Oral Chemotherapy Challenges: Safety, Adherence, Access and Cost

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Objectives
• Define challenges and advantages associated with the use of oral chemotherapy
• Describe the importance of ensuring safety checks for oral agents are as rigorous as those for IV chemotherapy
• Discuss opportunities for pharmacist involvement in improving patient access and adherence to oral chemotherapy
• Describe efforts at the state and national level to address the oral chemotherapy coverage disparity

Background
• OCAs are used for a wide variety of malignancies
• Use has increased significantly due to new drug development
  ▶ 11 OCAs FDA approved in last 10 years
  ▶ 25% - 30% of new cancer drugs in development planned as OCA

Oncology Drug Approvals

<table>
<thead>
<tr>
<th>Oral</th>
<th>Parenteral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vismodegib</td>
<td>Brentuximab 11</td>
</tr>
<tr>
<td>Axitinib</td>
<td>Eminera chrysanthemi 11</td>
</tr>
<tr>
<td>Potoxitinib</td>
<td>Ipilimumab 11</td>
</tr>
<tr>
<td>Sunitinib</td>
<td>Entinib 10</td>
</tr>
<tr>
<td>Vandetanib</td>
<td>Cabazitaxel 10</td>
</tr>
<tr>
<td>Crizotinib</td>
<td>Sipuleucel-T 10</td>
</tr>
<tr>
<td>Vandetanib</td>
<td>Ramotoposum 09</td>
</tr>
<tr>
<td>Aminoratene</td>
<td>Olahumumab 09</td>
</tr>
<tr>
<td>Everolimus</td>
<td>Prolactin 09</td>
</tr>
<tr>
<td>Pazopanib</td>
<td>Plenaxfor 09</td>
</tr>
<tr>
<td>Degarelix</td>
<td>Blendamustine 08</td>
</tr>
</tbody>
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Cancers Treated with Oral Agents

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Oral Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast cancer</td>
<td>capecitabine, cyclophosphamide, lapatinib, methotrexate</td>
</tr>
<tr>
<td>Brain tumors</td>
<td>temozolomide, procarbazine, temozolomide</td>
</tr>
<tr>
<td>Leukemias</td>
<td>hydroxyurea, mercaptopurine, methotrexate, thioguanine, tedizole</td>
</tr>
<tr>
<td>Chronic leukemias</td>
<td>chlorambucil, fludarabine, dasatinib, nilotinib</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>capecitabine</td>
</tr>
<tr>
<td>GI stromal/pancreatic tumors</td>
<td>nilotinib, sunitinib, pazopanib</td>
</tr>
<tr>
<td>Kidney cancer</td>
<td>everolimus, pazopanib, sunitinib, sunitinib, temozolomide, actinib</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>erlotinib, etoposide, crizotinib</td>
</tr>
<tr>
<td>Lymphomas</td>
<td>chlorambucil, cyclophosphamide, etoposide, lenalidomide, procarbazine, vincristine, bexarotene</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>lenalidomide, melphalan, thalidomide, vincristine</td>
</tr>
<tr>
<td>Prostate cancer</td>
<td>Abiraterone, enzalutamide, sipuleucel-T, cabazitaxel</td>
</tr>
<tr>
<td>Skin cancers</td>
<td>vismodegib, vemurafenib</td>
</tr>
<tr>
<td>Thyroid cancer</td>
<td>vandetanib</td>
</tr>
</tbody>
</table>
OCA Advantages

• Reduction in healthcare resources (personnel, supplies)
• Increase in patient convenience, satisfaction, and quality of life
  ➢ Greater sense of control over their treatment
  ➢ Less interference with daily work and social activities
  ➢ Reduced travel time to and costs of an infusion clinic
  ➢ Reduced discomfort associated with IV line

OCA Challenges

• Drug/food interactions
• Adverse drug reactions
• Medication errors
• Patient adherence
• Education (patient and provider)

OCA Challenges

• Monitoring
• Handling/disposal
• Patient perception (i.e., less dangerous)
• Restricted access
• Multiple providers
• Coverage/cost

OCA Challenges

Key Point from Practice Perspective

Resource intense
(education, monitoring, access, etc.)
with NO reimbursement!

