Principles of Cancer Treatment

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MultiCare Health System

Objectives

• Discuss goals of treatment
• Describe modalities and mechanism of action for the following cancer treatments
  – Chemotherapy
  – Biotherapy and Targeted Therapy
  – Surgery
  – Complementary and Alternative Medicine
• List potential side effects of cancer treatments
SURGERY

Surgery…

• Is the oldest form of cancer treatment
• Is precise and local
• Is a method of diagnosing and staging cancer
• May be curative alone
• May be used with other modalities
• May remove some or all of the primary tumor
• May be palliative in nature
Goals of Cancer Surgery

• Preventative/Prophylactic
  – To prevent/reduce risk of cancer in high-risk patients
    • Barrett’s esophagus: Esophagectomy
    • Familial Breast Cancer: Mastectomy
    • Familial Ovarian Cancer: Oophorectomy
    • Polyposis Coli or Ulcerative Colitis: Colectomy
  – Only used in high-risk patients after careful consultation with oncologist and genetic counselor/geneticist

Diagnosis and Pathologic Staging

• Treatment is based on biopsy results and tissue analysis
  – Determine extent of disease (staging)
  – Used for tumor markers and genetic testing
Diagnosis and Pathologic Staging

- Aspiration Biopsy
- Needle or Core Biopsy
- Incisional (sampling)
- Excisional (removal)
- Thorascopic or Laparoscopic

Blue marking dye for sentinel lymph node
Surgical margins marked with green ink

Posterior surface
Mastectomy has been cut into slices.

Breast Cancer
Radiographic markers left during the needle biopsy
On a Cellular Level…

• “Negative Margins”

Goals of Cancer Surgery

• Cure!?!?!?
• Surgical Resection: To remove entire tumor, which may include…
  – “Negative Margins”
  – Affected regional lymph nodes
  – Adjacent affected organs (salpingo-oophrectomy)
  – Biopsy tracts (renal cancer)
Goals of Cancer Surgery

• Surgical Palliation
  – To improve comfort when cancer is not curable
  – Cytoreduction
    • Decrease tumor burden
    • Improve chemo/radiation effects
  – Decompression or diversion
    • Tube
    • Ostomy
    • Stent
    • Removal of metastasis deposit (spine)

Multimodal Surgical Treatment

• Chemotherapy, biologics, and immunotherapies
  – Preop (neoadjuvant)
  – Intraop
  – Postop (adjuvant)

• Radiation
  – Preop (neoadjuvant)
  – Intraop
  – Postop (adjuvant)
Surgical Technique

• Local excision
• Wide excision
• En bloc resection (contiguous tissues)
• Debulking
  – Decrease tumor mass
  – Improve chemosensitivity
  – Intraop?

Other “Surgery”

• Cryotherapy/Cryosurgery/Cryoablation
  – thermal-based energy to lyse small lesions
  – cryoprobe inserted to desired site
  – treat primary lesion (Renal/Prostate) or metastatic lesion
• Transarterial Chemo Embolization (TACE)
  – chemotherapy-filled microspheres injected directly into tumor
  – treat large volume lesions (often liver primary)
TACE & Cryo

Microspheres injected during transarterial therapy "lock in" chemotherapy and block the blood supply to the tumor.

http://erabillings.com/services/transarterial/chemoembolization-tace/

http://keyholeurology.co.uk/kidnecancertreatment.html
Nursing Role

• Preoperative teaching and care
• Post-operative care
  – Hemodynamic/cardiovascular stability
  – Skin/wound/drain/tube assessment and care
  – Communication
  – Pain management
  – Prevention and management of SE associated with surgery and cancer
  – DVT prophylaxis
  – Pulmonary toileting
  – Nutrition
  – Bowel function
  – Psychosocial support

Nursing Role

• For Discharge:
  Continuous patient education and follow-up
  – Wound care
  – Discharge meds
  – Nutrition
  – Activity
  – Follow up appointment and plan
• Psychosocial support is key
QUESTIONS ABOUT SURGERY?

