Oral Anti-Neoplastics: History
Background

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February 2015
A BRIEF & VERY INCOMPLETE HISTORY OF THE DEVELOPMENT OF ANTI-CANCER MEDICATIONS
History of Anti Cancer Medications Including Orally Available Therapy

- 1890’s: Beatson Discovers that Estrogen Ablation Shrinks Breast Tumors
- 1930’s: Nitrogen Mustard (An Alkylating Agent) Shrinks Lymphomas
- 1940’s: Anti-folates Cause Regression of Pediatric Leukemia
- 1940’s: DES (estrogen) used to Treat Advanced Prostate Cancer
- 1950’s: Oral Anti-folate, Methotrexate, Used in Cancer Therapy
History of Anti Cancer Medications Including Orally Available Therapy

• 1950’s: Multiple Oral Alkylating Agents Become Available (Cyclophosphamide, Melphalan & Chlorambucil)
• 1950’s: Oral Purine Antagonists (6MP) Introduced
• 1950’s & 1960’s: Multiple Classes of IV Anti-neoplastic Introduced: Vinca Alkaloids, Anti-neoplastic Antibiotics, and Platinum Analogues
• 1960’s & 1970’s: Oral Androgens and Progestins Used to Treat Metastatic Breast Cancer
History of Anti Cancer Medications Including Orally Available Therapy

• 1970’s & 1980’s: Taxol (Paclitaxel) Approved to be Administered IV & Etoposide Approved to Be Administered IV & PO
• 1970’s & 1980’s: Anastrozole, Exemestane and Tamoxifen Approved as Oral Hormonal Therapy for Breast Cancer
• 1990’s: Rituximab Approved to Be Administered IV and Imatinib, an Oral Agent, Approved to be Administered P.O.
• This Ushers in the ERA of “Targeted Cancer Therapy”
• 1990”s: Capecitabine, an Oral Form of 5FU, Approved
History of Anti Cancer Medications Including Orally Available Therapy

• A Partial List of the Oral Anti-Neoplastic Medications Approved 2000 – 2009 { 12 Agents}
  – Thalidomide
  – Lenalidomide
  – Erlotinib
  – Lapatinib
  – Sunitinib
  – Sorafenib
  – Pazopanib
  – Nilotinib
  – Dasatinib
  – Raloxifene
  – Eltrombopag
  – Everolimus
History of Anti Cancer Medications Including Orally Available Therapy

- A Partial List of the Oral Anti-Neoplastic Medications Approved 2010 – 2014 (5 Years) {20 Agents}:
  - Vandetanib
  - Vemurafenib
  - Crizotinib
  - Deferiprone
  - Ruxolitinib
  - Axitinib
  - Enzalutamide
  - Aberaterone
  - Bosutinib
  - Regorafenib
  - Cabozatinib
  - Ponatinib
  - Pomalidomide
  - Trametinib
  - Dabrafenib
  - Afatinib
  - Ibrutinib
  - Idelablesib
  - Ceritinib
  - Olaparib
# Table of the Approximate Number of Oral Anti-Neoplastic Agents Available to Oncologist per Decade

<table>
<thead>
<tr>
<th>Decades</th>
<th>Number of Oral Agents Added per Decade</th>
<th>Number of Oral Agents Available to Oncologist per Decade</th>
</tr>
</thead>
<tbody>
<tr>
<td>1950</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>1960</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>1970</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>1980</td>
<td>3</td>
<td>11</td>
</tr>
<tr>
<td>1990</td>
<td>2</td>
<td>13</td>
</tr>
<tr>
<td>2000</td>
<td>12</td>
<td>25</td>
</tr>
<tr>
<td>2010</td>
<td>40*</td>
<td>65*</td>
</tr>
<tr>
<td>*</td>
<td>Adjusted to Decade</td>
<td></td>
</tr>
</tbody>
</table>
A Semi-Quantitative Graph of the Number of Oral Anti-Neoplastic Agents Available to Oncologist per Decade

- **Total Number of New Oral Agents Available**
- **Number of New Oral Agents Added Per Decade**
Common Misconceptions About Oral Anti-Neoplastic Drugs

