Opportunities in the Rise of Oral Oncologic Therapy

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Disclosures

• Becky Fahrenbruch
  • Board of directors for Upper Midwest Oncology Education Network (UMOEN) and Kappa Psi Pharmaceutical Foundation
  • Advisory Board for Tesaro, Amgen, Exelixis, BMS, Takeda and Oncology Reimbursement Management

• Jolynn Sessions has no financial disclosures
  • Board of directors as treasurer of the Hematology Oncology Pharmacy Association (HOPA)
CPE Information

- Target Audience: Pharmacists
- ACPE#: 0202-0000-19-090-L01-P
- Activity Type: Knowledge-based
Learning Objectives

At the completion of this knowledge-based activity, participants will be able to:

• Identify important counseling and education points associated with oral oncologic medications.

• Discuss challenges associated with obtaining reimbursement for oral oncologic medications and strategies to address those challenges.

• List appropriate medication management strategies to mitigate the common adverse effects associated with many oral oncologic therapies.

• Explain a plan to support patient adherence to oral oncologic therapy.
Assessment Questions

When counseling a patient on a new oral chemotherapy medication, which of the following would be important to include?

A. Mix your chemotherapy in the same pill box as other medications
B. If you have problems swallowing, chew the medication before to make it easier
C. Anyone may help give the medication to the patient with no precautions
D. Store medication at room temperature in a dry location away from pets and children
Which of the following is a Foundation that can be used to assist in the cost of oral oncology medications?

A. Cancer Alliance  
B. HealthWell Foundation  
C. Patient Financial Assistance Foundation  
D. Good Weeks
Which of the following therapies is an accepted treatment option for epidermal growth factor inhibitor TKI rash:

A. Benzoyl peroxide 
B. Retinoids 
C. Topical steroids 
D. Sunlight/Ultraviolet exposure
Assessment Questions

The best adherence plan may include which of the following?

A. Involves tailoring the education, administration schedule, compliance plan, and monitoring plan to the patient
B. Uses microelectronic monitoring systems (MEMs) caps
C. Includes a written administration calendar
D. Involves setting an app on the patient’s phone to remind when to take dose(s)
With oral oncolytics, which of the following is true regarding diarrhea

A. An uncommon toxicity and can occur in less than to 10% of patients taking certain oral oncolytics
B. Usually mild (grade 1-2 toxicity) and can be managed with octreotide
C. Caused by a cholinergic reaction of the drug
D. Self-care such as adequate hydration, avoidance of irritating factors (greasy, spicy foods, milks and cheeses, excessive fiber, etc.) should be encouraged
University of Minnesota Health Pharmacist-Managed Oral Oncology Program

• System wide program including 4 major outpatient clinics
  • Started Spring 2013
  • Around 500 patients managed at any given time

• Completely managed by pharmacists and pharmacy liaisons (technicians)
  • All in the outpatient/clinic setting
  • 3 full-time equivalent (FTE) pharmacists/3 FTE liaisons at University main campus
  • Off-university sites managed by infusion pharmacists (in conjunction with daily infusion workload)
    • Liaisons for all sit
University of Minnesota Health Pharmacist-Managed Oral Oncology Program

• Oral Medications
  • All oral oncology medications included in program (exception: hormonal agents)
• Comprehensive service including initial assessment, education, monitoring, visit/calls to patients, adherence and financial assistance
• Patient Financial Assistance

<table>
<thead>
<tr>
<th>Year</th>
<th>Assistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>$6 Million</td>
</tr>
<tr>
<td>2017</td>
<td>$12 Million</td>
</tr>
<tr>
<td>2018</td>
<td>$25 Million</td>
</tr>
</tbody>
</table>
Oral Chemotherapy Counseling

• Team approach
  • Physician
  • Nurse/care coordinator
  • Clinical pharmacist
  • Retail/specialty pharmacist

• Education not a one-time event, must be continued through treatment

• Common misconceptions
  • Oral oncology medications have minimal/no side effects
  • Drug interactions are negligible
  • Oral chemotherapy is less effective than intravenous
Financial Toxicity

