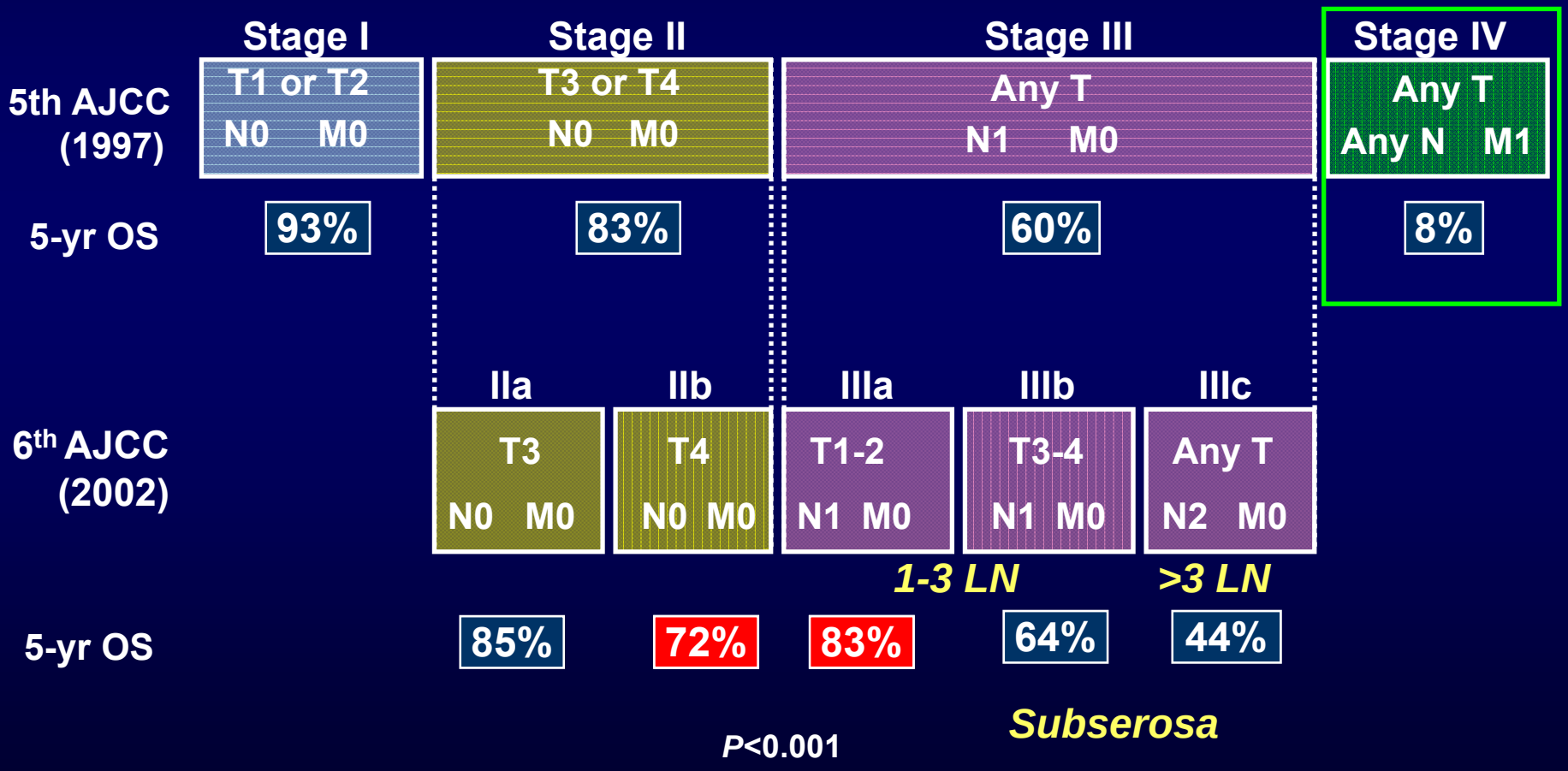
Colon Cancer: Case Presentation

- 58 yo construction worker with no sign. PMH presents with rectal bleeding of 1 months duration
- Diagnosed with non-obstructing colon cancer (transverse colon) on colonoscopy
- Initial work-up includes CBC, LFTs, CEA and CT C/A/P reveals 2 metastatic lesions in right lobe of liver, CEA=11
- What is his prognosis and what treatment should he receive?