CHEMOTHERAPY
Chemotherapy Overview

• Systemic therapy using a chemical substance
  – Frequently given in combination with other chemotherapy or non-chemotherapy drugs
  – Toxic to both normal and cancerous tissues
    • Can be a limiting factor in dosage/use
  – Many routes of administration available
  – Often given in specific sequences (cycles) to maximize response and minimize side effects

Role of Chemotherapy

• Curative
  – intended to cure disease

• Control
  – increase length and quality of life when cure not possible

• Palliative
  – relieve tumor-related symptoms
  – comfort when cure/control not possible
Role of Chemotherapy

• Adjuvant
  – used after primary treatment
    • chemo after surgery or radiation

• Neoadjuvant
  – used before primary treatment
    • Chemo used to shrink a tumor before surgery

• Myeloablative
  – obliterate bone marrow
  – used before HSCT

Chemotherapy

• Significant role in solid and liquid malignancy

• Impact based on cellular kinetics
  – Cell cycle
  – Cell time
  – Cell growth fraction
  – Tumor burden
Chemotherapy - Cell Cycle

- **G0**—Resting/dormant phase
- **G1**—Synthesis of proteins and RNA; growth
- **S**—DNA is replicated
- **G2**—Preparation for mitotic spindle formation; growth
- **M**—Cell division occurs

Cell Cycle Specificity

**Cell Cycle Specific**
- Exert an effect at a specific part of the cell cycle
- Work best when given in cycles, divided doses, or continuously
- Most effective when patient kept on regular treatment schedule

**Cell Cycle Non-Specific**
- Exert effects in all phases of cell cycle, including **G0**
- Cell kill is directly proportional to the amount of drug administered
- Dose dependent—easier to delay treatment so that higher dose can be given
Cell Cycle Specificity

- Cell Cycle-Specific
  - Antimetabolites
  - Plant alkaloids
    - Camptothecins
    - Epipodophyllotoxins
    - Taxanes
    - Vinca alkaloids
  - Miscellaneous

- Cell Cycle-Nonspecific
  - Alkylating agents
  - Antitumor antibiotics
  - Nitrosureas

Chemotherapy- Cell Time

- Cell time= Mitosis to mitosis
- Based on cell type
  - Highly mitotic cells include epithelial cells, embryonic tissue, and blood stem cells… and cancer cells
  
  Short cell cycle=

  $\uparrow$ cell kill

  Continuous infusion of a cell-cycle specific agent =

  $\uparrow$ cell kill
Breast, Grade 3/3
- Mitotic rate is factored into grading
- Generally on a 0/4 scale
- Breast (Nottingham) and Prostate (Gleason) are special

Breast, Grade 1/3
- Glandular breast tissue
- Minimal solid tumor
Breast, Grade 3/3
• Invading muscle

Chemotherapy- Growth Fraction

• Tumor Growth Fraction: proportion of cells dividing at one time
  - ↑% = ↑ increased kill with cell cycle-specific drugs
  - ↓% = ↑ sensitivity to cell cycle-nonspecific drugs
Chemotherapy - Tumor Burden

• Small tumors = increased chemosensitivity

• Growth slows as tumor burden increases

• The more tumor, the more types of cells, the more likely chemo-resistant baby cells will proliferate = scary

Routes of Administration

• Oral
• Intramuscular
• Subcutaneous
• Intravenous
• Intraperitoneal
• Intra-arterial
• Intrathecal
• Intrapleural
• Intravesicular

• Advantages and disadvantages for each route

• Additional care areas may administer by specialized route
  – Interventional radiology
  – Operating suite

• Review your institution’s policies and procedures
Chemotherapeutic Approaches

• Single agent
  – Favored in recurrent disease
  – Single-agent can lead to chemo-resistant clones

  – e.g. docetaxel in advancing NSCLC

Chemotherapeutic Approaches

**Combo Therapy**
- Additive/synergistic effects
- Different phases of cell cycle
- Alternating toxicities
- Decreased resistance potential
- Add targeted agents

**Criteria for Combo**
- Singularity effective on specific cancer
- Different toxicities
- Toxicities happening at alternating times
- Biologically enhanced cytotoxicity
How Chemotherapy is Ordered

• Cycles
  – Frequency drug delivered

• Days
  – The point at which the patient is in a cycle

• Example:
  – The very first day the patient receives treatment is Cycle 1 Day 1
  – Cycle 2 - the drugs repeat starting back at day one
  – Sometimes of labs/follow up you might see orders for Day -1

Throw Your Patient a Line!

