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

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 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)
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
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
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
# Combination Therapy: Example

<table>
<thead>
<tr>
<th>Agent</th>
<th>Toxicity</th>
<th>MOA</th>
<th>Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Carboplatin</strong></td>
<td>BM</td>
<td>DNA Cross-linking</td>
<td>Repair of damage</td>
</tr>
<tr>
<td></td>
<td>Renal</td>
<td></td>
<td>Reduced uptake</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Increased GSH</td>
</tr>
<tr>
<td><strong>Paclitaxel</strong></td>
<td>BM</td>
<td>Microtubule stabilizer</td>
<td>Cell export (MDR)</td>
</tr>
<tr>
<td></td>
<td>Neurotoxic</td>
<td></td>
<td>Structural alterations in tubulin</td>
</tr>
<tr>
<td></td>
<td>Edema</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Allergic Rxn</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Uses: NSC Lung, breast, ovarian, endometrial, bladder, H&N
Give paclitaxel, then platin (reduced myelosuppression) - order matters

Common combo therapy: carboplatin + Paclitaxel = SYNERGY

What are model aspects for combo therapy?

Efficacy is the same for any order of administration, but the toxicity is what drives the administration.
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)
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
  - rapidly dividing cells
  - also reproductive organs
- Almost all cause BM suppression, only a few that don’t/mild (bleomycin, cisplatin, methotrexate and vincristine)
NSC Lung Cancer: Case Presentation

• 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

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

• 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?
Most NSCLC is diagnosed at advanced stages.

**Extent of Disease at Diagnosis**

- **Unstaged**: 8%
- **Localized**: 16%
- **Regional**: 37%
- **Distant**: 39%
- **Unstaged**: 8%

- 55% of patients present with stage IIIIB or stage IV disease
  - Most cancers are diagnosed in advanced stage
- ~5–6 months median survival for untreated stage IIIIB/IV NSCLC
- ~15% 5-year survival rate with standard therapy
ECOG 1594: Alternative Doublets, Similar Outcomes

All eligible patients (N = 1155)
Response rate, 19%
Median survival, 7.9 months

Survival (%)

Months

100
90
80
70
60
50
40
30
20
10
0

Cisplatin/paclitaxel
Cisplatin/gemcitabine
Cisplatin/docetaxel
Carboplatin/paclitaxel

Pop Quiz:
common chemotx toxicities:

Treatment Options for Advanced NSCLC

Unresectable stage III (dry*)

Chemotherapy with radiotherapy

Progression/recurrence

Stage IIIB (wet†) stage IV (metastatic)

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

Progression/recurrence

Second-Line
Docetaxel
Pemetrexed
Erlotinib

Third-Line
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.

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)

  - 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 hemicolecotomy-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

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

5th AJCC
(1997)

<table>
<thead>
<tr>
<th>Stage I</th>
<th>Stage II</th>
<th>Stage III</th>
<th>Stage IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 or T2 N0 M0</td>
<td>T3 or T4 N0 M0</td>
<td>Any T N1 M0</td>
<td>Any T Any N M1</td>
</tr>
</tbody>
</table>

5-yr OS
| 93% | 83% | 60% | 8% |

6th AJCC
(2002)

<table>
<thead>
<tr>
<th>Stage Ia</th>
<th>Stage Ib</th>
<th>Stage IIa</th>
<th>Stage IIb</th>
<th>Stage IIc</th>
<th>Stage IIIa</th>
<th>Stage IIIb</th>
<th>Stage IIIc</th>
</tr>
</thead>
<tbody>
<tr>
<td>T3 N0 M0</td>
<td>T4 N0 M0</td>
<td>T1-2 N1 M0</td>
<td>T3-4 N1 M0</td>
<td>Any T N2 M0</td>
<td>Any T Any N M1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

5-yr OS
| 85% | 72% | 83% | 64% | 44% |

Subserosa

\(P < 0.001\)

## MOSAIC Trial: 6 year update

<table>
<thead>
<tr>
<th></th>
<th>Disease Free Survival (%)</th>
<th>5-FU/LV (n=1123)</th>
<th>FOLFOX-4 (n=1123)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage II</strong></td>
<td></td>
<td>81.3%</td>
<td>85.1%</td>
<td></td>
</tr>
<tr>
<td><strong>Stage III</strong></td>
<td></td>
<td>61%</td>
<td>69.7%</td>
<td></td>
</tr>
<tr>
<td><strong>Grade III Neuropathy (1mo)</strong></td>
<td></td>
<td>0%</td>
<td>12.4%</td>
<td></td>
</tr>
<tr>
<td><strong>Neuropathy (1 yr f/u)</strong></td>
<td></td>
<td>0%</td>
<td>1.1%</td>
<td></td>
</tr>
<tr>
<td><strong>Overall Survival</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Stage III (6 years)</strong></td>
<td></td>
<td>68.3%</td>
<td>72.9%</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td><strong>All patients (4 years)</strong></td>
<td></td>
<td>70.4%</td>
<td>76.2%</td>
<td>0.008</td>
</tr>
<tr>
<td><strong>All patients (3 years)</strong></td>
<td></td>
<td>72.9%</td>
<td>78.2%</td>
<td>0.002</td>
</tr>
</tbody>
</table>
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

- 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? hmmmm...unknown
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?
5-year colon cancer survival by stage
5th and 6th edition AJCC system


5th AJCC (1997)
- Stage I: T1 or T2 N0 M0
  - 5-yr OS: 93%
- Stage II: T3 or T4 N0 M0
  - 5-yr OS: 83%
- Stage III: Any T N1 M0
  - 5-yr OS: 60%
- Stage IV: Any T Any N M1
  - 5-yr OS: 8%

6th AJCC (2002)
- Stage I: T1-2 N0 M0
  - 5-yr OS: 85%
- Stage II: T3-4 N1 M0
  - 5-yr OS: 72%
- Stage III: Any T N2 M0
  - 5-yr OS: 64%
- Stage IV: Any T >3 LN
  - 5-yr OS: 44%

*Subserosa*

P<0.001

### Hepatic resection

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

*Hepatic resection brings 5 yr Overall Survival from 8% up to >35%*  
*This translates to ~95% certainty of cure*
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.

