Oncology 101

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September 2006
Fundamentals

- Biology of Cancer
- Diagnosis
- Pathology
- Principles of therapy
- Schedules/Delivery
- Toxicities
- Staging
- Evaluation of response
- Phases of trials
Biology of Cancer Cells

- Abnormal cell structure
- Uncontrolled growth
- Immortality
- Ability to spread
- Ability to invade other tissues
- Heightened sensitivity to growth factors
- Ability to divide
- Accelerated use of nutrients
- Angiogenesis
Diagnosis

- Physical Examination
- Biopsy
- Staging evaluation
  - What to choose? Alphabet soup?
  - CT, Mammo, PET, MRI, US, CT/PET, MUGA, ECHO, CXR,
- Surgical evaluation
Biopsy Methods: What’s the difference?

- Shave biopsy
- Fine needle biopsy
- Guided aspirate
- Full resection-wide excision/full surgical

- Cytology Bronchoscopy
- Bone Marrow Biopsy
- Paracentesis
- Thoracentesis
- Lumbar Puncture
- Colonoscopy
Pathology

- Preliminary vs Confirmatory biopsy
- Dermato- vs Surgical pathology

Terms
- Depth
- Markers
- Stains
- Borders
- Invasion
Therapeutic Options

- Surgery
- Radiation Therapy
- Chemotherapy
- Biologic therapy/Immunotherapy
- Targeted therapy
Biotherapy

• The use of agents derived from biologic sources or agents that affect biologic responses

• Mechanisms of action:
  – Enhance the patients own immune response
  – Altering responses of the body to allow cancer to grow
  – Increase vulnerability of cancer cells to the body’s own immune system
  – Prevent metastasis
  – Enhance the repair of normal cells
Immunotherapy

• Therapy that stimulates the immune system as its mechanism of action. (Immunotherapy is a form of biotherapy)

• Actions:
  – Defense against foreign organisms
  – Destruction of worn out cells
  – Identify foreign or non-self cells
Cells of the Immune System

- B cell - Ib+, CD 19+
- Th - CD3+, CD4+
- Tc - CD3+, CD8+
- NK - CD16+, CD56+
- Dendritic cell - CD80+, CD86+, CD40-
- Monocyte - CD45+, CD14-
- Neutrophil - CD45+
Chemotherapy - Goals

- **Cure:** Complete response, > 5 yrs
- **Control:** Extension of life
- **Palliation:** Comfort when cure or control is impossible
- **Adjuvant:** Use of therapy after surgery. Surgery is primary tx.
- **Neoadjuvant:** Use of chemo before surgery.
- **Chemoprevention**
- **Myeloablation**
Cell Cycle

- The cell life cycle is a five-stage reproductive process occurring in both normal and malignant cells.
- Chemotherapy drugs are classified according to pharmacologic action or effect on cell reproduction.
Cell Cycle

- **G0**: Resting Phase
- **G1**: RNA and Protein Synthesis
- **S**: DNA Synthesis
- **G2**: Construction of mitotic apparatus
- **Mitosis**
Pharmacology of Chemotherapy

- Cell cycle specific drugs: exert effect within a specific phase of the cell cycle; greatest potential when given in divided doses or continuous.
- Non-specific drugs: exert effect in all phases of the cell cycle.
Angiogenetic Agents
Administration Schedule

- **Bolus therapy**: Rapid infusion
- **Infusion therapy**: Parenteral therapy that lasts for 30 minutes to 24 hours or longer.
Dosing Schedules

- Milligrams per kilogram (mg/kg) of body weight
- Body surface area (BSA) (milligrams per meter squared [mg/m²])
  - Multiply the amount of drug by the BSA
  - In the case of obese patients, ideal body weight might be recommended
  - In the case of ascities, edema, ideal body weight recommended

AUC-calculation of dosing
Treatment Phase

- **1\textsuperscript{st} line treatment:** no prior treatment has been administered; Protocols may separate out biologics from cytotoxics
- **2\textsuperscript{nd} line treatment:** One prior cytotoxic agent regimen
- **3\textsuperscript{rd} line:** Two prior cytotoxic agent regimens
Safety of Administration

- Handling of medications (oral/IV)
- Handling of bodily fluids (after tx)
- Handling of linen’s after tx
- Disposal of cytotoxic materials
- Spill management
Immediate Complications of Therapy

