CLINICAL PEARLS: ONCOLOGY

SATURDAY/2:00-3:00PM

ACPE UAN: 0107-9999-17-017-L01-P 0.1 CEU/1.0 hr

Activity Type: Application-Based

Learning Objectives for Pharmacists: Upon completion of this CPE activity participants should be able to:
1. Review the management of patients receiving oral chemotherapy including common drug interactions and adverse events
2. Discuss barriers to patient adherence to oral chemotherapy
3. Describe strategies to help patients overcome barriers to adherence

Speaker: Kathryn Schiavo, PharmD
Kathryn Schiavo, is the Outpatient Oncology Pharmacy Manager at the NorthShore University Healthsystem Kellogg Cancer Centers located in the northern suburbs of Chicago. She graduated with her Doctor of Pharmacy degree from the Drake University College of Pharmacy and Heath Sciences in 2007. She completed an ASHP accredited Community Pharmacy Residency at NorthShore in 2008 and following her residency began work on opening Kellogg’s first oral oncology pharmacy in 2008. She now oversees a total of 3 oral oncology pharmacies as well as serves as the corporate contract for specialty pharmacy services at NorthShore. She serves as a pharmacy preceptor for both pharmacy residents and students in the oncology departments and serves on several corporate committees. She currently sites on the ASHP Advisory Group on Patient Care Quality and the HOPA (Hematology Oncology Pharmacy Association) Health Policy and Advocacy Committee.

Speaker Disclosure: Kathryn Schiavo reports that she is on a speaker’s bureau for Celgene Corp, Pfizer, Inc. Off-label use of medications will not be discussed during this presentation.
Clinical Pearls-Oncology
Kathryn Schiavo, PharmD

Disclosure

• Kathryn Schiavo reports:
  • Speaker’s bureau member for Pfizer Inc. and Celgene Corporation
**Audience Response Q1**

- What is your current practice setting?
  - Community/Retail based
  - Hospital based
  - Ambulatory/Clinic based
  - Oncology based
  - Academia
  - Other

**Audience Response Q2**

- Have you ever dispensed any oral chemotherapy drugs in your pharmacy setting?
  - Yes
  - No
### NorthShore Kellogg Cancer Center (KCC)
- Established in 1981
- Located at three different sites in the northwest suburbs of Chicago, IL
- Comprised of multiple disciplinary healthcare team
- Utilizes electronic medical record and physician order entry system

### Kellogg Pharmacy
- Offers both outpatient infusion and point of care services
- Comprised of specialty oncology pharmacists and certified technicians
- Utilize EMR computer system to monitor, verify, and dispense various cancer treatments

### Background
- Point of Care Pharmacy
- Established initial site in August 2009
- 2 Additional sites opened in 2012 & 2013
- Located within each of the Kellogg Cancer Center locations
- Dispenses oral chemotherapy, supportive care medications, and various outpatient medications and OTC products for KCC patients
- Has access to the hospital computer system for charting and documentation

### Kellogg Outpatient Pharmacy (KOP)
Learning Objectives

- Upon successful completion of this activity, participants should be able to:
- Discuss barriers to patient adherence with oral chemotherapy agents
- Describe strategies to help overcome barriers to adherence
- Review the management of patients receiving oral chemotherapy including common drug interactions and adverse events of selected agents

History of Oral Chemotherapy
### Oral Chemotherapy agents on the market in 2007

- Methotrexate - 1953
- Mercaptopurine - 1953
- Busulfan - 1954
- Chlorambucil - 1957
- Cyclophosphamide - 1959
- Melphalan - 1964
- Hydroxyurea - 1967
- Lomustine - 1976
- Tamoxifen - 1977
- Etoposide - 1986
- Anastrozole - 1995
- Bicalutamide - 1995
- Letrozole - 1997
- Thalidomide - 1998
- Capecitabine - 1998
- Exemestane - 1999
- Temozolomide - 1999
- Imatinib - 2003
- Erlotinib - 2004
- Sorafenib - 2005
- Lenalidomide - 2005
- Sunitinib - 2006
- Dasatinib - 2006
- Lapatinib - 2007