NCI Survey – Issues Identified

• A survey of 42 of the 54 National Cancer Institute (NCI) designated cancer center pharmacy directors revealed significant gaps in current practices
• Focused on six non-hormonal oral agents: capecitabine, cyclophosphamide, gefitinib, imatinib, methotrexate, temozolomide

NCI Survey – Issues Identified

• Safeguards for infusion chemotherapy have not been adopted for oral chemotherapy
• No apparent consensus among oncology professionals about safe practices for OCAs
• Development of safe practice guidelines is needed
National Guidelines

• ASHP Guidelines for Handling of Hazardous Drugs
  ➢ Revisions underway, expected release 2012

• ASCO/ONS Standards for Safe Chemotherapy Administration
  ➢ Revisions underway, expected release 2012

Other Published Guidelines

• Guidelines for the Safe Prescribing, Dispensing and Administration of Cancer Chemotherapy; a consultative report prepared by Clinical Oncological Society of Australia, November 2008.

Recent Publications


Recommendations for Practice

• Ensure patient can swallow medication
• Assess competency and readiness for self-administration
• Require patient consent
• Utilize generic name
• Utilize standardized orders
  ➢ Electronic templates, pre-printed order forms, CPOE
• Include OCAs with IV chemo treatment plan
• Prohibit handwritten and called in prescriptions (except to hold or discontinue treatment)
### Prescribing
- Provide prescriptions with required elements (diagnosis, ht, wt, BSA, prescribed dose, total daily dose, start/stop date, cycle #, and protocol when appropriate)
- Do not allow/limit refills
- Ensure appropriate supportive care medications are prescribed
- Provide independent double check
- Add OCAs to home medication list
- Perform medication reconciliation

### Dispensing
- Minimize number of dosage forms and concentrations available
- Provide independent double check
- Utilize bar code scanning
- Add OCAs to home medication list
- Provide clear and specific directions
  - Number of tablets of each strength to be taken
  - Never use “as directed”
- Perform medication reconciliation

### Administration
- Instruct patients to:
  - Not crush or chew
  - Not make dose adjustments unless physician has ordered
  - Immediately wash hands or wear gloves
- Request unused meds and empty containers to be returned to pharmacy for disposal

### Monitoring
- Include frequency of office visits and monitoring in the treatment plan
- Utilize follow-up phone calls between visits and ask probing questions to monitor for adherence and side effects
- Review medication journals/calendars at each visit to evaluate adherence
- Evaluate adverse effects, drug interactions, and financial situations at each visit
- Reinforce importance of adherence and communication at each visit

### Storage and Handling
- Cytotoxics should be stored in a designated area and separate from non-cytotoxic agents
- Use PPE to minimize exposure and health risks
- Do not use automatic counting machines
- Use disposable gloves, wash hands before and after glove applications
- Use separate equipment for cytotoxic and non-cytotoxic agents

### Storage and Handling
- Agents in powder form should be prepared in the pharmacy
- Oral liquid doses should be placed in an oral syringe in the pharmacy
- Have a written emergency plan for accidental spill or exposure and conduct drills
- Keep an updated list of hazardous medications readily available
Storage and Handling

• PPE should be disposed as cytotoxic waste
• Non-disposable items (counting trays, tools, surfaces, etc.) should be washed or decontaminated thoroughly
• Minimize or eliminate handling by pregnant staff
• Ensure all staff who may come in contact with OCAs or waste from patients have undergone appropriate training (clerks, sanitation workers, etc.)

Staff Education

• Designate a primary educator
• Develop and implement a plan for education specific to health care professional roles
  ➢ medications (indications, dosing, side effects, etc.)
  ➢ safe handling and disposal
  ➢ patient education materials
  ➢ assessing/monitoring adherence
  ➢ cost and access issues (e.g. specialty pharmacies, prior authorization, manufacturer and copay assistance programs)
  ➢ documentation requirements

Staff Education

• Ensure competency to perform education and monitor adherence
• Ensure information/knowledge is current
• Assign responsibility for patient education and follow up (i.e. primary education vs. reinforcement)
• Create checklists to guide and remind staff of key elements required for education
• Provide access to written protocol/treatment plan
• Develop policies and procedures to support safe practice guidelines

Patient Education

• Key to ensuring adherence and safety
• Barriers to adherence include
  ➢ Complex drug regimen
  ➢ Multiple chronic conditions
  ➢ Psychological problems, e.g. depression
  ➢ Perceptions
  ➢ Age, cognitive impairment
  ➢ Lack of social support
  ➢ Literacy level
  ➢ Inadequate follow-up

Patient Education

• Develop patient education materials that include:
  ➢ name of medication and what it looks like
  ➢ side effect management
  ➢ drug and food interactions
  ➢ safe handling and disposal (e.g. do not crush or chew, keep away from children)
  ➢ handling of missed or vomited doses
  ➢ when and how to contact provider 24/7