**PIV**
• Placed at bedside/chair side by competent RN/LPN
• High risk for extravasation
• Risk for sclerosis of veins
• Risk of phlebitis
• Low risk of infection

**CVC**
• PICC may be placed at bedside by specialized RN
• OR suite/IR placement
• Lower risk for dislodgement/ extravasation
• High risk of infection
Alkylating Agents

• Cell cycle-nonspecific
• Interfere with DNA replication by breaking DNA helix strand
• Examples:
  – Carboplatin/Cisplatin
  – Cyclophosphamide
  – Oxaliplatin
  – Ifosphamide
  – Dacarbazine

Side Effects

• Additional:
  – Hemorrhagic cystitis
    • ifosphamide
    • cyclophosphamide
  – Nephrotoxicity
    • cisplatin
  – Anaphylactic Reactions
    • oxaliplatin, thiopera, carboplatin

• Common:
  – Nausea/vomiting/diarrhea, decreased fertility, skin irritation, mucositis, alopecia, fatigue, neuropathy
Mesna?

- Urothelial protective agent
  - High dose cyclophosphamide
  - Ifosfamide
- Dosage is based on % of chemo dose
- IV or Oral

Antitumor Antibiotics (Alkylating Agents)

- Cell cycle-nonspecific
- Bind with DNA; inhibits DNA/RNA synthesis
- Examples:
  - Bleomycin
  - Mitomycin
  - Mitoxantrone
  - Anthracyclines
    - Doxorubicin
    - Epirubicin
    - Idarubicin
    - Daunorubicin
Side Effects

• Myelosuppression is the most common dose limiting toxicity
• Many agents are vesicants
• Drugs are colored (not clear)
  • Teach patient that urine/sclera might be discolored after administration

• Additional:
  • Cardiotoxicity
    • Anthracyclines
      – Lifetime cumulative dose limits
  • Pulmonary toxicity
    • Bleomycin
      – Test dose often used
  • Radiation Recall
  • Photosensitivity
  • Nephro/hepatotoxicity

• Common:
  – Nausea/vomiting, alopecia, electrolyte imbalance, decreased fertility, PPE (hand-foot syndrome), mucositis

Nitrosoureas (Alkylating Agents)

• Cell cycle non-specific
• Interfere with DNA replication by breaking DNA helix
• Cross blood-brain barrier
• Examples:
  – Carmustine
  – Lomustine
  – Streptozotocin
Side Effects

• Myelosuppression is the most common dose limiting toxicity
  • Also renal toxicity
• Delayed nadir: 4-6 weeks after treatment
• Agents can be irritating to veins if given rapidly

• Additional:
  – Nephrotoxicity
  – Hepatotoxicity
  – Pulmonary fibrosis
    • Lomustine
  – Altered glucose metabolism
    • Streptozocin

• Common:
  – Nausea/vomiting, anorexia, impaired fertility

Antimetabolites

• Cell cycle-specific
• Act in S phase; inhibit DNA synthesis and/or repair
• Given via many different routes
• Examples:
  – Capecitabine
  – Cytarabine
  – Fluorouracil
  – Gemcitabine
  – Methotrexate
  – Pemetrexed
Side Effects

- Major dose-limiting toxicity is myelosuppression
  - Also nephrotoxicity, hepatotoxicity, diarrhea, PPE, neurotoxicity, mucositis
- Dosing is highly variable depending on route and indication

- Additional:
  - Many agents are folic acid agonists or antagonists
    - Folic acid is either supplemented OR avoided!
  - Patients with hematologic malignancy may require hydration/allopurinol to prevent TLS

- Common:
  - Nausea/vomiting, alopecia, photosensitivity, constipation, fatigue, peripheral edema

Leucovorin?