### Oral Chemotherapy agents on the market in 2016

- Alectinib (venetoclax)
- Almacene (alendronate)
- Alkeran (melphalan)
- Anorex (anastrozole)
- Aromasin (exemestane)
- Bosulif (bosutinib)
- Caprelsa (velpatasertib)
- Casodex (bicalutamide)
- Cimelizumab (cikkizumab)
- Cytarabine (cytarabine)
- Cyclophosphamide (Cyclocystophosphamide caps)
- Droxi (hydroxyurea)
- Emoct (extastimine)
- Enzalut (enzolodine)
- Etoptoside
- Fermera (letrozole)
- Flutamide
- Gilotrif (lilidirin)
- Gleo-vrc (matribin)
- Geodine (lumazine)
- Hexas (hexas)
- Ibrance (palbociclib)
- Ishigui (isonitid)
- Irinotec (irtiniber)
- Iressa (geffonin)
- Jakafi (ruxolitinib)
- Lenvima (lenvatinib)
- Lenvarin (lenvarin)
- Leupetin (leupetin)
- Lomustine
- Lomustine (hiprofex)
- Lynparza (olaparib)
- Lysulin (lysuline)
- Matulane (procarbazine)
- Megace (megestrol acetate)
- Melanoma (melanotene)
- Mesnex (menos)
- Mithotelatase
- Myleen (busulfen)
- Nexavar (sorafenib)
- Nifedron (nifedipine)
- Nitrol (roxozim)
- Odonato (sonidegib)
- Pomalyst (pomalidomide)
- Purixan (mercaptopurine susp)
- Respilim (lenalidomide)
- Rheuminate (methylazat)
- Rylmild (lenalidomide)
- Soltamox (tamoxifen citrate)
- Sorbolz (desitin)
- Streps (diphenhydramine)
- Taltag (taltagin)
- Tafinlar (dabrafenib)
- Tagrisso (osimertinib)
- Tamoxifen
- Tarceva (erlotinib)
- Tarceva (erlotinib)
- Tazizia (ftarbine)
- Temodar (temozolomide)
- Thalidomide (thalidomide)
- Tickrin (tizanidine)
- Traylar (lapatinib)
- Vencor (dabrafenib)
- Vemidr (dabrafenib)
- Xeloda (capecitabine)
- Xstrahl (enoxatamide)
- Zelboraf (vemurafenib)
- Zelboraf (vemurafenib)
- Zytel (dabrafenib)
- Zetux (dabrafenib)
- Zetux (dabrafenib)
Why oral drugs?

- Convenience
- Ease of administration
- Flexibility of drug exposure (Timing of doses)
- Portability
- Patient preference/empowerment
  - 90% of patients prefer the oral route vs. IV administration
  - Primarily because of convenience
- Reduction of healthcare resources
- Perceived decrease in toxicity

Audience Response Q3

Why not oral drugs?

- Complicated dosing
- Cost
- Documentation
- Drug interactions
- Lack of availability
Availability of oral oncolytic therapy

Chart 15: Targeted Oncology Medicine FDA Approval Type by Year

Challenges of oral chemotherapy

- New hurdles for Clinicians
  - Prescribing
  - Documentation
  - Monitoring
  - Patient Access
- Cost
- Adherence
- Drug Interactions
- Adverse Events
New hurdles for Clinicians

A) Prescribing
• Many safe guards in place for IV chemotherapy
  • Only attending oncologist can order
  • Verbal orders typically not allowed
  • Pharmacy verification requires knowledge of indication, regimen, body surface area, labs, etc.
• Lack of safe guards in place for oral chemotherapy
  • Written on standard prescriptions pads or verbal/electronic orders
  • Limited distribution of many new oral agents

Ordering Concerns
• Electronic order
  • Who has authority to order?
  • Where are these orders sent?
  • How does the order translate into pharmacy system?
• Handwritten order

New Challenges to Clinicians cont.