POOR survival of 8% for metastatic Colon Cancer

5-year colon cancer survival by stage 5th and 6th edition AJCC system

119,363 patients with colon cancer in the SEER[1] US registry (1991-2000)



1. Surveillance, Epidemiology, and End Results registry; 2 O' Connell et al, J Natl Cancer Inst 2004, 96: 1420-25

hepatic resection brings 5 yr Overall Survival from 8% up to >35%

Hepatic resection

this translates to ~95% certainty of cure

R0 resection	Patients	Median survival (mo)	5 year OS (%)
Scheele	473	44	41
Fong	895	45	37
Meta-analysis			
S	140	47	41
S + 5-FU	138	61	53
Kemeny			
S + 5-FU	82	58	48
S + HAI/5-FU	74	68	56
OPTIMOX 1			
FOLFOX + S	98	32	36

Colon Cancer: FOLFOX or FOLFIRI maybe with Avastin

when thinking Colon Cancer>>go after metastatic disease

Colon Cancer: Case Presentation

- Prognosis- chance of 5 year survival 8%, but if receives neo-adjuvant chemotherapy and able to resect primary and both metastatic lesions in liver-goes up to 35-50%

- Options include oxaliplatin with infusional 5-FU (FOLFOX) or irinotecan with infusional 5-FU (FOLFIRI) plus targeted therapy against VEGF-bevacizumab until best response 2-3 months, then surgical resection, followed by 3-4 months of same as an adjuvant

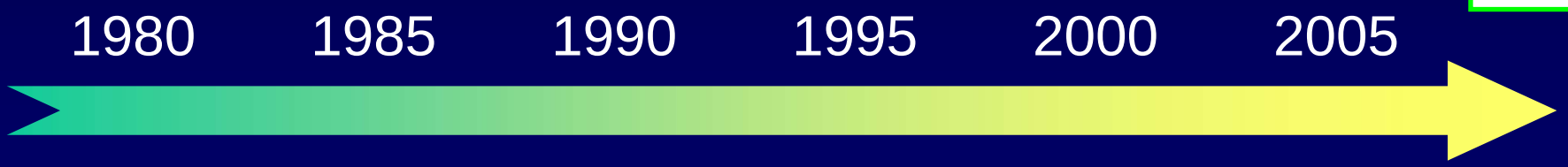
neo-adjuvant therapy, then adjuvant therapy

- What if he had widely metastatic disease (not resectable)?

for widely metastatic disease (nonresectable)

Integrating Therapy: Treatment of Colorectal Cancer

not included in lecture, but I thought you might be interested in the mechanisms....



5-FU

Irinotecan

Capecitabine

Oxaliplatin

Cetuximab

Bevacizumab

Panitumumab

Therapeutic concepts

Palliative chemotherapy

Adjuvant chemotherapy

Neoadjuvant chemotherapy

data data data: treatments work, but not superbly

Efficacy of Chemotherapy in First-Line CRC: Phase III Trial Results

overall survival

Trial	Regimen	RR (%)	Median PFS or TTP (mo)	Median OS (mo)
Saltz	5-FU/LV	21	4.3	12.6
	IFL	39*	7.0†	14.8
Douillard	5-FU/LV (CI)	22	4.4	14.1
	FOLFIRI	35†	6.7*	17.4
de Gramont	5-FU/LV	22	6.2	14.7
	FOLFOX4	51*	9.0*	16.2
N9741 Goldberg	IFL	31	6.9†	15*
	IROX	35	6.5*	17.4
	FOLFOX4	45	8.7	19.5

*$P \leq 0.001$.
†$P < 0.01$.

Saltz et al. *N Engl J Med*. 2000;343:905; Douillard et al. *Lancet*. 2000;355:1041; de Gramont et al. *J Clin Oncol*. 2000;18:2938; Goldberg et al. *J Clin Oncol*. 2004;22:23.