- Folinic acid (broken down folic acid)
- When given with fluorouricil
  - Improves binding of 5-FU to cancer cells
  - 5-FU lasts longer
- When given with methotrexate
  - About 24 hours after
  - Rescues the normal cells
Camptothecins

• Plant alkaloid
• Cell cycle specific
• Act in S phase; inhibits topoisomerase I, causing double-strand DNA changes
• Examples:
  – irinotecan
  – topotecan

Side Effects

• Diarrhea is major dose-limiting toxicity
  • Early onset (within 24 hours) usually cholinergic
  • Treated with atropine

• **Additional:**
  – Myelosuppression
  – Interstitial lung disease
    • Topotecan

• **Common:**
  – Nausea, vomiting, alopecia, anorexia, fatigue, mucositis
Epipodophyllotoxins

- Plant alkaloid
- Cell cycle specific
- Act in G2 and S phase; interfere with topoisomerase II
- Examples
  - etoposide
  - teniposide

Side Effects

- **Additional:**
  - Hypersensitivity reactions
  - Secondary malignancy

- **Common:**
  - Nausea, vomiting, alopecia, anorexia

- Myelosuppression is major dose-limiting toxicity
- Can cause hypotension if administered rapidly
- Consider dose reduction in patients with renal/hepatic impairment
Taxanes

- Plant alkaloid
- Cell cycle specific
- Act in G2 and M phases; inhibit cell division by stabilizing microtubules
- Examples:
  - cabazitaxel
  - docetaxel
  - paclitaxel

Side Effects

- Additional:
  - Use of in-line filter is required in some agents
    - paclitaxel
  - Consider dose adjustment or alternative agent in hepatic or renal dysfunction

- Common:
  - Hypersensitivity reactions
    - Premedicate with H2 antagonist, antihistamine, corticosteroid
  - Alopecia, facial flushing, fatigue, nausea, vomiting, myelosuppression, fluid retention

- Peripheral neuropathy is major dose-limiting toxicity
- Agents are irritants/vesicants
- Do not use PVC bag/tubing to administer
Vinca Alkaloids (Plant Alkaloid)

• Plant alkaloid
• Cell cycle specific
• Act in G2 phase to block DNA production, and M phase to prevent cell division
• Examples:
  – Vinblastine
  – Vincristine
  – Vinorelbine

Side Effects

• Myelosuppression and neurotoxicity are major dose-limiting toxicities
• Agents are vesicants

• Additional:
  – FATAL IF GIVEN INTRATHECALLY!
  – Nephrotoxicity
  – Hepatotoxicity

• Common:
  – Constipation, alopecia, nausea, vomiting
Miscellaneous Agents

• Cell cycle specific
• Have varied mechanisms of action
• Examples:
  – arsenic trioxide
  – hydroxyurea
  – vorinostat
  – asparaginase
  – procarbazine
  – ixabepilone

Side Effects

• Myelosuppression is most common dose-limiting toxicity
  • Also peripheral neuropathy

• Given by different routes, many PO

• Additional:
  – Alcohol should be avoided with procarbazine use
    • Antabuse-like reactions
  – Regular monitoring of labs and ECG needed with several agents
  – Asparaginase carries risk of anaphylactic reactions

• Common:
  – Nausea, vomiting, mucositis, hepatotoxicity, nephrotoxicity, fatigue, diarrhea
Complications of Chemotherapy

• Hypersensitivity reaction
  – Often prevented by premedications

• Extravasation
  – Irritants
  – Vesicants

• Anaphylaxis
  – True allergic response
  – Can be a Code situation!

• **Know your institutional policies!!**

• You will all take a closed-book test on everything you just learned regarding every drug that I just named.

• Good Luck! 😊
Why is this a ridiculous expectation?

So about Mr. Potter

- Harry Potter, age 57 in overall good health presented to his primary with hematochezia x3 months (has not had screening colonoscopy)
- Colonoscopy biopsy shows poorly differentiated adenocarcinoma of the colon
- CT of chest, abdomen, pelvis shows no distant metastases and limits the disease to loco/regional
- Sent to Dr. McGonagall: Surgical Oncologist
Post Op Mr. Potter

• Laparoscopic versus open?
  – Outcomes are similar 😊 Thanks New England Journal of Medicine!
• Dr. McGonagall completed a laparoscopic resection of a sigmoid colon with en bloc lymph node sampling
• What are our immediate interventions!?!
• What do we want to make sure he has before he leaves us?