B) Documentation
• Varies based on pharmacy systems in use
  • Electronic medical records vs. paper charts
  • Not linked to physician system or health record
• IV chemo orders typically require specific documentation and records
  • Patient’s weight, lab results, etc.
• Varying standards for oral chemotherapy orders
  • Verbal order documentation
  • Medication management systems/Medication reconciliation
New Challenges to Clinicians cont.

C) Monitoring
- Decreased hands on healthcare provider contact when receiving oral chemotherapy
- Patient education critical to appropriate use and management of adverse events
- Lack of standardized follow up

D) Patient Access
- Limited distribution medications
- Access to contracts/payers
- Lack of payment for clinical services

Clinical Pearl:
Management Challenges

- Cost
- Adherence
- Drug Interactions
- Adverse Events
Cost

The Growth of Oral Oncology Agents

- Expenditures for oral oncolytics increased to 6 billion in 2012 from 1 billion in 2003
- The percentage dispensed through specialty pharmacy increased to 61% in 2012 from 26%


Adherence

- The World Health Organization (WHO)
  - “the extent to which a person’s behavior – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider.”

- Adherence can decrease the need for more extensive and often expensive care of patients
  - However studies continue to demonstrate that adherence is a challenge
    - 7% of patients never filled prescriptions
    - 9% of patients did not refill their prescription
    - 10% of patients stopped taking their medications

Am J Manag Care. 2012;16(12):e461-e467
“Drugs don’t work in patients who don’t take them.”

-C. Everett Koop, MD

Types of Adherence

- Clinical studies show varying rates of adherence
- Studies are still lacking in oncology patients
- Compliance rates range from 20%-100%
  - Ideal Patient-Complete Adherence
  - Partial Adherer
  - Erratic User
  - Over user
  - Dropout
- Most patients are all of the above
Barriers to Adherence

1. Social & Economic Factors
   • Inadequate support
   • General attitude toward treatment options
   • Cost

2. Healthcare System Related
   • Access
   • Drug shortages
   • Barriers to care

3. Condition Related Factors
   • Co-morbidity
   • Disease related factors
Barriers to Adherence

4. Therapy Related
   • Adverse effects of drugs
   • Dosing complexity
   • Length of treatment
   • Availability

5. Patient Related
   • Poor understanding of treatment
   • Cultural beliefs
   • Reluctance to change

Clinical Pearl: Barriers to Adherence

• Social & Economic Factors
• Healthcare System Related
• Condition Related Factors
• Therapy Related
• Patient Related
Impact of Nonadherence

- Decreased therapeutic effect
- Increased adverse events
- Morbidly/Mortality
- Increased healthcare costs
  - Both to patient and facility
- Increased hospital admissions/physician visits
- Decreased quality of life
- Negative view of care

Clinical Consequences

Examples

- Tamoxifen in breast cancer patients
  - <70% adherence resulted in 16% increased risk of death from breast cancer
- Reports of death from over adherence to Temozolomide
  - Poor communication and lack of patient education
- Reports of death from overdose of CEENU
  - Poor documentation and lack of patient counseling

More reports available at ISMP.org
Clinical Pearl:
Factors that Affect Adherence

- Patient
- Drug Regimen
- Education
- Healthcare System
- Cost

Patient Factors

- Physical
  - Cognition
  - Ability to take oral medications
- Psychological
  - Lifestyle changes
  - Level of understanding
- Psychosocial
  - Health beliefs
  - Support system
Patient Nonadherence

Examples

- Adjuvant hormonal therapy in breast cancer patients
  - 2+ years post-diagnosis survey
    - 50% admit to forgetting doses
    - 13% admit to deliberately skipping doses
  - Other studies have demonstrated similar results
    - After 1 year, adherence rate was 87%
    - After 4 years, adherence rates decreased to 50%

Drug Regimen

- Dosing Complexity
- Dosing Frequency
- Duration of Therapy
- Regimen Prescribed
- Toxicity/Adverse Event Profile
What does the dose look like?