PFS: progression free survival
TTP: time to progression
OS: overall survival
RR: response rate

Phase III TREE-2 Trial in First-Line MCRC: Efficacy and Safety

	Percent of Patients		
	mFOLFOX6 + bevacizumab (n=71)	**bFOL + bevacizumab (n=70)**	**CAPEOX + bevacizumab (n=72)**
CR	6	5	3
PR	47	37	45
SD	39	31	32
PD	6 (28)	13 (29)	9 (14)
ORR	53 (43)	41 (22)	48 (35)
TTP	9.9 (8.7)	9.3 (5.9)	10.3(5.9)
mOS	26 (19.2)	20.7 (17.9)	27 (17.2)

Hochster et al. *ASCO*. 2006,

Impact of Treatment on Metastatic Colon Cancer

- Median Survival
  - BSC — 6.0 months
  - 5-FU — 12.0 months
  - 5-FU+ininotecan/oxali — 24.0 months
  - 5-FU+ininotecan/oxali +targeted (bev, cetuximab) — ~30.0 months

using our full arsenal (chemotx and targeted therapies)

choose between irinotecan and oxaliplatin based on PATIENT'S TOXICITIES

we are beginning to better know the biology of the tumor to predict greater efficiacy or increased toxicity

examples are for 5-FU (DPD), irinotecan (UGT1A1) and erbitux (Ras)

Individualizing Cancer Therapy

- Exposure to 5-FU
  - Do they have a dihydropyrimidine dehydrogenase (DPD) deficiency? Affects 1-3% of population.
  - DPD is the initial/rate-limiting enzyme in 5FU metabolism.
  - Results in severe/fatal diarrhea, mucositis, neutropenia
- Exposure to irinotecan
  - Do they have UDP-glucuronosyltransferase 1A1 (UGT1A1) polymorphisms?
  - SN-38 is conjugated and detoxified by UGT1A1
  - Specific polymorphisms (UGT1A1*27) predict increased toxicity
- Exposure to erbitux
  - Do they have a Ras mutation? If so, won't respond.

BCa is largely responsive to hormonal therapy; this is good because hormonal therapy generally has milder toxicity when compared to chemotx

Breast Cancer: Case Presentation

- 55 yo postal worker, postmenopausal, with no PMH has a lump on her left breast on self-examination, mammography reveals mass with suspicious calcifications

