Oral Chemotherapy Medication Make Up 40% of All Recently Approved Cancer Drugs: “What Does the Pharmacist Need to Know?"

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Speaker Disclosures

- Speakers Bureau
  - Pharmacyclics
  - Seattle Genetics
  - Merck
  - Celgene

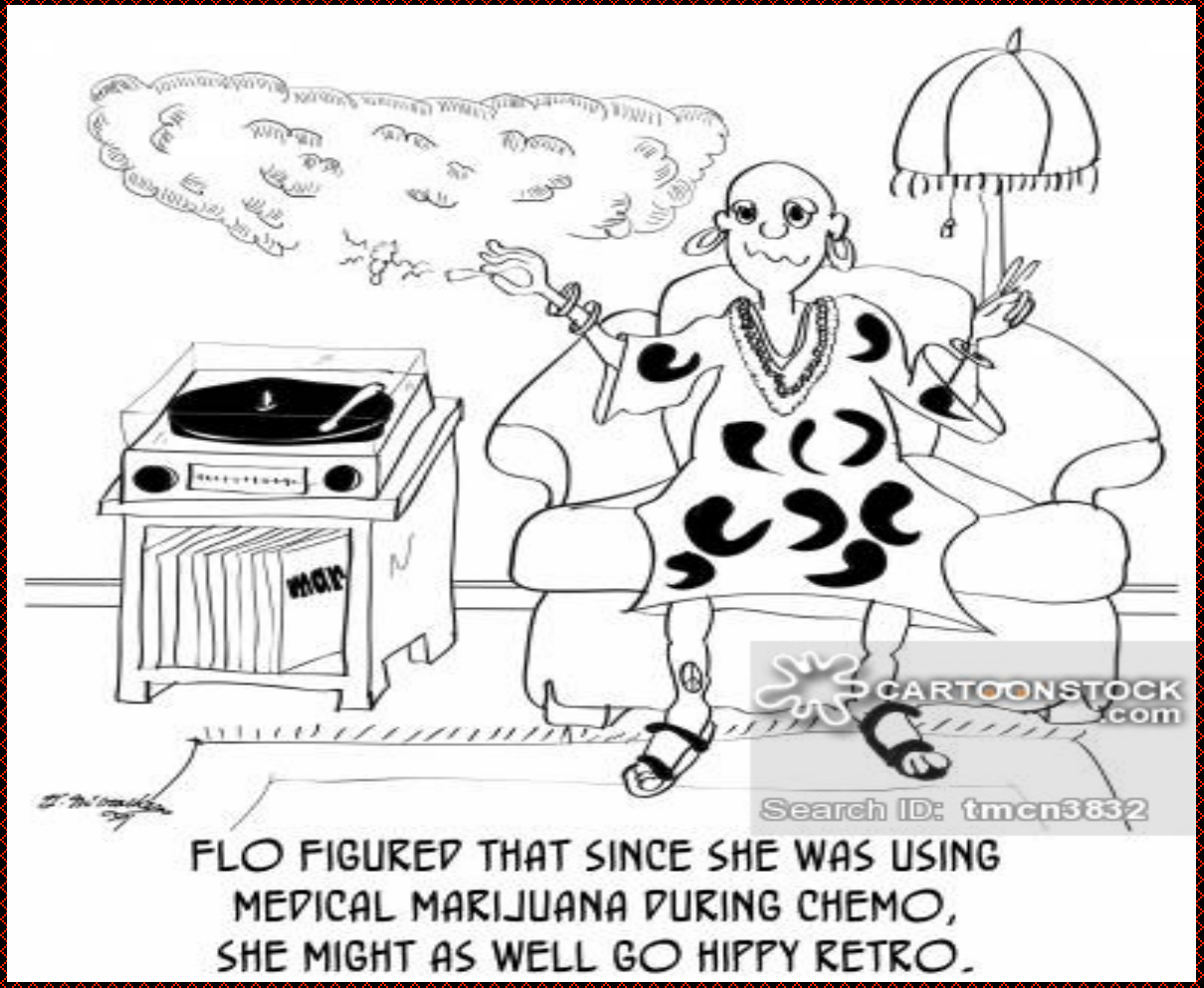
Learning Objectives

1. Recall the indication for each oral chemotherapy medication presented.

2. Identify the most important counseling point for 3 medications presented.

3. Discuss the dosing guidelines for the oncology medications presented.

4. Explain the general types of oncology drug interactions.


FLO FIGURED THAT SINCE SHE WAS USING
MEDICAL MARIJUANA DURING CHEMO,
SHE MIGHT AS WELL GO HIPPY RETRO.
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Oral Chemotherapy Agents

- Up to 2012 over 40 oral cancer therapies have been FDA approved.
- Since 2015 to the first half of 2016 over 21 therapies were approval. (11 are oral)
  - Eleven are "first in class" agents
  - Sequencing therapy
  - Pharmacogenomics
  - Continuing education will be mandatory

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Oral Chemotherapy Drugs

- Two major problems with oral therapies
  1. Patients have less contact with health –care providers
     - Less contact with physician
     - Less chance for double checking therapy
     - Less chance for laboratory double checks
     - Nursing have less contact with patients
     - Less chance for discharge follow-up

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Oral Chemotherapy Drugs

- Two major problems with oral therapies (cont.)
  2. Even dispensed through Specialty Pharmacies less counseling is seen with each patient
     - Most prescriptions are mailed
     - Less relationship with your pharmacist