Education

- Literacy
- Language barriers
- Lack of patient counseling/teaching
- Prior experiences with chemotherapy
- Patient expectations
Healthcare System

• Access to medication
  • Community Pharmacies
  • Specialty Pharmacies
• Responsibility of care shifted from healthcare providers to the patient
  • Infusion Center vs. Home Administration
• Lack of communication and follow up
  • Loss of control by healthcare practitioners

Cost

• Drug Cost
  • Branded medications
  • Additional supportive care medications
• Insurance Coverage
  • Medicare B vs. Medicare D
  • Commercial insurance plans
• Patient Assistance Programs
Most people taking Rx drugs say they can afford their treatment, but about 1 in 4 have a difficult time affording their medicine

Among those who are currently takingRx medicines, percent who report some or difficulty affording the cost of their prescription medications:

- Very easy, 45%
- Somewhat easy, 27%
- Somewhat difficult, 16%
- Very difficult, 8%
- Don’t have to pay, 3%
- Other, 1%

Source: Kaiser Family Foundation Health Tracking Poll (Conducted Aug 6 – 11, 2013)

Who is paying?
Medicare Billing

• Cover different drugs
  • Does the drug have an IV equivalent
• Patients may still be responsible for out-of-pocket payments with both
  • Medicare B - 20% without supplemental coverage
  • Medicare D - based on patient’s plan*
    • Initial out-of-pocket cost= $3700
    • Coverage gap/Donut hole= $4950
    • Catastrophic coverage= 5% of price of drug

Medical coverage does not always mean prescription drug coverage

Co-pays vs. Percentage Payments

Formulary Management
  • Restrictions
  • Amendments/Updates

Prior Authorizations and Step Therapy

Each plan is different and can/will change!!!
### Patient Assistance Programs

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
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</thead>
<tbody>
<tr>
<td>• Provide financial assistance to patients in need</td>
<td>• Availability of programs</td>
</tr>
<tr>
<td>• Increase access to expensive medications</td>
<td>• Inconsistencies in programs</td>
</tr>
<tr>
<td>• Improve patient adherence</td>
<td>• Qualifications</td>
</tr>
<tr>
<td>• Improve patient outcomes</td>
<td>• Complex application process</td>
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<td></td>
<td>• Lengthy processing times</td>
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<td>• Limited funds available</td>
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**Who is the ideal oral chemotherapy patient?**
Clinical Pearl: Predictors of Poor Adherence

- Past non-compliance
- Patients that skip appointments
- Patient’s with previous poor communication
- Patients with financial difficulties

Patient Case: JZ

- 46 year-old female
- Full time teacher
- 3 children
- Starting combination therapy for advanced disease
- She is currently taking medications for hypertension and depression
- She has difficulty scheduling appointments due to her work/childcare schedules

What concerns would we have?
- Lifestyle /adherence issues
- Drug interactions
- Toxicity
Clinical Pearl: Strategies to Improve Adherence

- Initial Assessment
- Patient Education
- Behavior Methods
- Follow Up
- Patient Resources

Initial Assessment

- Focus on the patient’s risk for poor adherence
- Collaborate with other healthcare team members
- Formulate an individualized care plan
- Communicate regimen
- Patient-centered care
Patient Education

- Provide individualized patient education
  - Regimen
  - Drug toxicity profile
- Who/when to follow up regarding adverse events
- Include all members of the healthcare team
- Include patients support system when possible
  - Family members, caregivers, etc.
- Target high-risk patients
- Emphasize the importance of adherence

Behavioral Methods

- Patient medication calendar
  - Online programs available
- Pill box
- Medications diary
- Telephone reminder
- Text reminders
- Email reminder
- Mail reminder
- Electronic monitoring device
  - Costly
Follow Up

- Scheduled call or appointment
- Provider initiated
- Healthcare team approach
- Document interaction
  - Who?
  - What?
  - When?