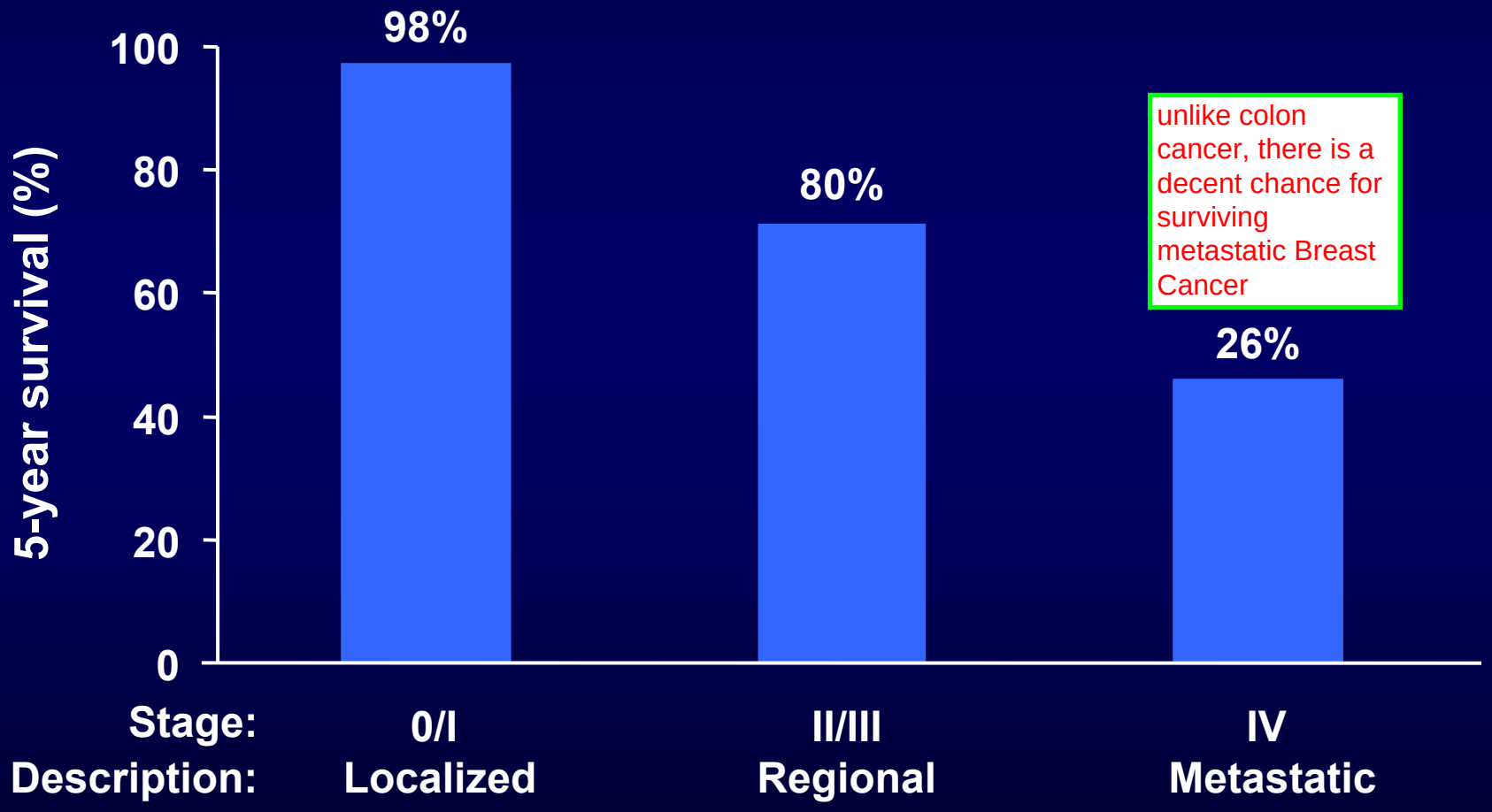
MUGA-nuclear medicine study that detects heart function (studies ejection fraction)

- Patient undergoes a lumpectomy and sentinel lymph node biopsy with pathology demonstrating a 1.2-cm, estrogen receptor-positive, progesterone receptor-positive, HER2-2+positive (by IHC) tumor. Surgical margins are negative, and 1 of 4 LN is positive for disease. Fluorescence in situ hybridization analysis confirms HER2-positive disease.
- A MUGA scan reveals normal ejection fraction, CT C/A/P reveals no metastatic diseas

would want to consider heart function when thinking of using Herceptin or anthracyclines (doxorubicin) to gather a baseline before (toxic) treatment

- What is her prognosis and what treatment should she receive, if any?

Breast Cancer: 5-Year Survival by Stage



American Cancer Society. *Cancer Facts and Figures 2005*.

"Systemic Therapy in Metastatic Breast Cancer Based ...

on Tumor Characteristics

HER2-Positive MBC

- Anti-HER2 monoclonal antibody: trastuzumab

ER/PgR-Positive MBC

- Aromatase inhibitors: letrozole, anastrozole, exemestane (primarily post-menopausal)
- Antiestrogens: tamoxifen, toremifene (primarily pre-menopausal)
- Progestin: megestrol acetate
- Fulvestrant (estrogen-receptor antagonist used when disease progresses after prior hormonal therapy)
- LHRH agonists (e.g. goserelin)

MBC = metastatic breast cancer; HER2 = human epidermal growth factor receptor 2; ER = estrogen receptor; PgR = progesterone receptor; LHRH = luteinizing hormone-releasing hormone.