• Financial burden of oral chemotherapies
  • 10% of patients abandon their first prescription of an oral chemotherapy agent
    • High cost sharing, increased prescription activity, lower income and Medicare coverage associated with higher abandonment
    • 25% of patients had some delay in initiating another oncolytic, potentially causing delay in treatment
  • Cost-sharing amounts > $500 was 4X more likely to be abandoned than < $100
    • Did not follow up with another oncology prescription within 90 days

Key Counseling Points with Oral Oncology Medications

- Drug name
- Food and Drug Administration (FDA) indications
- Dose and schedule
- Storage, handling and disposal
- Handling of body fluid and waste
- Side effects and management
- Drug interactions
- Pregnancy, sexual activity and contraception

Oral Chemotherapy Education sheet. The Association of Community Cancer Centers (ACCC), Hematology/Oncology Pharmacy Association (HOPA), National Community Oncology Dispensing Association, Inc. (NCODA), and Oncology Nursing Society (ONS). http://www.oralchemoedsheets.com/
Key Counseling Points with Oral Oncology Medications

• Other items that may be covered specific to oral chemotherapy
  • Monitoring parameters (ie blood pressure, electrocardiogram (EKG) monitoring)
  • Blood testing requirements (ie blood counts, glucose, liver enzymes, etc)
  • Drug access
  • Refill process

• These will vary per institution, patient insurance, split fill requirements, etc

Examples of Oral Chemotherapy Patient Counseling Sheets

• The Association of Community Cancer Centers (ACCC), Hematology/Oncology Pharmacy Association (HOPA), National Community Oncology Dispensing Association, Inc. (NCODA), and Oncology Nursing Society (ONS)
  • [http://oralchemoedsheets.com/](http://oralchemoedsheets.com/)

• Chemocare
  • [http://chemocare.com/](http://chemocare.com/)

• British Columbia (BC) Cancer Agency
Key Counseling Points with Oral Oncology Medications

- Drug name
  - Including brand and generic names
  - FDA-approved indications/mechanism of action

- Dose and schedule
  - Extremely important for oral oncology medications
  - Various schedules/cycles used (ie 2 weeks on, 1 week off; Mon-Friday days of radiation; Day 1-5, 8-12 q 28 days)
  - Food recommendations
    - Defining an empty stomach, low-fat breakfast, with food
  - Food interactions
    - Grapefruit, grapefruit juice, Seville oranges, star fruit, pomelo, etc
  - Swallow whole and do not chew, crush, cut or dissolve
  - If a dose is missed, do not take an extra dose or two doses at one time
Storage, Handling and Disposal

- Store at room temp (68°F–77°F) in a dry location away from light.
- Keep out of reach of children and pets.
- Leave in the provided packaging until it is ready to be taken.
- Whenever possible, give oral chemotherapy to yourself and follow these steps:
  1. Wash hands with soap and water BEFORE AND AFTER
  2. Put on gloves to avoid touching the medication (if caregiver gives)
     - Gloves are not necessary if you give the drug to yourself
  3. Gently transfer from its package to a small medicine or other disposable cup
  4. Administer the medicine immediately by mouth with water
  5. Remove gloves and do not use them for anything else. Throw gloves and medicine cup in household trash.
Storage, Handling and Disposal

- **Pill box**
  - Use a separate one for oral chemotherapy. Do not mix other medications into the box.
  - Person filling the box should wear gloves if it is not the patient.
  - When empty, the box should be washed with soap and water before refilling. Be sure to wash hands with soap and water after the task is complete, whether or not gloves are worn.

