Current State of Oncology Care

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April 6, 2017  
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Where I am privileged to be located

Side view with Terrace
The Past - Still Current

• Diagnostics
  — Breast: from 2-D to 3-D, Screening Debate
  — Colon: Colonoscopy remains gold standard
  — Prostate: “Watch and Wait”
  — Lung: Low dose CT Screening - Access

Surgical

Shift towards increasing specialization:

- General Surgeon
- Surgical Oncologist
- Organ Site Specialist (GYN, Colo-Rectal, Breast, Hepatobiliary, Thoracic)
- Genomics: genetic mapping and DNA sequencing of sets of genes

Considerations Before Surgery

• Genomics: genetic mapping and DNA sequencing of sets of genes
• Proteomics: structure, function, and interactions of the proteins produced by the genes
Breast Exams Have Changed

Treatments for Cancer

• Chemotherapy - Higher Doses with Fewer Side Effects. Not universally selective.
• Hormonal Therapy
• Antibody Therapy to Boost the Immune System: “mab’s: Monoclonal AntiBody”
  • Monoclonal antibodies are laboratory-produced molecules engineered to serve as substitute antibodies that can restore, enhance or mimic the immune system’s attack on cancer cells

Privacy Expectations
Public Spaces in Treatment

Just Get Away

Move Away From Hospitals
“Environment Counts”
Expectations of Patients and Staff

Treatments for Cancer

- **Radiation therapy** – Increase precision has meant increase in Dosages:
  - Accelerated Breast
  - Stereotactic Radiosurgery
  - Stereotactic Radiotherapy
  - High Dose Radiotherapy (HDR)

Much More than a “Radiation” Machine
Treatments for Cancer

Radio-immunotherapy

- MAB’s can be engineered as a delivery vehicle for other treatments. Example: attaching a small radioactive particle to transports the radiation treatment directly to cancer cells minimizing the effect of radiation on healthy cells.

Treatments for Cancer

Immunotherapy

- Training your immune system to recognize cancer cells. Immunotherapy uses your immune system to kill cancer cells. Sipuleucel-T (provenge), a form of immunotherapy, has been developed to genetically engineer your immune cells to fight prostate cancer.

Treatments for Cancer

Infused Targeted Radiation

Example: radium-223 (Xofigo)
- Targets fast-growing prostate cancer cells in the bones
- Used to relieve bone pain.
Terminology

- The “-mab” family is used when receptor targets are overexpressed on the outside of cancer cells.
- The sub-stem of the generic names of the “-mabs” identifies the source where the antibodies were generated or cloned:

...MAB Family

- Chimeric antibody (mixed species) = substituting the mouse Fc region of the antibody with that from human—drugs ending in “-ximab” (i.e., rituximab, infliximab)
- Humanized mouse—drugs ending in “-zumab” (i.e., bevacizumab)
- Fully human—drugs ending in “-mumab” (i.e., ipilimumab).

...mab family- continued

- Humanized mouse—drugs ending in “-zumab” (i.e., bevacizumab)
- an antibody is developed to have the desired properties in a mouse (or other non-human), the DNA coding for that antibody can be isolated, cloned into a vector and sequenced.
- a strategy can be devised for inserting these sequences appropriately into a construct containing the DNA for a human antibody variant.
Use of bacteria to Humanize antibodies

- creation of antibody gene “libraries” which can be wholly derived from human RNA isolated from peripheral blood. The immediate products of these systems are antibody fragments created by the “phage display”.
- Example: Adalimumab (Humira)

the “-ib” family

- targets processes within the cell and therefore must be small enough in molecular weight to enter the cell and interfere with proteins on both the inside and outside of the cell.
- Proteins that code for growth or inhibit growth are some of the targets of these small but powerful family of drugs.

the “-ib” family

- Tyrosine kinase inhibition—sub stem “-tinib” (i.e., imatinib)
- Proteasome inhibition—“-zomib” (i.e., bortezomib)
- Clyclin-dependent kinase inhibition—“-ciclib” (i.e., seliciclib)
Newer Supportive Treatments
-Photopheresis-

Palliative Care (Supportive Care)

Supportive Treatments
Lymphedema Management
We are more alike than Different Rheumatology

Treat the whole person before and after Surgery (or Medically)- BLOOD MANAGEMENT

Children’s and Young Adult Clinic

4 Clinical Trials = Young Adults have been left behind on the survival advances

Movement nationwide to treat using pediatric protocols.
Children’s and Young Adult Clinic

Children Involved in Design

Open feel for Teens
Variety of Ages

Targeted Therapies – New and Research Driven

• Targeted therapies look at molecular alterations and seek to address ONE Variant.

• Alphabet Soup of Molecular Alterations:

Normal DNA Gene Sequencing
Abnormal DNA Gene Sequencing

TCG\_TGA
TCGA\_TGA
TCGG\_TGA
TCGGGG\_TGA

normal DNA
SNV - Single Nucleotide Mutation
INSertion
Deletion
Indel – deletion and insertion
Duplication

Increasing complexity

Big Question

• What is the functional impact on the protein caused by these molecular variations?

Depends........

VUS – Variant of Uncertain (Unknown) Significance

Targeting Agents

• BRAF V600E – Votrient (pazopanib)
• EGFR R521K – EGFR inhibitors
• JAK3 activating mutations – Jakafi (ruxolitinib)
  * Caution as does not work for JAK 3 mutation

Comfort level of interpretation increasingly an issue
Example of How Used

- **microsatellite instability**: A change that occurs in the DNA of cells in which the number of repeats of microsatellites (short, repeated sequences of DNA) is different than the number of repeats that was in the DNA when it was inherited. The cause of microsatellite instability may be a defect in the ability to repair mistakes made when DNA is copied in the cell.

MSI Used in Colorectal Cancer

- MSI – H tumors harbor genetic variations that are potentially recognizable by the immune system creating an inflamed environment with high expression of immune checkpoints such as PDL-1 (Programmed Death)
- PDL-1 Receptors = suppress ability of T-Cells to work at killing cancer cells
- Pembralizumab was 1st PDL-1 blockade agent
- Nivolumab (Obdivo) – lung, melanoma, renal, Hodgkins, H&N, Bladder

Tumor genetics rather than patient genetics
Sample Analysis prior to research

Hematology as well as Solid Tumors

Environment is Important
How Patients Look is Important

Thank You