Mr. Potter Pathology

• https://cancerstaging.org/references-tools/quickreferences/Documents/ColonMedium.pdf
• Tumor invades into the pericolon tissues
• 3/12 lymph nodes positive for malignancy
• T3, N1b, M0
• Stage?
• Medical Oncologist is consulted: Dr. Dumbledore!
• So………. Now what?
At Tumor Board

- Dr. McGonagall presents Mr. Potter’s case
- Radiologist review scans
- Pathologists review slides
- Tumor Registrar provides the NCCN guidelines
- Medical Oncologist Dr. Dumbledore reviews standard of care
- Research nurse looks for a clinical trial
- Office nurse anticipates patient needs
- Radiation therapy says “not today”

Chemo Regimen

- Dr. Dumbledore orders FOLFOX

- FOL - folinic acid (leucovorin)
- F - flurouricil (5-fu)
- OX - (oxaliplatin)

- Every two weeks x 12 cycles… OR a clinical trial comparing 6 and 12 cycles
Ordering

- Leucovorin 400 mg/m2 iv over 2 hrs, prior to 5-FU d1
- 5-FU 400 mg/m2 iv bolus d1 followed by 2400 mg/m2 iv over 46 hrs
- Oxaliplatin (Eloxatin) 100 mg/m2 in 500 ml dextrose 5% iv over 2 hours d1
- Q2w x 12 cycles

Summary

- Chemotherapy can be classified according to effect on cell cycle and pharmacologic class
- Each class has different mechanisms of action and side effect profiles
- Myelosupression is the most lethal and most common side effect of chemotherapy
- ?????????????????????????????????????????????????????????????????????
  ????
Biotherapy: NCI Definition

• *N.*: “Treatment to boost or restore the ability of the immune system to fight cancer, infections, and other diseases. It also is used to lessen certain side effects that may be caused by some cancer treatments.”

• Biologic agents mimic or impact signaling pathways to control cellular functions
Biotherapy

• Alters the body’s immune system
• Enhances immune response
• Prevents metastasis of cancer cells
• Helps normal cells repair following treatment

• Biologic Response Modifiers Includes:
  – vaccines
  – interleukins
  – interferons
  – colony stimulating factors
  – Monoclonal antibodies

Transition to Targeted Therapy

Approach to Targeted Therapy

• Neoadjuvant
  – Downsize tumor $\rightarrow$ complete response

• Primary Treatment
  – Single agent
    • *imatinib* for the treatment of Philadelphia chromosome-positive CML
  – Combo agent
    • CHOP (cyclophosphamide, doxorubicin, vincristine (oncovin), and prednisone + rituximab

Approach to Targeted Therapy

• Adjuvant Setting
  – Single
    • Postop imatinib to maintain disease-free interval after GIST resection
  – Combo
    • TCH- docetaxel (Taxotere) and carboplatin + trastuzumab in HER2+ breast cancer
Targeted Therapy

• Drugs that block cancer growth/spread
  – Interfere with molecules that act on tumor growth and progression
  – Therapies focus on signaling pathways
  – Mutations in signaling pathways are found in many cancers
  – These mutations can be targets of therapy

Targeted Therapy

• Substantial growth in field in last 15 years
  – The first: rituximab approved 1994
  – Targets and blocks CD20 receptors on cancer cells
  – Within the last three years, 36 new oncology drugs received FDA approval
    • Most were targeted therapies
• Monoclonal antibodies (mAbs)
• Small Molecule Inhibitors
Monoclonal Antibodies

• Cell signaling directs cellular growth, function, and death
  – Done by biochemical or molecular messengers
    • Cytokines, enzymes, etc
    • Cancer cells have super signals

• Mechanism of action
  – Signal transduction
  – Generated inside or outside of the cell
  – Triggers a signaling cascade that directs the cell
to do a specific activity
Monoclonal Antibodies

Monoclonal Antibodies in Action

**Rituximab**
- Targets the CD20 extracellular antibodies on B lymphocytes
- Binds to receptors, recruiting NK cells
- Activates compliment

**Bevacizumab**
- Targets vascular endothelial growth factor (VEGF)
- Prevents VEGF from binding to and inhibiting new vessel growth
Examples of mAbs