• Patients Prefer Them; NO:
  – These Drugs are Complicated to Administer
  – These Drugs are Complicated to Take
  – They are Expensive

• They have Fewer Side Effects; NO:
  – See the Subsequent Slide

• They are Easier for Patients than IV Chemo; NO:
  – The Patient Receiving IV Chemotherapy Can Be a Passive Recipient of Treatment with No Responsibilities About When & How to Take the Medication
  – The Patient on Oral Anti-neoplastic Drugs Must Actively Participate in the Administration and Monitoring of these Medications

• The Cost of Oral Anti-neoplastic Drugs is Offset by Less Staff & Facility Resources; NO:
  – Currently Providers and Facilities are Not Reimbursed for Helping Patients Obtain and Manage These Complex Drugs
  – As the Number & Complexity of These Drugs Increases, the Reimbursement System Will Need to Change to Support this Type of Cancer Treatment
### Representative Costs of Oral Anti-neoplastic Drugs Per Decade

<table>
<thead>
<tr>
<th>Drug &amp; Decade Drug Introduced</th>
<th>Est. Cost for a 30 Day Supply @ Average Dose @ Today’s Prices</th>
<th>20% Co-Pay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytoxan 1950’s</td>
<td>$100</td>
<td>$20</td>
</tr>
<tr>
<td>Megace 1960’s</td>
<td>$25</td>
<td>$5</td>
</tr>
<tr>
<td>Etoposide (VP 16) 1970’s</td>
<td>$3,000</td>
<td>$600</td>
</tr>
<tr>
<td>Anastrozole 1980’s</td>
<td>$100</td>
<td>$20</td>
</tr>
<tr>
<td>Imatinib (Gleevec) 1990’s</td>
<td>$8,500</td>
<td>$1,700</td>
</tr>
<tr>
<td>Thalidomide 2000’s</td>
<td>$8,500</td>
<td>$1,700</td>
</tr>
<tr>
<td>Dasatinib (Sprycel) 2000’s</td>
<td>$10,000</td>
<td>$2,000</td>
</tr>
<tr>
<td>Sorafenib (Nexavar) 2000’s</td>
<td>$3,000</td>
<td>$600</td>
</tr>
<tr>
<td>Crizotinib (Xalkori) 2010’s</td>
<td>$3,000</td>
<td>$600</td>
</tr>
<tr>
<td>Vemurafenib (Zelboraf) 2010’s</td>
<td>$5,600</td>
<td>$1,120</td>
</tr>
<tr>
<td>Aberaterone (Zytiga) 2010’s</td>
<td>$3,000</td>
<td>$600</td>
</tr>
</tbody>
</table>

• Results of Study:
  1. Mean OOP Cost per Month for Medicare Patients:
     • Anastrozole $88.80
     • Erlotinib $850.50
     • Thalidomide $1,124.10
  2. The Percentage of Medicare Patients Who Delayed or Discontinues Rx was:
     • Anastrozole 58%
     • Erlotinib 61%
     • Thalidomide 70%
  3. For Each $10 Increase in OOP Cost the Likelihood of Rx Delay or Discontinuation Increased:
     • Anastrozole N/S
     • Erlotinib 14%
     • Thalidomide 20%
### Not Only Oral Anti-neoplastic Drugs Expensive, They are Toxic: Common Side Effects