- **Extravasation**: tissue damage due to drug infiltration (some anecdotes)
- **Hypersensitivity**: flare reaction and anaphylaxis.
Therapy Toxicities

- Most rapidly dividing cells are cells most affected by cytotoxic therapies.
  - Bone Marrow
  - Cells of the gastrointestinal tract (GI) (from mouth to anus)
  - Hair follicles and skin
  - Organs of the reproductive system
Monitoring of Toxicities

- Hematologic (myelosuppression)
  - Neutropenia - WBC, ANC
  - Anemia - RBC, Hgl, Hct
  - Thrombocytopenia - platelets
  - Nadir

- Risks of alterations
Monitoring of Toxicities

• GI and mucousal effects
  – Nausea
  – Vomiting
  – Diarrhea
  – Constipation
  – Mucositis
  – Anorexia
Monitoring Toxicities

- Fatigue
- Alopecia
- Myalgias/Arthralgias
- Cardiac/Pulmonary toxicities
- Nephrotoxicity
- Hepatotoxicity
- Neurotoxicity
- And more............
Staging - Purpose

- To compare/ analyze groups of patients
- Selection of primary and adjuvant therapy
- Estimation of prognosis
- Assistance in evaluation of results of tx
- Facilitates the exchange of information among treatment centers
- Contributes to the continues investigation of human cancer.
Staging - Categories

- TNM system
- T The extent of the primary tumor, size/extent
- N The presence/absence of regional lymph nodes
- M The presence/absence of distant metastasis
TNM Subsets

• cTNM- clinical classification
  – Based on clinical evaluation
  – Based on blood work, scans, exam

• pTNM-pathalogic classification
  – Based on full surgical evaluation
T- Primary Tumor

- Tx- cannot be assessed
- T0-no evidence
- Tis- Carcinoma in situ
- T1, T2, T3, T4- increasing size and location; specific measurements are disease dependent
N-Regional Lymph Nodes

- **Nx**: Regional nodes cannot be assessed
- **N0**: No regional nodes of metastasis
- **N1, N2, N3**: Increasing involvement of regional lymph nodes
M- Distant Metastasis

- **Mx**: Distant metastasis cannot be assessed
- **M0**: No distant metastasis
- **M1**: Distant metastasis
Histologic Grade

- Gx- Grade cannot be assessed
- G1- Well differentiated
- G2- Moderately differentiated
- G3- Poorly differentiated
- G4- Undifferentiated.
Other Descriptors

- **Lymphatic Vessel Invasion (L)**
  - Lx-Cannot be assessed
  - L0- No lymphatic vessel invasion
  - L1- Lymphatic vessel invasion

- **Venous Invasion (V)**
  - Vx-Cannot be assessed
  - V0- No venous invasion
  - V1-Microscopic venous invasion
  - V2- Macroscopic venous invasion
## Colon & Rectum

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Evaluation of Responses

- Complete response (CR)
- Partial response (PR)
- Stable disease (SD)
- Progressive disease (PD)
- Relapse
Evaluation Tools

- History
- Physical Exam
- CT scan
- PET scan
- MRI
- Tumor markers
Tumor Markers

- Prostate: PSA
- Breast:
- Ovarian:
- Melanoma: LDH
Tumor Measurements

- WHO Criteria
- RECIST Criteria
## Phases of Trials

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<th>Phase</th>
<th>Primary Goals</th>
<th>Characteristics</th>
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| I     | •Establish maximum tolerated dose and dosing schedule  
       •Evaluate toxicity  
       •Determine pharmacokinetics | •Relapsed/refractory disease  
       •Small number of patients  
       •Dose escalating cohorts  
       •Variety of tumor types  
       •Pharmacokinetic studies |
| II    | •Determine antitumor activity in specific tumor types  
       •Evaluate toxicity | •Groups of patients with similar tumors  
       •Measurable disease to assess response rates |
| III   | •Establish efficacy by assessing survival, time to progression  
       •Obtain quality of life data | •Randomization between experimental treatment and standard treatment and/or control groups  
       •Large number of patients |
| IV    | •Expand “off-label” use  
       •Further assess toxicity | •Postmarketing trials of commercially available drugs. |
Attribution of Toxicities

- What is expected?
- What is our experience?
- Interactions?
- Reactions?
- Possible effect?
- Probable effect?
- Definite effect?