Chemotherapy 2.0
Dispensing Oral Chemotherapy

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Objectives

- Discuss emergence of oral therapies for cancer treatment
- Discuss benefits and risks of oral chemotherapy
- Understand various considerations for dispensing and handling oral chemotherapy
- Review the benefits of having dedicated pharmacist monitoring
- Understand barriers related to costs and paying for oral chemotherapy
Emergence of Oral Chemotherapy

- Oral Chemotherapies have been available for decades
  - Chlorambucil, MTX, 6-MP, cyclophosphamide
- New era started with approval of Xeloda in 1998
- Last 6 years have seen an explosion in development
- 25 Million doses annually
- One–Fourth of all new cancer agents are oral
  - Currently 5% of all antineoplastics

1953-1997: 17 Oral Chemo Agents
1998- Present: 26 New Agents

1953-6: 6-MP & MTX
1954: Busulfan
1957: Chlorambucil
1959: Cyclophosphamide
1961: Melphalan
1966: Thioguanine
1967: Hydrea
1969: Procarbazine
1970: Mitotane
1976: Lomustine
1977: Tamoxifen
1986: Etoposide
1989: Eulexin
1995: Casodex
1996: Nilandron
1997: Femara
1998: Xeloda & Thalidomide
1999: Aromasin, Temodar, Targetin
2000: Gleevec
2003: Iressa
2004: Tarceva, Vesanoid
2005: Nexavar & Revlimid
2007: Hycamtin, Tasigna & Tykerb
2009: Afinitor & Votrient
2011: Jakafi, Caprelsa, Xalkori, Zelboraf & Zytiga

1953-1997: 17 Oral Chemo Agents
1998- Present: 26 New Agents
Trends in Oral Chemo Prescribing

Figure 1: Proportion of Total Pharmacy Benefit Spending for Oral Chemotherapy Drugs

Thalidomide is excluded from these data since the drug was not approved for a cancer indication until May 26, 2006; summary data for claims with dates of service from January 1, 2002, through May 31, 2006, for more than 2,000 small, self-insured employers.
What are the benefits of Oral Chemotherapy?

A) Better Convenience
B) Cheaper Cost
C) Better Insurance Coverage
D) Better Adherence
E) I don’t have to handle it
Benefits of Oral Chemo

- CONVENIENCE!!!
  - Mostly for the patient, of course
  - Preference provided efficacy is not compromised
- Less interruption of day to day life
Risks of Oral Chemotherapy

- Adherence/Compliance
- Work Flow
- Accessibility
- Food & Drug Interactions
- Side-Effects
  - Can be severe, not observed in clinic
- Perceived Lack of Efficacy
- Costs
Factors Influencing Adherence

Disease Factors
- Disease Type & Stage, Side-Effects of Disease, Medications Required to Treat

Patient Factors
- Age, Race, Education, Income Level, Depression, Belief about Medications, Health Literacy, Social Support

Med Factors
- Pill Size, Pill Number, How to Take, DDIs, ADRs, Costs

System Factors
- Relationship with providers, System Processes, Monitoring, Costs

Adherence
Risks of Oral Chemotherapy

Accessibility
- Insurance frequently requires prior auth, inhibiting ease of access
- Outpatient pharmacies don’t stock these regularly
- Many require specialty pharmacy licenses to dispense
- Most pharmacies require pts to pay before obtaining medication
Pros/Cons of Mail Order Programs

Pros
- May provide better contract prices based on mass purchasing
  - Rarely if ever passed on to patient
- Good for practices without direct involvement

Cons
- Contact not as direct as on-site programs
- Don’t know the patients as well
- Can’t control dispensing as tightly
- On site programs can provide this and more!
Changes in work flow
- Moves patients out of infusion centers
- Decreases income if scripts are sent to outside pharmacies
  - A lot of unreimbursed staff time
    - Education
    - Co-pay & patient assistance
- Complex reimbursement strategies
- Difficulty in ensuring adherence

Hede K. JNCI. 2009;101(22): 1534-36
Rx Written for Oral Chemotherapy (MD/RN)

**Pharmacist**: Check labs, Drug Interactions, Patient Education

**Outpatient Pharmacy**: Benefits Investigation

**Pharmacist**: Prior Authorization

- Coordinate with Outpatient Pharmacy
- Medication Filled and Sent to Patient
- Patient Follow-up for Side Effects

**Patient Advocate**: Copay Assistance Programs

**Social Worker**: Free Medication Programs

- Return Patient Without Dose Change: Monthly Follow-up
- New Patient or Dose Change: Weekly Follow-up