Patient Resources

- Health System Groups
- Foundations
- Pharmaceutical Industry Programs
- Outside Support Groups
- The Internet
  - Beware
  - Good and Bad
Clinical Pearl: Management Challenges

- Cost
- Adherence
- Drug Interactions
- Adverse Events

Kellogg Outpatient Experience

- Cost
- Adherence
- Drug interactions
- Adverse events
Clinical Pearl: Community Experience

How can community based pharmacists make an impact in management of patients on oral chemo like clinic providers?

- Patient Counseling and Education
- Drug Interactions
- Adverse Event Education vs. Monitoring

Clinical Pearl:

Community Experience

- Correct dosage and adherence technique
- Common toxicities and management tips
- Proper storage
- Safe handling and disposal
- Advice on when to call clinic
- Provide written information where possible
Drug Interactions

- Acid reducing agents
- Anticoagulants
- Antibiotics
- CYP metabolism
- OTCs
- Herbal supplements

Acid reducing agents

- Proton pump inhibitors (PPIs)
- Histamine blockers (H2 blockers)

Considerations

- Can increase or decrease the serum concentration of oral drugs
- Can interfere with the normal release of drug from the delayed-release capsules or timing specific drug delivery systems
- Can increase concentrations of active metabolites leading to adverse events and variable doses

Recommendations can include:

- Separating doses by 2-8 hours
- Switching between classes
- Avoiding combination all together
Anticoagulants

- Warfarin
- NOACs

- Considerations:
  - Can increase patients risk for bleeding
  - Specific drug interactions may exist
  - Increased need for monitoring

- Recommendations:
  - Counsel patient on effects of combination
  - Encourage patient to follow up with provider for increased drug monitoring/ labs

Antibiotics

- Drug interactions will vary by agents used

- Considerations:
  - Who is prescribing the medications?
  - Drugs can have direct effect on metabolism of each other
  - Drugs can have additive toxicity

- Recommendations
  - Contact providers involved
  - Counsel patient on effects of combination
  - Encourage patient to follow up with provider for increased drug monitoring/ labs as needed
CYP Metabolism

- CYP3A inducers and inhibitors
- CYP2D6 inducers and inhibitors
- CYP2C9 inducers and inhibitors

Considerations:
- May reduce or increase blood levels of oral chemotherapy
- May require dose adjustments when used together
- May require discontinuation or therapy modification

Recommendations
- Contact providers involved
- Counsel patient on effects of combination

OTCs & Herbal Supplements

- Interactions will vary by agents used

Considerations:
- Is this issue related to chemotherapy management or separate issue
- Determine if issue requires medical attention
- Patient may require discontinuation or therapy modification

Recommendations
- Contact providers involved
- Counsel patient on effects of combination
- Counsel patient on when to seek medical advice
Adverse Event Education

- Education vs. Management
- Focus on anticipated effects
  - Nausea
  - Education on dosing and timing of medications
  - Constipation
  - Use of OTC laxative options
  - Education on when to seek medical help
  - Diarrhea
  - OTC products and when to seek medical help
  - Rash
  - Hand hygiene
  - Assessment

Knowing WHEN and WHO to call
Resources for Patients

• Support Organizations
  • American Cancer Society (ACS) [www.cancer.org](http://www.cancer.org)
  • National Cancer Institute (NIH) [www.cancer.gov](http://www.cancer.gov)
  • Needy Meds [www.needymeds.org](http://www.needymeds.org)
  • RX Assist [www.rxassist.org](http://www.rxassist.org)
  • State and local support groups

• Foundation Groups
  • Chronic Disease Fund
  • Patient Advocate Network Foundation
  • HealthWell Foundation

• Pharmaceutical Companies

Resources for Pharmacists

• National organizations
  • Hematology/Oncology Pharmacy Association (HOPA)
  • Association of Community Cancer Centers (ACCC)
  • American Society of Clinical Oncology (ASCO)
  • National Comprehensive Cancer Network (NCCN)

• State and regional organizations
• Pharmaceutical Companies
THANK YOU

Questions ??

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