     - Less chance for laboratory and imaging checks
     - Less chance for discharge follow-up

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Oral Chemotherapy Drugs

- Oral cancer agents on the market (1 July 2016)
  - Seventy-seven agents approved for use in the US
  - Seventeen are now generic
  - Five or more are long-term agents (compassionate approval)
  - At least 20 have been dispensed in general retail settings such as Costco and CVS

Important Oral Chemotherapy

- Definition
  - High use in cancer
  - Higher cure rate then previous therapy
  - High possibility of general retail dispensing
  - Newer therapy

Palbociclib	**Multiple Myeloma**
Ixazomib	Basal Cell Ca
Ibrutinib	NSCLC
Sonidegib	Breast Cancer
Alectinib	Melanoma
Cobimetinib	CLL

Palbociclib

- Indication: Postmenopausal, hormone receptor +, HER2 -, advanced stage breast cancer. Used with endocrine therapy.

- MOA: Reversible, selective inhibitor of cyclin dependent kinase (CDK) 4 and CDK 6 (cell cycle regulation)

- Two trials: with letrazole and with fulvestrant, doubled or tripled PFS, both combinations were statistically significant.

Package Insert Ibrance 2/2015

Palbociclib

- Dosage: 125mg daily – 3 weeks on and 1 week off

Dose reductions for grade 3 hematologic or 4 non-heme: 100mg daily then 75mg daily

- Counseling: higher incidence of neutropenia and leukopenia with combination

- Endocrine therapy is given at the standard package insert level for both drugs

Package Insert Ibrance 2/2015

Ixazomib

- Indication: Multiple myeloma after one prior therapy. Admin c lenalidomide and dexamethasone (2nd line)

Ixazomib	Day 1	Day 8	Day 15	Week off
Lenalidomide	Days 1-7	Days 8-14	Days 15-21	Week off
Dexamethasone	Day 1	Day 8	Day 15	Day 22

- MOA: Reversible proteasome inhibitor, (beta 5 subunit of the 20S proteasome).