<table>
<thead>
<tr>
<th>Agent</th>
<th>Target</th>
<th>Source</th>
<th>Indication</th>
<th>Year Approved</th>
</tr>
</thead>
<tbody>
<tr>
<td>rituximab</td>
<td>CD20</td>
<td>Chimeric</td>
<td>Non-Hodgkins Lymphoma</td>
<td>1994</td>
</tr>
<tr>
<td>trastuzumab</td>
<td>HER-2</td>
<td>Humanized</td>
<td>Breast, gastric cancer</td>
<td>1998</td>
</tr>
<tr>
<td>cetuximab</td>
<td>EGFR</td>
<td>Chimeric</td>
<td>HN, colorectal cancer</td>
<td>2004</td>
</tr>
<tr>
<td>bevacizumab</td>
<td>VEGF</td>
<td>Humanized</td>
<td>Colorectal, GBM, NSCLC</td>
<td>2004</td>
</tr>
<tr>
<td>panitumumab</td>
<td>EGFR</td>
<td>Human</td>
<td>Colorectal cancer</td>
<td>2006</td>
</tr>
<tr>
<td>ofatumumab</td>
<td>CD20</td>
<td>Human</td>
<td>CLL</td>
<td>2009</td>
</tr>
<tr>
<td>Brentuximab vedotin</td>
<td>CD30</td>
<td>chimeric</td>
<td>HD, anaplastic lymphoma</td>
<td>2011</td>
</tr>
</tbody>
</table>

Adapted from [http://www.actip.org/pages/library/Table_Monoclonal_Antibodies.pdf](http://www.actip.org/pages/library/Table_Monoclonal_Antibodies.pdf)
Side Effects

• Highly dependent on the cellular pathway being disrupted and agent administered
• Hypersensitivity reactions are possible
• Dermatologic toxicities can be severe (acneiform rash, PPE, dry/cracked skin, fissuring); can be dose-limiting
• Also cardiac dysfunction, hepatotoxicity, nausea, vomiting, hypertension, fatigue

Small Molecule Inhibitors

• Mechanism of Action
  – Act on signaling pathways that control tumor growth, proliferation, and invasion
  – Either moderate, control, and/or kill cancer cells
  – Most require chronic or long-term therapies
• Tyrosine Kinase Inhibitors (TKIs)
  – Erlotinib, Sorafenib, Sunitinib
• Mammalian target of rapamycin (mTOR)
  – Temsirolimus, everolimus
Signaling Pathways

EGFR Pathway

• https://www.youtube.com/watch?v=TAm4twCwOUU
### Examples Small Molecule Inhibitors

<table>
<thead>
<tr>
<th>Agent</th>
<th>Target</th>
<th>Indication</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bortezomib (Velcade)</td>
<td>26S proteasome</td>
<td>Multiple myeloma, mantle cell lymphoma</td>
<td>IV, SC</td>
</tr>
<tr>
<td>Erlotinib (Tarceva)</td>
<td>EGFR</td>
<td>NSCLC, pancreatic cancer</td>
<td>PO</td>
</tr>
<tr>
<td>Everolimus (Afinitor)</td>
<td>mTOR</td>
<td>Breast, renal cell</td>
<td>PO</td>
</tr>
<tr>
<td>Imatinib mesylate (Gleevec)</td>
<td>MCR-ABL</td>
<td>Ph+ CML</td>
<td>PO</td>
</tr>
<tr>
<td>Sorafinib (Nexavar)</td>
<td>Multikinase inhibitor</td>
<td>Hepatocellular, renal cell carcinoma</td>
<td>PO</td>
</tr>
<tr>
<td>Temsirolimus (Torisel)</td>
<td>mTOR</td>
<td>Renal cell carcinoma</td>
<td>IV</td>
</tr>
</tbody>
</table>

### Not-so-small Molecule Side Effects

- Very drug specific!
- Dermatologic toxicities
  - Rash, acneiform/maculopapular, itching, stomatitis (oral lesions)
  - Topical corticosteroids, oral antihistamines, oral corticosteroids
- Cardiac dysfunction
  - Edema, fluid retention, cardiomyopathy, decreased LVEF, QT prolongation, hypertension
- Miscellaneous
  - Electrolyte imbalances, hair color changes, hepatotoxicity, skin discoloration, bleeding
**mAb v. Kinase Inhibitors**