- **Disposal**
  - If you have any unused medication, do not throw it away; do not flush it down the sink or toilet. Talk to your care provider about proper disposal.
    - Manufacturer may provide instruction for disposal
    - Free local drop boxes
Handling Body Fluid and Waste

• Pregnant women should avoid touching anything that may be soiled with body fluids from the patient

• Toilet and septic systems
  • Patients may use the same toilet, septic tank, and/or sewer that they usually use. If they have a low-flow toilet, close the lid and flush twice to ensure all waste has been discarded.
  • If the toilet or toilet seat becomes soiled with urine, stool or vomit, clean the surfaces before other people use the toilet
  • Wash hands with soap and water after using the toilet

• If patients do not have good control of bladder or bowels, use a disposable pad with a plastic back, a diaper or a sheet to absorb body waste
Handling Body Fluid and Waste

• Wash any skin that has been exposed to body waste with soap and water
• Linens or clothing that are soiled with body fluids or body waste should be washed separately from other linens and clothing. If you do not have a washer, place the soiled linens in a plastic bag until they can be washed.
  • Wash hands with soap and water after touching linens or clothing that may be soiled with body fluids
Drug Interactions

- Many drug interactions with oral oncology medications
  - Always run a drug interaction screen
  - Common
    - Warfarin
    - Cytochrome P450 (CYP) inducers/inhibitors
    - Antacids/proton pump inhibitors (PPI)
  - Make alternative recommendations to the health care team
- Ask about over-the-counter medications, supplements and herbs
Pregnancy, Sexual Activity, and Contraception

• Women should not become pregnant and men should not get a partner pregnant
• Men and women of childbearing age should use effective contraception during therapy and for a minimum of one week after the last dose
  • Interval required may differ based on medication
• Inform care provider if you become pregnant
• It is safe to hug and kiss
• Special precautions may be needed for sexual activity
  • Encourage patient to ask another care provider if needed
Challenges with Reimbursement

• Medications are expensive
  • 20% copay on $15,000/month medication is $3,000
• Differences between private vs public insurance
• Patients’ lack of knowledge and understanding
• Almost everything needs a Prior Authorization (PA)
  • Maybe even an appeal
• Money/grants disappear toward the end of the year
Pharmacy Technician/Liaison Workflow

- Meet patient and discuss role

- Run test claim
  - Participating pharmacy as determined by insurance
  - Prior Authorization
  - Coverage appeals

- Release e-scribe prescription to specialty pharmacy
Pharmacy Technician/Liaison Role

- Expedite prescriptions though insurance and specialty pharmacies
  - Discuss co-pay obligation
  - Complete PA, appeals and paperwork
  - Attempt to track the prescription all the way through various systems until prescription reaches the patient
    - Daily check of status of prescriptions
- Provide information on financial assistance and complete paperwork
  - Discussion with patient
  - Obtain assistance through free drug, grants, co-pay cards
  - Private vs. public insurance
    - Private insurance or no insurance
      - Manufacturer sponsored assistance programs
    - Public insurance
      - Co-pay assistance programs through various private foundations
Pharmacy Technician/Liaison Workflow

- Monitor prescription refill needs
  - Dates and timing is correct
- Continual communication with various Specialty Pharmacies
- Obtain medication
  - Sent to patient’s home
  - Available for pick up
Financial Assistance for Oral Oncology Medications

• Financial Assistance
  • Where to start?
    • Fund Finder/Patient Access Network (PAN) Foundation
    • Zitter Health Insights (ZHI) Reimbursement portal
  • Criteria to be eligible
    • Insurance type
    • Household financials
  • Completion and submission of application
  • Obtaining funds
Financial Assistance Foundations

Common Adverse Effects with Oral Oncolytics

Epidermal growth-factor receptor (EGFR) inhibitor skin toxicities

Diarrhea

Vascular endothelial growth factor (VEGF) inhibitor toxicities
  Hypertension
  Decreased wound healing
  Thrombosis
  Proteinuria

Hand-foot skin reaction (HFSR)

Cardiac Effects
**Patient Case**

- 41 year old, never-smoker woman of Asian decent
- Presents to her primary care provider with a 2 month history of a non-productive cough and left sided chest pain
- Has been prescribed, and was compliant with:
  - Amoxicillin X 10 days
  - Doxycycline X 10 days
  - Azithromycin X 5 days

- Primary care provider orders a chest X-ray
- Which reveals a large mass
- Pathology of mass:
  - Adenocarcinoma
  - EGFR mutation +
  - ALK and ROS –
- She is referred to a medical oncologist