Patient Education

• Provide both written and verbal education
  ➢ ask patient to repeat key points (e.g. dosing schedule, total daily dose, missed doses, adherence)
  ➢ confirm understanding
  ➢ document comprehension
  ➢ provide calendars and journals as needed
  ➢ reinforce information at each visit
• Ensure materials are comprehensive and routinely updated
Patient Education

- Include family, caregivers, and others based on patient’s ability to assume responsibility for managing therapy
- Provide follow up phone call to assess understanding, answer questions, ensure prescription has been filled
- Offer online educational and management tools for addressing adverse effects
- Dedicate follow up appointment specifically for medication education

Patient Education

- Assess adherence, treatment tolerance, and adverse effects at each visit
  - Encourage use of dosing aids
  - Encourage patients to bring medication bottles to appointment
- Encourage patients to report medication errors and near misses
- Discuss access and cost issues (e.g. specialty pharmacies, prior authorization, manufacturer and copay assistance programs)

Coverage/Cost Concerns

- Most OCAs require prior authorization which can lead to therapy delay
- Many insurance plans disadvantage oral chemotherapy medications by placing them into the specialty tier benefit of the plan’s prescription program
  - Results in decreased drug costs for payers at the expense of patients
  - Patients pay exorbitant out of pocket copayments

Coverage/Cost Concerns: Physician Prescribing

- Physicians twice as likely to check patient coverage prior to making treatment decision
  - 46% discussed out of pocket costs in 2007
  - 67% discussed out of pocket costs in 2008

Coverage/Cost Concerns: Patient Adherence

- Oral oncolytics abandonment rate is 10%
  - Associated with cost sharing and Medicare coverage
  - High costs delay initiation in 25% of patients
- Patients with costs >$200 per month are 3 times more likely to not fill prescriptions

Oral Chemotherapy Parity Legislation

- Ensures equal coverage for oral and IV chemotherapy drugs
State Oral Parity Legislative Update

Cancer Patient Protection Bill
Ohio SB 194 and HB 237

- Efforts led by James Cancer Hospital Pharmacy staff
- Sponsored by Senator Olslaeger (originally sponsored by Karen Gilmore) and Representative Deborah Newcomb
- Requires equal coverage for oral and intravenous chemotherapy drugs

Cancer Drug Coverage Parity Act of 2011

- Amends the Employee Retirement Income Security Act, Public Health Service Act, and Internal Revenue Code
- Requires health insurance and group plans to cover oral anticancer drugs at equitable rate to intravenous drugs
  - Does not mandate chemotherapy coverage

Solution Case Example:
Ohio State University Health Plan

- All oral chemotherapy has been moved under preferred tier plan
- The James has been successful adding new medications to the preferred tier plan through appeal

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<thead>
<tr>
<th>Chemotherapy Type</th>
<th>Benefit Payment/Co-Pay</th>
<th>Out of Pocket Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parenteral</td>
<td>80%-20%</td>
<td>$2,000</td>
</tr>
<tr>
<td>Oral</td>
<td>80%-20%</td>
<td>$80/prescription $2,500 total</td>
</tr>
</tbody>
</table>

Questions

Appendix
Recommendations for Patients & Caregivers

“Dos” for Oral Chemotherapy

- Use gloves or tip tablets/capsules from their blister pack/container into a disposable medicine cup
- Wash hands before and after medication administration
- Keep a journal of adverse effects
- Inform other health care professionals that you are on oral chemotherapy (e.g., surgeons and dentists)
- Minimize the number of individuals coming in contact with the cytotoxic medication
- Wash clothes and bed linens separately and handle with gloves
- Double-flush the toilet after use, during use of and 4 to 7 days after discontinuing chemotherapy
- Return unused (discontinued/expired) medication to the pharmacist or hospital for disposal

“Don’ts” for Oral Chemotherapy

- Do not leave near sources of water or direct sunlight
- Do not leave where it can be accessed by children or pets
- Do not store near where food/drinks are stored or consumed
- Do not crush, break, or chew tablets
- Do not double-up on doses or skip doses, unless instructed by a health care professional
- Do not assume that oral chemotherapy is safer than intravenous chemotherapy
- Do not discard medication down the toilet or in the garbage

Recent Published Literature: Patient Adherence

- Streeter SB, Schwartzberg L, et al. Patient and plan characteristics affecting abandonment of oral oncolytic prescriptions. Am J Manag Care 2011;17(Spec No.):SP38-SP44.