"Systemic Therapy in MBC Based ...

on Tumor Characteristics (cont'd)

Other Types of MBC (ie, HER2-Negative, ER/PgR-Negative)

aka "triple negative" BCa

- Chemotherapy
  - Anthracyclines: doxorubicin, pegylated doxorubicin, epirubicin
    cardiac toxicity
  - Taxanes: docetaxel, *nab*-paclitaxel, albumin-paclitaxel
  - Antimetabolites: 5-fluorouracil, capecitabine, gemcitabine
  - Others: vinorelbine, cyclophosphamide, carboplatin
  - Combination of chemotherapeutic agents

in general, for breast cancer, we use sequential single-agent therapy to balance toxicities when treating metastatic disease (not combo therapy as for other cancers)

more mechanisms (see if you remember the ones from before):

Breast Cancer: Case Presentation

- Prognosis- chance of 5 year survival 80%, but if receives adjuvant chemotherapy and targeted therapy, increases to >90%

- Treatment includes chemotherapy (doxorubicin and cyclophosphamide) followed by docetaxel and trastuzumab (targeting Her-2)
  - need to repeat MUGA to follow cardiac status (Why?)
- Needs to receive XRT for local control
- Finally-needs to receive adjuvant hormonal therapy- choices are tamoxifen or an aromatase inhibitor (causes bone denstity loss-can minimize with oral bisphosphonate, calcium, Vit D and weight bearing exercise)

cardiac toxicity, especially from doxorubicin and trastuzumab

x-ray therapy

clots, loss of bone mineral density--problem for post-menopausal women to begin with

Breast Cancer: Case Presentation

- 46 yo legal assistant, premenopausal, notes right breast mass, mammography reveals 7 X 8 cm mass with calcifications, bx reveals ER-/PR-/Her2- tumor. Pt gets neoadj chemo (ECF) followed by mastectomy and axillary node dissection (3/12 LN positive),chest wall XRT and adjuvant chemo docetaxel for 4 months.

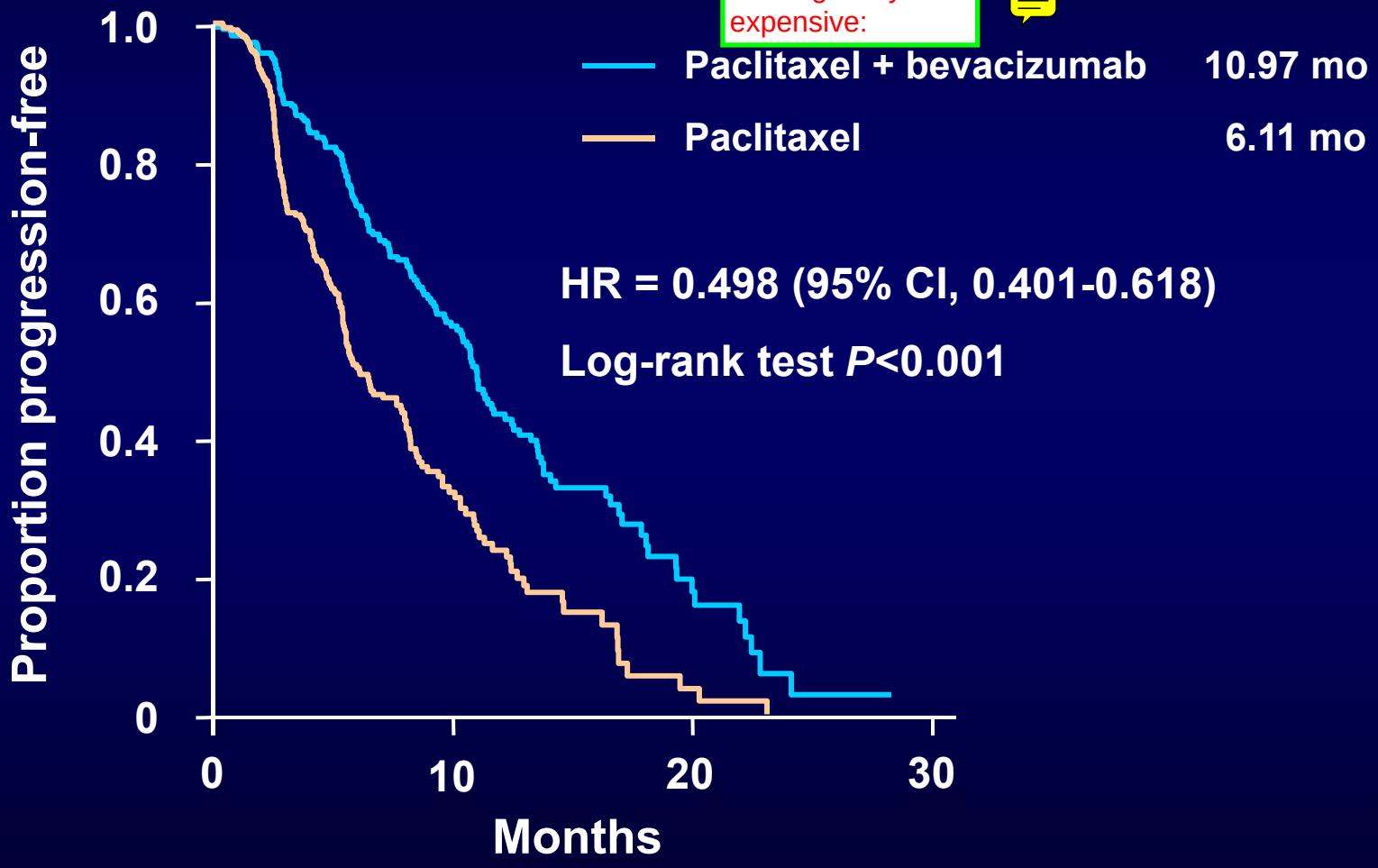
- Then followed closely for 4 years, presents with palpable supraclavicular mass-bx reveals triple negative breast cancer. Imaging reveals multiple lung nodules.