ALK=anaplastic lymphoma kinase  ROS=proto-oncogene, driven by ROS1 gene rearrangement
Oncologist prescribes:

- Erlotinib 150 mg PO daily

What do you want to educate the patient about?
EGFR-Rash

- Epidermal growth factor receptor inhibitor
- Very specific rash secondary to the mechanism
- +/- pruritus
- +/- skin tenderness

EGFR Rash

- Generally present on face, neck, back, chest, scalp
  - Papulopustular
- Dry skin in these areas and extremities (especially hands)
- Much different from traditional acne
- Most common tyrosine kinase inhibitor (TKI): erlotinib
### EGFR-Rash Management

**Recommend:**
- Moisturize
  - Scent-free
- Protect: SPF (sun protection factor) 15+
- Do use
  - Hydrocortisone cream
  - Antibiotic Creams (metronidazole or clindamycin)
  - Oral tetracycline derivatives: minocycline and doxycycline
  - Oral antihistamines for itching

**Avoid:**
- Sun exposure
- Hot showers, hot baths, saunas
- Preventative retinoids
- Topicals that dry:
  - Alcohol containing
  - Benzoyl peroxide
  - Vitamin K cream
  - Pimecrolimus cream
  - Tazarotene cream

# EGFR-Rash Prevention vs. Treatment

<table>
<thead>
<tr>
<th>Prevention</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Topical</strong></td>
<td>• Topical</td>
</tr>
<tr>
<td></td>
<td>• Hydrocortisone 1% cream with moisturizer and</td>
</tr>
<tr>
<td></td>
<td>• Sunscreen twice daily</td>
</tr>
<tr>
<td></td>
<td>• Systemic</td>
</tr>
<tr>
<td></td>
<td>• Minocycline 100mg PO daily or</td>
</tr>
<tr>
<td></td>
<td>• Doxycycline 100mg PO twice a day (preferred in renal dysfunction)</td>
</tr>
<tr>
<td></td>
<td>• Systemic</td>
</tr>
<tr>
<td></td>
<td>• Fluocinonide 0.05% cream twice daily</td>
</tr>
<tr>
<td></td>
<td>• Clindamycin 1% twice daily</td>
</tr>
<tr>
<td></td>
<td>• Systemic</td>
</tr>
<tr>
<td></td>
<td>• Doxycycline 100mg PO twice a day</td>
</tr>
<tr>
<td></td>
<td>• Minocycline 100 mg PO daily</td>
</tr>
<tr>
<td></td>
<td>• Isotretinoin at low doses (20–30 mg/day) PO</td>
</tr>
</tbody>
</table>

Other EGFR Skin Toxicities

Hair Changes
- trichomegaly
- brittleness
- rare alopecia

Increased Radiation Dermatitis

Xerosis and Skin Fissures

Pruritus
- Occurs in ~50%
- moisturizer
- topical steroids
- gabapentin/pregabalin
- doxepin

Paronychia
- Bleach soaks: final concentration of 0.005% (approximately 1/4–1/8 cup of 6% bleach for 3–5 gal water)
- Biotin

Diarrhea

- Common with TKIs
- Generally mild
  - Grade 1 – 2: increase in stool frequency not exceeding 6 times above baseline
  - A little diarrhea all the time is not favorable
- Greatly affects quality of life