- What if he had widely metastatic disease (not resectable)?
Integrating Therapy: Treatment of Colorectal Cancer

Therapeutic concepts

Palliative chemotherapy
Adjuvant chemotherapy
Neoadjuvant chemotherapy


5-FU
Irinotecan
Capecitabine
Oxaliplatin
Cetuximab
Bevacizumab
Panitumumab

for widely metastatic disease (nonresectable)

not included in lecture, but I thought you might be interested in the mechanisms....
Efficacy of Chemotherapy in First-Line CRC: Phase III Trial Results

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

*P ≤ 0.001.
†P < 0.01.


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

<table>
<thead>
<tr>
<th></th>
<th>mFOLFOX6 + bevacizumab (n=71)</th>
<th>bFOL + bevacizumab (n=70)</th>
<th>CAPEOX + bevacizumab (n=72)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CR</strong></td>
<td>6</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td><strong>PR</strong></td>
<td>47</td>
<td>37</td>
<td>45</td>
</tr>
<tr>
<td><strong>SD</strong></td>
<td>39</td>
<td>31</td>
<td>32</td>
</tr>
<tr>
<td><strong>PD</strong></td>
<td>6 (28)</td>
<td>13 (29)</td>
<td>9 (14)</td>
</tr>
<tr>
<td><strong>ORR</strong></td>
<td>53 (43)</td>
<td>41 (22)</td>
<td>48 (35)</td>
</tr>
<tr>
<td><strong>TTP</strong></td>
<td>9.9 (8.7)</td>
<td>9.3 (5.9)</td>
<td>10.3 (5.9)</td>
</tr>
<tr>
<td><strong>mOS</strong></td>
<td>26 (19.2)</td>
<td>20.7 (17.9)</td>
<td>27 (17.2)</td>
</tr>
</tbody>
</table>

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 + irinotecan/oxali: 24.0 months
  - 5-FU + irinotecan/oxali + targeted (bev, cetuximab): ~30.0 months

Choose between irinotecan and oxaliplatin based on PATIENT'S TOXICITIES.
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.

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

We are beginning to better know the biology of the tumor to predict greater efficacy or increased toxicity.
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.

- 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 disease.

- What is her prognosis and what treatment should she receive, if any?
Breast Cancer: 5-Year Survival by Stage

- **Stage 0/I (Localized):** 98% 5-year survival
- **Stage II/III (Regional):** 80% 5-year survival
- **Stage IV (Metastatic):** 26% 5-year survival

Unlike colon cancer, there is a decent chance for surviving metastatic Breast Cancer.

**Tumor Characteristics**

**HER2-Positive MBC**
- Anti-HER2 monoclonal antibody: **trastuzumab**

**ER/PgR-Positive MBC**
- Aromatase inhibitors: **letrozole, anastrozole, exemestane**
- Antiestrogens: **tamoxifen, toremifene**
- Progestin: **megestrol acetate**
- Fulvestrant
- 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.*
Other Types of MBC (ie, HER2-Negative, ER/PgR-Negative)

- **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

*Systemic Therapy in MBC Based on Tumor Characteristics (cont’d)*

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 density loss-can minimize with oral bisphosphonate, calcium, Vit D and weight bearing exercise)

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

HR = 0.498 (95% CI, 0.401-0.618)
Log-rank test $P<0.001$

Paclitaxel + bevacizumab  10.97 mo
Paclitaxel  6.11 mo

CI = confidence interval.
Miller et al. Presentation at ASCO, 2005.
Phase III Trial of Paclitaxel ± Bevacizumab as First-Line Therapy in MBC: Overall Survival

proportion surviving

HR = 0.674 (95% CI, 0.495-0.917)
Log-rank test $P=0.01$
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).
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

more treatment = longer survival
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

• 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?
Prostate Cancer: Case Presentation

- Prognosis - chance of 5 year survival 100%
- Treatment options include radiation (either external beam or brachytherapy) or surgery (radical prostatectomy)
- Goal is cure
- As there is a question of extracapsular invasion, he has a large prostate, and urinary sx-recommendation would be for surgery.
- Should he receive any adjuvant therapy?
Prostate Cancer: Case Presentation

- Should he receive any 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

- Bone scan and CT AP, and transrectal bx of prostatic fossa all negative for malignancy. Patient asymptomatic.

- What treatment should he receive now?
Prostate Cancer: Case Presentation

• What treatment should he receive now?
  – **Hormonal therapy** (GnRH agonist)-drops PSA to undetectable
    fairly easy to tolerate

treat prostate cancer recurrence with hormonal therapy, like leuprolide
Prostate Cancer Case Presentation

• 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