**Physician**: Follow-up for Drug Efficacy

**Patient Advocate**: Copay Assistance Programs

**Social Worker**: Free Medication Programs

- Return Patient Without Dose Change: Monthly Follow-up
- New Patient or Dose Change: Weekly Follow-up

**Physician**: Follow-up for Drug Efficacy
Trends in Oral Chemo Prescribing

Based on Current Trends
- Now: 7 new, 23 refills per week
- In 2 years: 14 new, 128 refills per week

Zytiga as an example
- 6 prescriptions first day it was available
- 21 new patients in first month
- If 25% of newly approved drugs are oral, what is likely to happen?
Pharmacy Considerations

- Are these meds routinely stocked?
- Can your pharmacy dispense these medications?
  - Specialty Pharmacy license required
  - Ex. Tasigna, Revlimid, Thalomid
- Insurance requirements
  - Most require prior authorizations
  - Exorbitant co-pays
  - What do you tell patients about this?
- Some require refrigeration
  - Ex. Etoposide, Melphlan, etc
Inpatient vs. Outpatient Considerations

- Should inpatient and outpatient formulary be the same?
  - Consider regulatory requirements
  - Consider what really needs to be “stat”
  - Consider likelihood of inpatient reimbursement

- Dispensing
  - Whole bottles vs individual pills
  - Who can administer
OC Handling

- Should be handled like chemotherapy
  - Counting trays should be used ONLY for these agents
  - Clean trays with bleach or alcohol mixture between each different agent
  - Use PPE to avoid direct contact
- Pregnant staff should avoid handling if possible
- Always double count
Sites should have policy on take back or disposal
- Dispose of in chemotherapy waste on site*
- Dispose of the same way your site disposes of other NIOSH hazardous medications

Educate patients on proper disposal
- Can they bring it back?
- How to dispose at home

Disposal Resources

- FDA Disposal Handouts
  - “How to Dispose of Unused Medicines”
    - [http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm101653.htm](http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm101653.htm)

- Drug Take-Back Programs
  - Check with local authorities for dates

- Manufacturer programs
  - Lenalidomide, Thalidomide
Benefits of Pharmacist Monitoring

- Pharmacist Interventions
  - Drug Interactions
  - Dose adjustments for renal/hepatic function
  - Protocol implementation (nausea, supportive care, etc)
  - Education
  - Lab monitoring

- Reduction in Non-fulfillment
  - <1% of patients unable to obtain meds due to cost

Pharmacists Interventions

- First 700 patients evaluated at MSTI
  - 82 drug–interactions found in 73 patients
    - 41% changed concomitant therapy
    - 50% required more frequent monitoring (i.e. warfarin)
    - 9% didn’t change (deemed insignificant)
  - 24 dose adjustments for renal/hepatic function
    - 92% accepted
  - 34 other documented interventions
    - 11 anti–emetic protocol needed
    - 5 dose or cycle corrections
    - 11 labs requested (not previously ordered)
    - 4 supportive care medications
    - 3 referrals to other disciplines (cardiology, psych, etc)
## Food & Drug Interactions

<table>
<thead>
<tr>
<th>Oral Oncologic</th>
<th>Drug Interactions</th>
<th>Food Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abiraterone</td>
<td>CYP2D6 substrates &amp; CYP3A4 inhibitors and inducers</td>
<td>Must be taken on empty stomach, high fat meals can increase exposure 10-fold.</td>
</tr>
<tr>
<td>Capecitabine</td>
<td>Phenytoin &amp; warfarin</td>
<td>Must be taken with food to reduce side-effect profile.</td>
</tr>
<tr>
<td>Dasatinib</td>
<td>Requires acidic environment, must evaluate patients on acid suppressors</td>
<td>May be taken with or without food. Interacts with grapefruit juice.</td>
</tr>
<tr>
<td>Erlotinib</td>
<td>Warfarin, Acid-Suppressors, CYP3A4 substrates</td>
<td>Must be taken on empty stomach to avoid polyvalent cations from binding medication and reducing absorption.</td>
</tr>
<tr>
<td>Imatinib</td>
<td>Potent inhibitor of CYP3A4, CYP2C19, CYP2D6</td>
<td>Must be administered with food to reduce GI irritation.</td>
</tr>
<tr>
<td>Lapatinib</td>
<td>Substrate of CYP3A4, caution with use of other agents that inhibit or induce</td>
<td>Must be taken on an empty stomach. Interacts with grapefruit juice.</td>
</tr>
<tr>
<td>Nilotinib</td>
<td>Substrate of CYP3A4, caution with use of other agents that inhibit or induce. Requires acidic environment, must evaluate patients on acid suppressors</td>
<td>Must be taken on empty stomach.</td>
</tr>
<tr>
<td>Sorafenib</td>
<td>Substrate for CYP3A4, inhibitor of CYP2C9</td>
<td>Must be taken on empty stomach.</td>
</tr>
<tr>
<td>Temozolomide</td>
<td>Valproic acid can increase systemic levels of temozolomide</td>
<td>Administer on empty stomach or at bedtime to reduce nausea and vomiting.</td>
</tr>
</tbody>
</table>
Benefits of Pharmacist Monitoring