<table>
<thead>
<tr>
<th>Common Suspects</th>
<th>Incidence %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capecitabine (Xeloda)</td>
<td>55</td>
</tr>
<tr>
<td>Erlotinib (Tarceva)</td>
<td>20-60</td>
</tr>
<tr>
<td>Ibrutinib (Imbruvica)</td>
<td>51-63</td>
</tr>
<tr>
<td>Afatinib (Gilotrif)</td>
<td>96</td>
</tr>
<tr>
<td>Axitinib (Inlyta)</td>
<td>55</td>
</tr>
<tr>
<td>Bosutinib (Bosulif)</td>
<td>82</td>
</tr>
<tr>
<td>Crizotinib (Xalkori)</td>
<td>43-60</td>
</tr>
<tr>
<td>Dasatinib (Sprycel)</td>
<td>18-31</td>
</tr>
<tr>
<td>Imatinib (Gleevec)</td>
<td>25-59</td>
</tr>
<tr>
<td>Lapatinib (Tykerb)</td>
<td>65</td>
</tr>
<tr>
<td>Nilotinib (Tasigna)</td>
<td>14-28</td>
</tr>
<tr>
<td>Pazopanib (Votrient)</td>
<td>52-59</td>
</tr>
<tr>
<td>Regorafenib (Stivarga)</td>
<td>43-47</td>
</tr>
<tr>
<td>Sorafenib (Nexavar)</td>
<td>43-68</td>
</tr>
<tr>
<td>Sunitinib (Sutent)</td>
<td>40-66</td>
</tr>
<tr>
<td>Trametinib (Mekinist)</td>
<td>43</td>
</tr>
</tbody>
</table>

References are package inserts of each drug
Potential Mechanisms of Diarrhea

• For EGFR inhibition:
  • EGFR is expressed by gastrointestinal epithelium
  • EGFR inhibition leads to reduced growth and healing, mucosal atrophy
  • Excess chloride secretion caused by dysregulated EGFR signaling
• Non-absorbed drug and metabolites cause local irritation via fecal elimination
• VEGF inhibition: decreased microcirculation
  
  We don’t really know (at this time)

Bowen JM. Current Opinion Supportive and Palliative Care 2013:7(2);162-7
Diarrhea Management

YOU can have a big impact here

• Encourage adequate hydration
• Avoid high-fiber foods that can cause diarrhea and cramping
• Avoid coffee, tea, alcohol and sweets
• Avoid milk and milk products if they make diarrhea worse
• Avoid very hot or cold liquids
• Avoid greasy and spicy foods
• Loperamide 4 mg PO at onset and 2mg after each loose stool for up to 8 tablets per day
• If >5 loose stools per day – contact provider
Diarrhea Management – Other Considerations

- If watery and more than 5 episodes, rule out infection
- Consider fluids with electrolytes
  - Renal function
  - Fluid issues, such as congestive heart failure (CHF)
VASCULAR Endothelial Growth Factor (VEGF) Inhibitors
Sample Drugs with Anti-VEGF Activity

- Axitinib (Inlyta ®)
- Cabozantinib (Cometriq®)
- Pazopanib (Votrient ®)
- Regorafenib (Stivarga ®)

- Sorafenib (Nexavar ®)
- Sunitinib (Sutent ®)
- Vandetanib (Caprelsa ®)
Mechanism/Toxicity VEGF

- Decreased wound healing
- Increased risk of clots
- Increased blood pressure
- Proteinuria
# VEGF-Inhibition Toxicities – Hypertension

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Pharmacist role</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gradual increases in blood pressure</td>
<td>• Encourage adherence</td>
</tr>
<tr>
<td>• Suppression of nitric oxide production?</td>
<td>• Encourage home monitoring and logging data</td>
</tr>
<tr>
<td>• Indicative of clinical benefit?</td>
<td>• Assist with dose adjustments of BP meds</td>
</tr>
<tr>
<td></td>
<td>• Assist with identifying need to start BP med</td>
</tr>
<tr>
<td></td>
<td>• Initiate/adjust therapy if BP&gt;130/80*, or diastolic BP &gt;20 mmHg over baseline</td>
</tr>
<tr>
<td></td>
<td>(unless other patient-specific goals exist)</td>
</tr>
<tr>
<td></td>
<td>• CYP inhibition by verapamil and diltiazem – avoid with sorafenib and sunitinib</td>
</tr>
</tbody>
</table>

### VEGF-Inhibition Toxicities – Wound Healing

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Pharmacist role</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased wound healing</td>
<td>• Education about timing of planned surgical/invasive procedures</td>
</tr>
<tr>
<td></td>
<td>• Holding doses 14-28 days before and after procedure is sometimes advisable</td>
</tr>
<tr>
<td></td>
<td>• Seek medical attention if bleeding exceeds 25 mL</td>
</tr>
</tbody>
</table>
**VEGF-Inhibition Toxicities - Clots**