- What is her prognosis and what treatment should she receive?

bevacizumab adds marginal success

Phase III Trial of Paclitaxel ± Bevacizumab as First-Line Therapy in MBC: Progression-Free Survival

this is ghastly expensive:

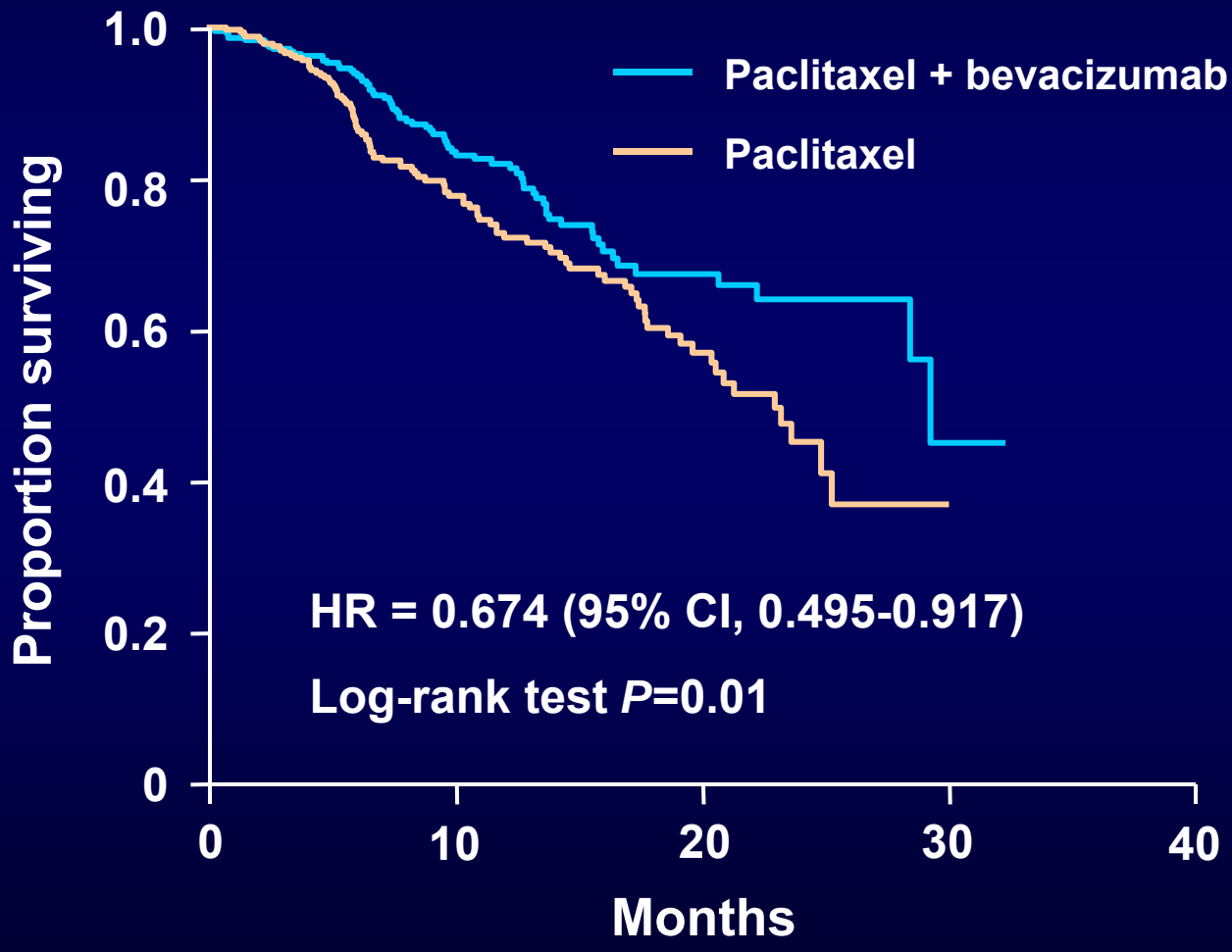


CI = confidence interval.

Miller et al. Presentation at ASCO, 2005.

bevacizumab adds marginal success

Phase III Trial of Paclitaxel ± Bevacizumab as First-Line Therapy in MBC: Overall Survival



Miller et al. Presentation at ASCO, 2005.

sad case where palliative chemtx is the course of action

Breast Cancer: Case Presentation

- Prognosis- chance of 5 year survival 25%, but palliative chemotherapy can increase mOS
- Treatment options includes chemotherapy (taxane) plus bevacizumab, capecitabine, cisplatin and navelbine
  which is vinorelbine
- Goal is for palliation and symptomatic control
- What if patient was ER+ and Her2+?

Breast Cancer: Case Presentation

- What if patient was ER+ and Her2+?'
- In this case-hormonal therapy would have been a good first choice (aromatase inhibitor)
- Then when refractory to hormonal therapy, can go on to target Her2 with trastuzumab and combine this chemo (paclitaxel).
- Other options down the line include capecitabine and lapatinib (targets Her2 and Her1)

name the aromatase inhibitors:

more treatment = longer survival

Impact of Treatment on Metastatic Breast Cancer

- Median Survival
  - BSC 12.0 months
  - Single agent chemo 18.0 months
  - Doublet chemo 22.0 months
  - Doublet chemo+targeted (trastuzumab) 30.0 months

Prostate Cancer: Case Presentation

- 56 yo tollbooth worker presents with urinary hesitancy, urology w/u reveals increased PVR, DRE reveals left sided prostate nodule, PSA= 8 ng/mL, bx reveals Gleason Grade 8 prostate CA in 4/6 cores

Gleason grading scheme goes to a max of 10

- Initial work-up includes MRI which reveals large lesion in left prostate and possible extracapsular invasion.

- What is his prognosis and what treatment should he receive?

goal for local prostate cancer is cure by surgery or radation

Prostate Cancer: Case Presentation

- Prognosis- chance of 5 year survival 100%

local treatments for CURE

- Treatment options includes radiation (either external beam or brachytherapy) or surgery (radical prostatectomy)

internal localized radiation source

- Goal is cure

- As there is a question of extracapsular invasion, he has a large prostate, and urinary sxs-recommendation would be for surgery.