- Cost Savings
  - Rounding to pill sizes
  - Controlled dispensing of quantities
  - On-site dispensing savings
    - Reduces dispensing of discontinued treatments
    - Saves patient a co-pay
    - Saves insurance cost of the medication
  - Financial Assistance/Free Drug Programs
Which is the most expensive Oral Chemotherapy Agent?

A) Capecitabine (Xeloda®)
B) Erlotinib (Tarceva®)
C) Imatinib (Gleevec®)
D) Lenalidomide (Revlimid®)
E) Dineromide (Expenceva®)
Risks of Oral Chemotherapy

FIGURE 6
Average Charge per 30-Day Supply* in 2006 and Distribution of Spending for the High-Cost Oral Chemotherapy Drugs for Small Self-Insured Employers

<table>
<thead>
<tr>
<th>Drug</th>
<th>Charge per 30-Day Supply</th>
<th>% Total Spending for Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lenalidomide</td>
<td>$7,083</td>
<td>39.6%</td>
</tr>
<tr>
<td>Sunitinib</td>
<td>$6,896</td>
<td>18.1%</td>
</tr>
<tr>
<td>Sorafenib</td>
<td>$4,646</td>
<td>14.2%</td>
</tr>
<tr>
<td>Imatinib</td>
<td>$3,015</td>
<td>8.6%</td>
</tr>
<tr>
<td>Erlotinib</td>
<td>$2,664</td>
<td>7.7%</td>
</tr>
<tr>
<td>Capecitabine</td>
<td>$2,277</td>
<td>6.9%</td>
</tr>
</tbody>
</table>

Allowed charge is discount pricing, comprising allowed ingredient cost and pharmacist professional fee, before subtraction of member cost share, for claims with dates of service in 2006 through May 31; from a PBM database for more than 2,000 small, self-insured employers. PBM=pharmacy benefits manager.
# Average Wholesale Prices

<table>
<thead>
<tr>
<th>Medication</th>
<th>Pill Size</th>
<th>Avg Monthly Cost</th>
<th>Avg #Number of pills/month</th>
<th>Cost/pill</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nexavar®</td>
<td>200mg</td>
<td>$9,552.78</td>
<td>120</td>
<td>$79.61</td>
</tr>
<tr>
<td>Revlimid®</td>
<td>25mg</td>
<td>$8,991.78</td>
<td>21</td>
<td>$428.18</td>
</tr>
<tr>
<td>Sutent® (28on/14off)</td>
<td>50mg</td>
<td>$6,245.87*</td>
<td>28</td>
<td>$334.60</td>
</tr>
<tr>
<td>Tarceva®</td>
<td>150mg</td>
<td>$4,648.98</td>
<td>30</td>
<td>$154.97</td>
</tr>
<tr>
<td>Tykerb®</td>
<td>250mg</td>
<td>$3,989.84</td>
<td>150</td>
<td>$26.60</td>
</tr>
<tr>
<td>Xeloda® (14on/7off)</td>
<td>500 mg</td>
<td>$3,069.92</td>
<td>84</td>
<td>$27.41</td>
</tr>
</tbody>
</table>

*Sutent 28 pills = 6 weeks supply = $9,368.80*
Risks of Oral Chemotherapy

- Costs
  - Some covered under major medical
  - Some covered only under prescription insurance
    - Medicare Part D “Donut Hole”
  - Exorbitant co-pays
  - Lack of coverage
  - Two pills = two co-pays