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Pharmacist role</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased risk of clots</td>
<td>• Education on signs/symptoms of blood clots</td>
</tr>
<tr>
<td>Arterial &gt; venous</td>
<td>• Decision support with when to seek further medical care</td>
</tr>
<tr>
<td></td>
<td>• Predisposing cardiovascular risk factors (ie, hypertension, hyperlipidemia, and diabetes) should be aggressively managed</td>
</tr>
</tbody>
</table>

A meta-analysis that included 10,255 patients in 10 studies

- 87 % with renal cell carcinoma
- Treated with sunitinib or sorafenib
- Incidence of arterial thrombotic events (ATE) was 1.4 % (Relative Risk 3.0 vs. controls)

Pazopanib = 3% ATE vs 0% placebo in renal cell carcinoma
Lenvatinib = 5% ATE vs 3% placebo
Ponatinib = 11%

RAF Inhibitors

- Sorafenib (Sutent®)
- Regorafenib (Stivarga®)
- Dabrafenib (Tafinlar®)
Hand-Foot Skin Reactions (HFSR)

• Palmar-plantar erythrodysesthesia
• Localized tender lesions, which appear in areas of trauma or friction
• VEGF–inhibition targets capillary endothelium?
• Clinically different from hand-foot syndrome with traditional chemotherapy
### Common Suspects

<table>
<thead>
<tr>
<th>Drug</th>
<th>% Incidence</th>
</tr>
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<tbody>
<tr>
<td>Capecitabine (Xeloda)</td>
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<td>Sorafenib (Nexavar)</td>
<td>21-69</td>
</tr>
<tr>
<td>Regorafenib (Stivarga)</td>
<td>45-67</td>
</tr>
<tr>
<td>Lapatinib (Tykerb) *with capecitabine</td>
<td>53</td>
</tr>
<tr>
<td>Dabrafenib (Tefinlar)</td>
<td>20</td>
</tr>
<tr>
<td>Axitinib (Inlyta)</td>
<td>27</td>
</tr>
<tr>
<td>Cabozantinib (Cometriq)</td>
<td>50</td>
</tr>
<tr>
<td>Sunitinib (Sutent)</td>
<td>14-29</td>
</tr>
<tr>
<td>Afatinib, Vemurafenib, Pazopanib</td>
<td>&lt;10</td>
</tr>
</tbody>
</table>

References: package insert of each drug
Hand-Foot Syndrome Management

Pharmacist Education:
- *Before* treatment, removal of pre-existing hyperhyperkeratotic areas (mani/pedi)
- Avoid hot water to hands and feet
- Avoid constrictive clothing and footwear
- Shoes with padded insoles

Options to treat:
- Emollients +/- cotton socks or gloves
- Keratolytics, such as topical urea or salicylic acid can be considered
- Topical steroids
- Topical analgesics (lidocaine 2%)
Cardiac Toxicities – QTc Prolongation

- Small but definite risks exist
- Correct hypokalemia and hypomagnesemia
- Obtain baseline ECG
- Obtain second ECG 7-10 days after start of TKI and any dose adjustment
- Concentration dependent

### Common Suspects

<table>
<thead>
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<tbody>
<tr>
<td>Nilotinib (Tasigna)</td>
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<tr>
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<tr>
<td>Lapatinib (Tykerb)</td>
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<tr>
<td>Dasatinib (Sprycel)</td>
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<tr>
<td>Vemurafenib (Zelboraf)</td>
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ECG = electrocardiogram
WARNING: QT PROLONGATION AND SUDDEN DEATHS

• Nilotinib prolongs the QT interval. Prior to Nilotinib administration and periodically, monitor for hypokalemia or hypomagnesemia and correct deficiencies. Obtain ECGs to monitor the QTc at baseline, seven days after initiation, and periodically thereafter, and following any dose adjustments.