<table>
<thead>
<tr>
<th>Drug</th>
<th>Fatigue</th>
<th>Nausea &amp; Vomiting</th>
<th>Bone Marrow Suppression</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytoxan</td>
<td>✓</td>
<td>✓✓✓</td>
<td>✓✓</td>
<td></td>
</tr>
<tr>
<td>Megace</td>
<td>✓</td>
<td></td>
<td></td>
<td>Weight Gain</td>
</tr>
<tr>
<td>VP 16</td>
<td>✓</td>
<td>✓✓</td>
<td>✓✓</td>
<td></td>
</tr>
<tr>
<td>Anastrozole</td>
<td>✓</td>
<td></td>
<td></td>
<td>Joint Pain</td>
</tr>
<tr>
<td>Gleevec</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>Diarrhea, Fluid Retention &amp; Shortness of Breath</td>
</tr>
<tr>
<td>Thalidomide</td>
<td>✓✓</td>
<td></td>
<td>✓</td>
<td>Constipation</td>
</tr>
<tr>
<td>Dasatinib</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>Diarrhea &amp; Fluid Retention</td>
</tr>
<tr>
<td>Sorafenib</td>
<td>✓✓</td>
<td>✓</td>
<td>✓</td>
<td>Rash &amp; Hypertension</td>
</tr>
<tr>
<td>Xalkori</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>Shortness of Breath; Heart Problems</td>
</tr>
<tr>
<td>Jakafi</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>Dizziness and Fluid Retention</td>
</tr>
<tr>
<td>Zytiga</td>
<td>✓</td>
<td></td>
<td></td>
<td>Fluid Retention &amp; Heart Problems</td>
</tr>
</tbody>
</table>
Oral Anti-Neoplastic Require Careful Monitoring & Management by the Patient and the Provider

• NCCN Recommendations and Guidelines for Oral Anti-Neoplastics  
  – Patient Selection
    • Intellectual Skills
    • Social Support
    • Physical Capacity to Take Rx
    • Economic Resources
  – Monitoring that the Provider Has Administered:
    • The Right Drug
    • To the Right Patient
    • At the Right Dose
    • With Proper Follow-up
  – Monitoring Adherence
    • What Mechanisms are in Place to Assure Adherence?
Oral Anti-Neoplastic Require Careful Monitoring & Management by the Patient and the Provider

• NCCN Recommendations and Guidelines for Oral Anti-Neoplastics
  — Monitoring Side Effects
    • Has the Patient Been Educated About How to Manage Side Effects?
    • Has the Patient Been Educated About When to Call the Provider?
    • Has the Patient Been Educated About What is a Medical Emergency?
  — On Going Counseling Re Dosage Adjusts
    • What Mechanisms are in Place to Assure Patients Understand if a New Drug Dosage is Required and How Comply with that Change?
  — Proper Provider Follow-Up Needed
  — Proper Biohazard Management Needed
National Professional Societies Have Created Minimum Standards for the Safe and Effective Administration of Oral Chemotherapy: It’s Complicated & Resource Intensive

• ASCO/ONS Chemotherapy Administration Safety Standards 2013*
  – Staffing Standards Supported by Appropriate Policies, Procedures, Training & CME
  – Qualified Providers
  – Chemotherapy Planning that is Consistent with:
    • the Patient’s Pathological Diagnosis
    • Their Stage
    • Performance Status
    • Updated Medical History & Physical
    • Assessment of the Ability of the Patient to Adhere to Rx
  – Standard Regimens Used According to Standard Guidelines, Pathways, Literature or Compendia References
  – Informed Consent Obtained Along with Patient Education
  – Financial & Psychosocial Support Available to Patient and Family
  – Proper Monitoring is in Place to Ascertain Response and Manage Toxicities
  – Protocol Adherence is Monitored & Support Given as Needed

* Neuss, MN et.al.: 2013 Updated ASCO/ONS Chemotherapy Safety Standards Including Standards of the Safe Administration and management of Oral Chemotherapy. JOP 2S; 5s – 13s, 2013
Oral Anti-neoplastic

- They are Complicated to Give
- They are Complicated to Take
- They are Expensive
- As a Society We Do Not have the Proper Financial, Psychosocial or Medical Systems in Place to Assure Safe Access to the Medications
National Effort to Bring Parity Between Oral and IV Anti-cancer Medications

- Established law in 34 states and District of Columbia
- Limits patient out-of-pocket costs for oral anti-cancer medications
- Parity laws typically feature one of two possible solutions:
  - Cost-share for an oral will be “no less favorable” than the cost-share for a IV/injected treatment
  - Cost-share for an oral will be capped at an amount stipulated in the law—e.g. $100.
Efforts in New Hampshire

• SB 137 submitted by Senate Majority Leader Bradley
  • [http://www.gencourt.state.nh.us/legislation/2015/SB0137.html](http://www.gencourt.state.nh.us/legislation/2015/SB0137.html)

• Broad coalition of Medical professionals and public health organizations.

• How can I get involved?
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  • mike.rollo@cancer.org