PERSONALIZED MEDICINE

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Director of Research
Carevive Systems, Inc™
Objectives

- Guide patients through the path of personalized medicine, including genetic testing and immunotherapies

- Identify the unique side effects that can affect the patient’s experience with personalized cancer therapies in order to prepare proper interventions and management.
The Path to Personalized Medicine and Beyond

- 1990s – Molecularly targeted therapies terminology was used to discuss agents designed to work at the molecular level
  - Rituximab
  - Trastuzumab

- 2003 – Human genome sequenced

- Personalized medicine – treatment personalized to the individual characteristics of each patient
  - Tumor histology
  - Tumor genetics
  - Tumor proteomics
  - No longer one size fits all
Precision Medicine

Identification of actionable mutations and agents that target the mutation pathway
Case Study 1

- 2002 Monthly education and support group for patients with lung cancer
  - Four patients recently diagnosed with Stage IV NSCLC
  - Each being treated with platinum doublet chemotherapy, either cisplatin or carboplatin with paclitxel.
  - Mary is able to provide information and education that is applicable to all in the group
  - All of the patients agree it is reassuring that they are getting the same treatment for the same disease

- 2017 Monthly education and support group
  - Four patients recently diagnosed with Stage IV NSCLC
  - Each patient is receiving a different treatment, some patients are receiving oral drugs and others receiving intravenous
  - Mary must explain that we have learned much in recent years about the differences within the diagnosis of NSCLC and now we have specific treatments for the different types of NSCLC
How are Targeted Therapies different than Cytotoxic Chemotherapy?

Different mechanisms of action, administration, and toxicity profiles
Standard of Care

- Actionable mutations
  - Function and testing
  - Patient characteristics likely to be positive
  - Is the marker prognostic, predictive or both

- Molecular testing in standard for many cancers. NCCN guidelines for
  - Lung
  - Breast
  - Colorectal
  - Myeloma
  - Leukemia
Tissue Collection, Processing, and Analysis

- Where was tissue obtained?
  - Your institution
  - Community
- Is there enough tissue for diagnosis and molecular testing?
- When will results be available?
- Who gets (and communicates) results?
Actionable mutations

- Colon cancer
  - KRAS
- Breast
  - HER2
  - ER/RH
- NSCLC
  - EGFR
  - ALK (anaplastic lymphoma kinase)
- Malignant melanoma
  - BRAF
Types of Targeted Therapies

http://www.cancer.gov/cancertopics/understandingcancer/targetedtherapies
Drugs are designed to attach and interfere with specific pathways.
# Small Molecule Targeted Therapies: Oral Agents

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<thead>
<tr>
<th>Name Suffix</th>
<th>Target</th>
<th>Examples</th>
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<tbody>
<tr>
<td>nibs (tinibs)</td>
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<td>erlotinib, sunitinib, ponatinib, imatinib, dasatinib, ibrutinib</td>
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<td>nibs (rafenibs, metanib)</td>
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Care Issues

- Adherence
- Possible drug/food, drug/drug response
- Education regarding taking medication correctly
- Symptom management
## Small Molecule Targeted Therapies: IV, Subq or oral

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<td>Proteozome inhibitors</td>
<td>bortezomib, carfilzomib, ixazomib</td>
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<tr>
<td>inostat (IV or oral)</td>
<td>Histone deacetylase inhibitors (HDAC)</td>
<td>vorinostat, belinostat, panobinostat</td>
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<tr>
<td>toclax</td>
<td>BCL-2 inhibitors</td>
<td>venetoclax</td>
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Once potential targets are identified, then drugs are designed to best attack the target

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Monoclonal Antibody Naming Conventions

- Prefix
- Infix
  - Target/Disease Class
  - Source
- Suffix
  - Monoclonal antibody = mab
What does the name mean?

Target/Disease Class Infix

- **Trastuzumab**
  - Infix: *tu/t = tumor*
  - Example: -tuzumab/-tumab/-tomab

- **Bevacizumab**
  - Infix: *ci/c = circulatory*
  - Example: -cixumab/-cumab

- **Ipilimumab**
  - Infix: *li/l = immunomodulator*
  - Example: -liximab/-lumab/-lixizumab

Source Infix

- **Tositumomab and iodine 131**
  - *mo = mouse*

- **Rituximab**
  - *xi = chimeric or cross between mouse and human*

- **Trastuzumab, bevacizumab**
  - *zu = humanized*

- **Panitumumab**
  - *u = fully human*
Enhancing the Immune Response

http://www.cancer.gov/cancertopics/understandingcancer/targetedtherapies
Checkpoint Inhibitors

Targets receptors that promote t-cell proliferation to allow the immune system to recognize tumor antigens

- **CTLA-4**: cytotoxic T-lymphocyte-associated antigen-4
  - Ipilimumab (Yervoy)

- **PD-1**: programmed cell death protein
  - Nivolumab (Opdivo)
  - Pembrolizumab (Keytruda)

- **PD-L1**: programmed cell death protein ligand 1
  - Atezolizumab (Tecentriq)
Blocking CTLA-4

B7-1/B7-2 binds to CTLA-4 and inhibits T cell killing of tumor cell

Blocking B7-1/B7-2 or CTLA-4 allows T cell killing of tumor cell
Blocking PD-1 and PD-L1

PD-L1 binds to PD-1 and inhibits T cell killing of tumor cell

Blocking PD-L1 or PD-1 allows T cell killing of tumor cell
Potentially Serious/Life-threatening Immune Related Adverse Events (irAEs)

- GI (diarrhea > colitis)
- Pulmonary (pneumonitis/interstitial lung disease [ILD])
- Endocrine (thyroid, adrenal, pituitary)
- Liver (hepatitis)
- Kidney (nephritis)
- Eye (uveitis)
- Skin
References

- http://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm279174.htm
- http://www.mycancergenome.org