• Sudden deaths have been reported in patients receiving nilotinib. Do not administer Nilotinib to patients with hypokalemia, hypomagnesemia, or long QT syndrome.

• Avoid use of concomitant drugs known to prolong the QT interval and strong CYP3A4 inhibitors.

• Avoid food 2 hours before and 1 hour after taking the dose.
**QT Prolongation & Drug Interactions**

<table>
<thead>
<tr>
<th>Strong CYP3A4 Inhibitors (examples)</th>
<th>Strong CYP3A4 Inducers (examples)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Ketoconazole</td>
<td>• Dexamethasone</td>
</tr>
<tr>
<td>• Itraconazole</td>
<td>• Phenytoin/Phenobarbital</td>
</tr>
<tr>
<td>• Voriconazole</td>
<td>• Carbamazepine</td>
</tr>
<tr>
<td>• Clarithromycin/Erythromycin</td>
<td>• Rifampin/rifabutin/rifapentine</td>
</tr>
<tr>
<td>• Atazanavir</td>
<td>• St. John’s Wort</td>
</tr>
<tr>
<td>• Indinavir</td>
<td></td>
</tr>
<tr>
<td>• Nefazodone</td>
<td></td>
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<tr>
<td>• Nelfinavir</td>
<td></td>
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<tr>
<td>• Ritonavir</td>
<td></td>
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<tr>
<td>• Saquinavir</td>
<td></td>
</tr>
<tr>
<td>• Telithromycin</td>
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</tbody>
</table>

**QT Prolonging Drugs (examples)**

• Amiodarone
• Sotolol
• Dofetilide
• Haloperidol
• Methadone
• Serotonin antagonists

*Your role = help to identify, monitor and adjust for potential interactions*
Heart Failure/Decreased LVEF with KIs

- Found in multi-kinase inhibitors including VEGF inhibitors
- Lapatinib (anti-HER-2)

<table>
<thead>
<tr>
<th>Drug</th>
<th>% with ↓ LVEF</th>
<th>Symptomatic/clinical CHF</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pazopanib</td>
<td>6.9%</td>
<td></td>
<td>van der Graaf WT, Tissue and Bone Sarcoma Group, PALETTE study group Lancet.</td>
</tr>
<tr>
<td>Ponatinib</td>
<td>4%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

LVEF=left ventricular ejection fraction, HER=human epidermal growth factor receptor
What Impacts Adherence?

**Personal factors**
- Health beliefs
- Social Support
- Socioeconomic status
- Education level
- Comorbid Illness

**Treatment factors**
- Schedule
- Onset of benefit
- Side effects
- Cost

**Interaction with System**
- Satisfaction with care
- Insurance coverage
- Convenience
- Educational Resources
- Access to healthcare/clinic

Tailor monitoring plan and follow-up based on standard initial assessment

Ruddy CA Cancer J Clin 2009:59:56-66
Improving Adherence and Persistence

Develop a tailored care plan with the patient

- Maintain calendar or medication list
- Complete a pill diary
- Establish a routine
- Set electronic reminders
- Use pillboxes with multiple compartments
- Engage family and support system
- Connect with local support group
Improved Follow-up

• Follow-up calls, emails, texts
• Standard toxicity/compliance visit at 1-2 weeks
• Use of technology:
  • MEMs caps: microelectronic monitoring systems
  • Digital ingestion tracking system
Sample flow - Pharmacist

Initial visit
- Counseling
- Consent
- Med rec
- Drug interaction assessment
- Establish adherence plan

2 week visit
- Toxicity assessment
- Lab review
- Adherence review (per patient)
- Follow-up education
- Plan for symptom management and adherence

1-2 month visits alternating with oncologist
- Toxicity assessment
- Lab review
- Adherence review (refills and per patient)
- Follow-up education
- Plan for symptom management and adherence
**Proof of Concept - Using Patient Reported Outcomes to Improve/Tailor Care**