Risks of Oral Chemotherapy

- Insurance Coverage– Medicare Part B
  - Per Center for Medicaid Services ([www.cms.gov](http://www.cms.gov)):
    - “Oral Anti–Cancer Drugs. Drugs taken orally during cancer chemotherapy provided they have the same active ingredients and are used for the same indications as chemotherapy drugs that would be covered if they were not self-administered and were administered as incident to a physician’s professional service.”
    - Capecitabine (Xeloda®)
    - Cyclophosphamide (Cytoxan®)
    - Methotrexate (Rheumatrex®)
    - Temozolomide (Temodar®)
    - Busulfan (Myleran®)
    - Etoposide (VePesid®)
    - Melphalan (Alkeran®)
  - Often still have to pay 20% of the cost!
Cost Savings

- Collaboration with Financial Advocates
  - Over $1 million in free drug obtained for patients
  - >$200,000 in co-pay assistance funds

- On-Site Dispensing
  - Patients seen on day 1 (or shortly before) of each cycle
  - 6 month evaluation of dispensing
    - 37 patients discontinued on start date of next cycle
    - Drug savings $103,567.33 (based on AWP)
    - Co-pay savings to patients: $13,850

# Free Drug

## Table 1

<table>
<thead>
<tr>
<th>Free Drug</th>
<th>Number of Patients</th>
<th>Total Cost Savings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sorafenib (Nexavar&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>5</td>
<td>$85,705</td>
</tr>
<tr>
<td>Lenalidomide (Revlimid&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>4</td>
<td>$153,903</td>
</tr>
<tr>
<td>Sunitinib (Sutent&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>11</td>
<td>$382,367</td>
</tr>
<tr>
<td>Erlotinib (Tarceva&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>6</td>
<td>$83,682</td>
</tr>
<tr>
<td>Temozolomide (Temodar&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>5</td>
<td>$78,783</td>
</tr>
<tr>
<td>Lapatinib (Tykerb&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>2</td>
<td>$31,919</td>
</tr>
<tr>
<td>Capecitabine (Xeloda&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>8</td>
<td>$73,447</td>
</tr>
<tr>
<td>Other*</td>
<td>6</td>
<td>$201,836</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>47</strong></td>
<td><strong>$1,007,960</strong></td>
</tr>
</tbody>
</table>

*Others include: Cyclosporine, Deferasirox (Exjade<sup>®</sup>), Imatinib (Gleevec<sup>®</sup>), Dasatinib (Spryce<sup>®</sup>), Pazopanib (Votrient<sup>®</sup>), and Abiraterone (Zytiga<sup>®</sup>).*

*Total cost savings in are based on average wholesale price (AWP) and reflect cost savings to both the patient and the pharmacy.*

Cycle Management Program

- Focus on early identification & management of side-effects
- Utilizes dose-monitoring plan (split-fill)
  - 16 day supply
  - Assesses need for remaining fill for month
  - Analysis of 823 CMP patients
    - 32% discontinued before second fill, saving $934 per patient
    - Estimated 2.9% reduction in hospital admission saving $440 per patient
    - Linear regression model to “predict” patients who would be hospitalized (no control group, no actual data)

Overcoming Barriers

- Is your pharmacy contracted?
  - Some insurances will allow you to fill if you fill out paperwork
  - Some manufacturers won’t let you dispense
    - Ex. Pfizer (Inlyta/Xalkori)

- Medicare vs Private Insurance
  - Part B vs Part D

- Exorbitant copays

- Non-FDA approved indications
Patient Resources

- Free Drug Programs
  - [http://www.ons.org/ClinicalResources/OralTherapies/Toolkit]
  - Tool 3, Table 1
  - Partnership for Prescription Assistance [www.pparx.org]

- Co-pay Assistance Programs
  - [http://www.ons.org/ClinicalResources/OralTherapies/Toolkit]
  - Tool 3, Table 2
  - CancerCare Co-Pay Assistance Foundation [www.cancercarecopay.org]

- Educational Handouts
  - ONS Toolkit linked above
  - CancerCare: *Taking Pills for Cancer Treatment: Tips for staying on your plan.* [http://www.cancercare.org/publications/111-the_importance_of_taking_your_pills_everyday_on_schedule]
Conclusions

- Issues with Oral Chemotherapy
  - Adherence/Compliance, Work Flow, Accessibility, Food & Drug Interactions, Side-Effects, Perceived Lack of Efficacy, Costs

- Dispensing Considerations
  - Handling, Disposal, Insurance Contracts, Manufacturer Contracts & REMS

- Cost Considerations
  - Prescription Drug Coverage vs Major Medical Insurance
  - Co-pay assistance & Free Drug Programs

- Oral Chemo is not as convenient as one might think!
Questions?

It's quite serious. Take this medicine when it's available... whenever you can afford it.
References