<table>
<thead>
<tr>
<th></th>
<th>Monoclonal Antibodies</th>
<th>Small-Molecule Kinase Inhibitors</th>
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</thead>
<tbody>
<tr>
<td><strong>Size</strong></td>
<td>Large</td>
<td>Small</td>
</tr>
<tr>
<td><strong>Site of Action</strong></td>
<td>Extracellular</td>
<td>Intracellular</td>
</tr>
<tr>
<td><strong>Usual Method of Admin</strong></td>
<td>IV</td>
<td>Oral</td>
</tr>
<tr>
<td><strong>Half-life</strong></td>
<td>Days</td>
<td>Hours</td>
</tr>
<tr>
<td><strong>Type of Target</strong></td>
<td>Single</td>
<td>Single/Multiple</td>
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<tr>
<td><strong>Immune system activation potential?</strong></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Drug/Drug Interaction</strong></td>
<td>No</td>
<td>ABSOLUTELY!</td>
</tr>
</tbody>
</table>

**Meet Dori**

- Dori is a 59 y.o. female presenting to the ED with increased shortness of breath, abdominal pain, also complains of fatigue and general malaise
- Physical assessment shows bulky cervical lymphadenopathy
- CT of chest/abdomen/pelvis shows bulky mediastinal, axillary, and cervical lymphadenopathy
- Admitted to floor to manage pain, correct electrolyte imbalance, and monitoring
Enter Dr. Marlin

• Dr. Marlin, Medical Oncologist is consulted
  – Orders U/S guided biopsy of mediastinal mass
  – Bone marrow aspirate to be performed at bedside
  – Many, Many, Many lab tests
  – Histochemical stains, flow cytometry, peripheral smear, HIV antibody, you name it, he ordered it
• Results of all that: CD20+ high-grade diffuse Large B cell lymphoma

Summary

• Effect specific cellular markers/signals on both healthy and cancerous cells
  – Cancerous cells over-express tumor markers
• Infusion reactions are common in mAbs
• Many agents are PO
  – Patient education is important
  – some agents cannot be crushed; know whether or not they can be taken with food
• Side effects are highly drug specific
The Regimen

- Dori is going to start her first cycle of EPOCH-R
- E- etoposide
- P-prednisone
- O-vincristine [Oncovin]
- C- Cyclophosphamide
- H- Doxorubicin [hydroxydaunorubicin]
- R- Rituxumab

Orders

- **Day 1**: Rituximab 375mg/m² IV day 1
- **Days 1–4**: Etoposide 50mg/m² IV, doxorubicin 10mg/m², and vincristine 0.4mg/m²
- **Day 5**: Cyclophosphamide 750mg/m² IV
- **Days 1–5**: Prednisone 60mg/m² PO BID.
- Administer G-CSF 5 mcg/kg SQ daily until an ANC >5 × 10⁹/L above nadir level starting day 6.
- Repeat cycle every 3 weeks for 6 cycles
What is happens next?

- What kind of line do we need?
- What are we monitoring?
- What are we teaching?

COMPLEMENTARY AND ALTERNATIVE THERAPIES OR COMPLEMENTARY AND INTEGRATIVE THERAPIES
Holism and Holistic Health Care

- Modalities that integrate mind/body/spirit/environment

- Integrative Medicine
  - “A personalized and holistic approach that takes into account each patient’s unique circumstances (e.g. diagnosis, patient values an preferences, expected toxicities related to standard treatment regimen) to customize treatment programs”

“CAM”

- Any medical system, practice, or product that is not thought of as standard care
  - Complementary Medicine
    • A CAM therapy used along with standard medicine
  - Alternative Medicine
    • A CAM therapy used in place of standard treatments
    • A domain of therapies that fall outside of conventional medicine
Prevalence in the US

• Approximately 38% of adults and 12% of children use CAM
  – Most use is underreported
  – Use has risen significantly in recent years
  – Spans all cultural/ethnic backgrounds
• $33.9 BILLION spent in 2007 alone
  – Out-of pocket visits, supplies, materials
• Some CAM practices are more regulated than others
  – Supplements/herbals are not always FDA regulated

Top Patient-Reported Reasons for Using

• Disease prevention
• Pain management
• Treatment of specific chronic health conditions
• Supplements to conventional medicine
Heath Care Providers are Catching On!