**Design:** Single-center, randomized

**Inclusion:**
- Advanced solid tumors
- Receiving outpatient chemotherapy

**Exclusion:**
- Investigational therapies

**Randomized 2:1**

**Intervention arm (STAR – symptom tracking and reporting):**
- Self-report on 12 common symptoms
  - Tablet or at computer kiosk
  - At each visit and/or weekly via home computer
- STAR triggered e-mail alerts to nurses when symptom score increased by
  - > 2 points (on 0-5 scale) or
  - > absolute grade 3

**Usual care**

<table>
<thead>
<tr>
<th></th>
<th>Intervention group</th>
<th>Usual Care group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=766</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health-related QOL improvement (%)</td>
<td>34</td>
<td>18</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Health-related QOL worsened (%)</td>
<td>38</td>
<td>53</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ER admission (%)</td>
<td>34</td>
<td>41</td>
<td>0.02</td>
</tr>
<tr>
<td>Hospital admission (%)</td>
<td>45</td>
<td>49</td>
<td>0.08</td>
</tr>
<tr>
<td>Duration of chemotherapy (m)</td>
<td>8.2</td>
<td>6.3</td>
<td>0.002</td>
</tr>
<tr>
<td>1-year overall survival (%)</td>
<td>75</td>
<td>69</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Closing remarks/conclusion

• Comprehensive oral chemotherapy counseling can help eliminate errors
• Challenges with oral chemotherapy reimbursement may be reduced with educated staff and financial assistant options
• Diarrhea, skin toxicities, and cardiac complications are common issues with oral therapies
• Pharmacists are in a key position to help manage chronic side effects to improve adherence and persistence
• Tailor your education and monitoring plan to the patient’s needs
Oral Parity Legislative Update

Oral Anti-Cancer Therapy Access Legislative Landscape - 2018

- Active Campaign
- Signed into law

43 states have enacted Oral Anti-Cancer Therapy access laws:

2008 Oregon
2009 Indiana, Iowa, Hawaii, District of Columbia
2010 Vermont, Connecticut, Kansas, Colorado, Minnesota
2011 Illinois, New Mexico, Texas, New York, Washington
2012 New Jersey, Virginia, Maryland, Nebraska, Delaware, Louisiana
2013 Massachusetts, Oklahoma, Utah, Nevada, Florida, Rhode Island, California
2014 Maine, Missouri, Wisconsin, Kentucky, Georgia, Arizona, Ohio
2015 Wyoming, South Dakota, West Virginia, Mississippi, North Dakota, New Hampshire
2016 Alaska, Pennsylvania
2017 Arkansas

http://peac.myeloma.org/oral-chemo-access-map/ accessed 10/5/2018
Assessment Questions

When counseling a patient on a new oral chemotherapy medication, which of the following would be important to include?

A. Mix your chemotherapy in the same pill box as other medications
B. If you have problems swallowing, chew the medication before to make it easier
C. Anyone may help give the medication to the patient with no precautions
D. Store medication at room temperature in a dry location away from pets and children
Which of the following is a Foundation that can be used to assist in the cost of oral oncology medications?

A. Cancer Alliance
B. HealthWell Foundation
C. Patient Financial Assistance Foundation
D. Good Weeks
Which of the following therapies is an accepted treatment option for epidermal growth factor inhibitor TKI rash:

A. Benzoyl peroxide
B. Retinoids
C. Topical steroids
D. Sunlight/Ultraviolet exposure
The best adherence plan may include which of the following?

A. Involves tailoring the education, administration schedule, compliance plan, and monitoring plan to the patient
B. Uses microelectronic monitoring systems (MEMs) caps
C. Includes a written administration calendar
D. Involves setting an app on the patient’s phone to remind when to take dose(s)
With oral oncolytics, which of the following is true regarding diarrhea

A. An uncommon toxicity and can occur in less than to 10% of patients taking certain oral oncolytics
B. Usually mild (grade 1-2 toxicity) and can be managed with octreotide
C. Caused by a cholinergic reaction of the drug
D. Self-care such as adequate hydration, avoidance of irritating factors (greasy, spicy foods, milks and cheeses, excessive fiber, etc.) should be encouraged
Opportunities in the Rise of Oral Oncologic Therapy

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