- Should he receive any adjuvant therapy?

no adjuvant therapy warranted for local prostate cancer

Prostate Cancer: Case Presentation

- Should he receive any adjuvant therapy? no known role for adjuvant therapy
  - No, there is no evidence that this improves outcome or survival.
  - Clinical trial would be appropriate
- After close follow-up for 3 years, patient's PSA begins to rise, from <0.1 to 1.2 to 3.1 ng/ml over 3 months cancer recurrence
- Bone scan and CT A/P, and transrectal bx of prostatic fossa all negative for maligancy. Patient asymptomatic.

but all the scans are negative?

- What treatment should he receive now?

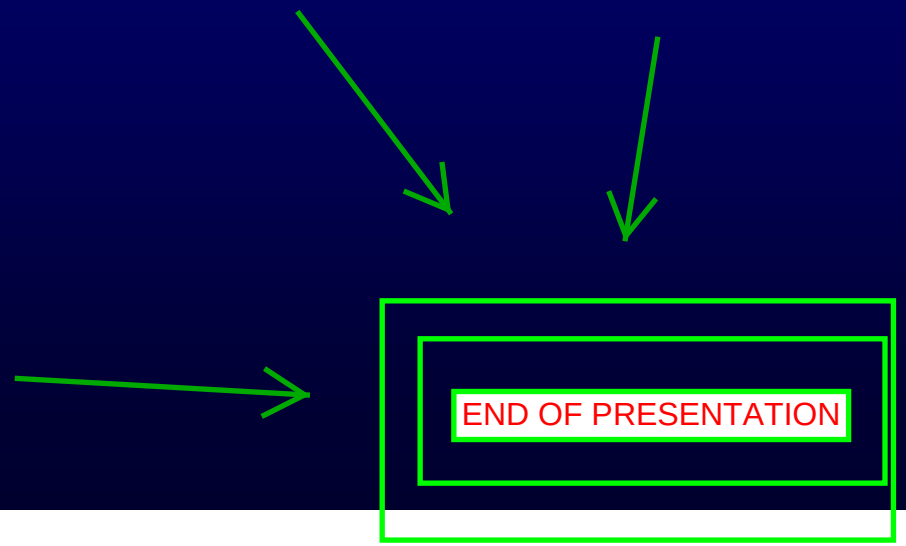
treat prostate cancer recurrence with hormonal therapy, like leuprolide

Prostate Cancer: Case Presentation

- What treatment should he receive now?
  - Hormonal therapy (GnRH agonist)-drops PSA to undetectable

e.g. leuprolide

fairly easy to tolerate



Prostate Cancer Case Presentation

STOPPED HERE STOPPED HERE STOPPED HERE STOPPED HERE

- 79 yo with 5 yr ho metastatic prostate cancer being treated with anti-androgen and GnRH agonist presents with increasing lower back pain.

- X-rays reveal sclerotic lesions in thoracic and lumbar spine, bone scan reveals spine disease and disease in right sacrum.

- What is his prognosis and what treatment should he receive?

Prostate Cancer: Case Presentation

- Prognosis- chance of 5 year survival 30%

- Treatment-should first get MRI to r/o cord compression, this is ruled out (if not needs XRT to the area)
- Treatment options include discontinuing antiandrogen (can often cause a response) and placing on the bisphosphonate zoledronic acid to reduce skeletal complications

- Goal is palliation
- Patient responds for 3 months with decreased pain, but then re-develops pain-CT reveals pelvic LAN, bone scan-new lesions
- What should we do now?

Prostate Cancer: Case Presentation

- What should we do now?
  - Chemotherapy with docetaxel and prednisone or extramustine
    - Improves survival for HRPC
  - Other choices down the line include retreatment with docetaxel and prednisone or extramustine or mitoxantrone and prednisone

Summary

- Cancer treatment becoming more complicated, less toxic, more effective
- While surgery, radiation and chemotherapy remain the backbone, targeted agents are increasingly carving their niche
- Better preclinical models are needed to understand how these treatment options can be combined
- New paradigms are needed to demonstrate the activity of these agents (old measures don't work for targeted agents)
- Patient selection may be critical to identifying appropriate patients for these agents
  - Matching patients with the appropriate agents for their tumor type is the future