- As number of providers offering complementary therapies increases, cancer care becomes more integrative
- Hospice care provider offerings:
  - Massage
  - Supportive group
  - Music

NCI Support of CAM

- $105,341,737 spent on CAM in 2011
  - $64 million for prevention research
  - $19 million for treatment
  - $16 million for symptom management
- Examples of NCI Funded Studies
  - Green Tea for Bladder Cancer
  - Curcumin for Radiation Dermatitis
  - Acupuncture for Dry Mouth
Types of CAM

• NCI’s office of Cancer and Complementary and Alternative Medicine lists 8 major categories:
  – Alternative medical systems
  – Energy therapies
  – Exercise therapies
  – Manipulative and body-based methods
  – Mind/body interventions
  – Nutritional therapeutics
  – Pharmacologic/biologic treatments
  – Spiritual therapies

NCI Reports: High Dose Vit C

• 2 studies show decrease AEs and increase in quality of life with HD Vit C
• Redox properties and decreasing tumor growth in vitro

NCI Reports: Mistletoe

• Most widely studied CAM therapies
• Injectable form not available in US
• Has been studied in humans with reports of increased survival and QOL… but reliability was highly questionable
• Should not be recommended outside of clinical trials
  • What is the challenge here?

https://www.cancer.gov/about-cancer/treatment/cam/hp/mistletoe-pdq

Whole Medical Systems

Ayurveda
• Mind/body/consciousness balance treat illness and preserve health
• Goals include proper diet/hydration
• Sleep-wake routines
• Mantras (specific movements/spoken words)

Chiropractic Medicine
• Re-establish CNS functioning
• Contraindicated in patients with:
  – Bone mets
  – Spinal cord compression
  – Thrombocytopenia
  – VTE
Whole Medical Systems

• Traditional Chinese Medicine
  – Acupuncture
  – Herbs
  – Mind-body therapy
  – Find balance between opposing complementary forces
    • Cold/heat, excess/deficiency

And the list goes on…

• Acupressure
• Aromatherapy
• Dance therapy
• Lymphatic therapy
• Massage
• Physical therapy
• Trigger point therapy
• Art therapy
• Color therapy
• Guided imagery
• Meditation
• Music therapy
• T’ai chi
• Yoga
Must Love Research!

• Pranayama
  – A series of breathing techniques
  – Taught in weekly classes
  – Instructed to practice at home

• Findings
  – Dose-response relationship found between pranayama use and improvements in chemotherapy-associated symptoms and quality of life

• Be on the look out for CAM-related research articles in Oncology and other journals!

Herbs and Supplements

• Herbs have been used to treat disease for 1000s of years
• Continue to be used by as many as 50% of Americans
• Many are proven to be beneficial
  – Ginger prevents nausea
  – St. John’s wort is effective at treating depression
  – English ivy leaf treats bronchitis and asthma
Drug Interaction: CYP3A4

- Goldenseal: topical antiseptic and systemic GI disorder treatment
  - CYP3A4 inhibitor (prevents drug metabolism)

- St. John’s Wort: depression
  - CYP3A4 inducer (increased drug metabolism)
  - Shortens the half life of alprazolam (Xanax) from 12 hours to 6 hours

Nursing Assessment

- Should include directed questions regarding CAM
- Question in culturally-sensitive and non-judgmental way
- CAM practices can be tied to cultural and spiritual beliefs
- All CAM therapies should be documented in assessment
- Are you taking any medications?
HAZARDOUS MEDICATIONS

Hazardous Medications

• Must meet one or more of these criteria:
  – Genotoxicity – causes DNA damage
  – Carcinogenicity – causes cancer development
  – Teratogenicity/developmental toxicity – fetal damage, loss
  – Reproductive toxicity– sterility, infertility
  – Organ toxicity – at low doses
Principles of Safe Handling

• Preparation in biologic safety cabinet (BSC) under laminar flow hood
• Safe handling techniques during storage, mixing, and transport
• Processes in place for labeling, administration, and disposal
• Personal Protective Equipment

Washington State Law

• Passed in 2012 by state legislature
  – Requires all facilities that handle hazardous drugs to comply with NIOSH recommendations
    • List of hazardous drugs defined by NIOSH and formulary
  – Implemented in three stages:
    • January 1st, 2015– written hazardous drug control program implemented
    • July 1st 2015– provided employee training
    • January 1st, 2016– installed appropriate ventilated BSC
• Be aware of your facility-specific policy and procedure for hazardous medication handling
Questions?

• Thank you!!

References