- ILD vs placebo LD – improved PFS 6 months in second line therapy. Statistically significant

Package Insert Ninlaro 11/2015

Ixazomib

- Dosage: 4mg on day 1, 8, 15 of 28 day cycle (empty stomach) (3 cap package), also 3mg and 2.3 mg sizes. Dose reductions for neuropathy, grade 3 hematologic or 4 non-heme: 3mg daily then 2.3mg daily

- Counseling: Peripheral neuropathy, thrombocytopenia, gastro-intestinal (diarrhea), peripheral edema, rash, and hepatotoxicity

- Can be all oral therapy, Don't take Ixazomib and Dexamethasone together. Refer to package insert for multiple dose guidelines and information

Package Insert Ninlaro 11/2015

Ibrutinib

- Indication: Mantle cell lymphoma (one prior), CLL/SLL (deletion 17p), Waldenström's macroglobulinemia
- MOA: inhibitor of Bruton's Tyrosine Kinase. Forms a covalent bond with a cysteine residue in the BTK active site, leading to inhibition of BTK enzymatic activity
- Multiple 1st and 2nd line studies. MCL approved based on response. CLL stopped without median stat for ibrutinib.

Package Insert Imbruvica 5/2016

Ibrutinib

- Dosage: 140mg capsules – MCL; 4 caps daily, CLL or WM; 3 caps daily. Dose reduction for toxicity outlined in package insert.

- Counseling: Hemorrhage, Infections, Cytopenias, Atrial Fibrillation, Hypertension, Second Primary Malignancies, Tumor Lysis Syndrome

- Interesting long history, different dose for MCL and CLL/WM, CYP 3A liver enzymes, and potentially high levels in the elderly

Package Insert Imbruvica 5/2016

Sonidegib

- Indication: Locally advanced basal cell carcinoma (Second line), (Hedgehog pathway)
- MOA: Sonidegib binds to and inhibits Smoothened, a transmembrane protein involved in Hedgehog signal transduction.
- One study – 58% overall response rate with 5% complete responses. Some patients have reached 18 months and median response rate has not been reached.

Package Insert Odomzo 7/2015

Sonidegib

- Dosage: 200mg daily on an empty stomach. Comes in 200mg capsule.
- Counseling: Embryo-fetal toxicity, musculoskeletal and laboratory chemistry changes
- Semen showed evidence of sonidegib exposure up to 8 months after therapy. An 800mg trial dose did not improve outcome.

Package Insert Odomzo 7/2015

Alectinib

- Indication: a kinase inhibitor for treatment of patients with anaplastic lymphoma kinase (ALK)-positive, metastatic non-small cell lung cancer (NSCLC) who have progressed or are intolerant to crizotinib

- MOA: Targets ALK and RET. Decreased tumor cell viability in multiple cell lines harboring ALK fusions, amplifications, or activating mutations.

- Two studies based on ORR and duration of response. 7 to 12 months response and 5 to 9 months duration.

Package Insert Anecensa 12/2015

Alectinib

- Dosage: 600 mg orally twice daily with meals. (150mg caps). Dose modifications to 450mg and 300 mg for adverse effects.
- Counseling: Hepatotoxicity, Interstitial Lung Disease (ILD)/ Pneumonitis, Bradycardia, and Myalgia and Creatine Phosphokinase (CPK) Elevation.
- No pharmacokinetic interactions, missed or vomited dose advised patients not to take an extra dose.

Package Insert Alecensa 12/2015

Cobimetinib

- Indication: treatment of unresectable or metastatic melanoma with a BRAF V600E or V600K mutation. Use with vemurafenib.
- MOA: reversible inhibitor of mitogen-activated protein kinase (MAPK)/extracellular signal regulated kinase 1 (MEK1) and MEK2. MEK proteins are upstream regulators of the extracellular signal related kinase (ERK) pathway
- One large study – 40% improvement in ORR. Statistically significant.

Package Insert Cotellic 11/2015

Cobimetinib

- Dosage: 60mg daily on days 1 – 21 of a 28 day cycle. (20mg tabs). For adverse rections or concurrent CYP3A dosing reductions to 40mg and 20mg occur.

- Counseling: Second Primary Malignancies, Hemorrhage, Rash, Cardiomyopathy, Retinopathy, Hepatotoxicity, Rhabdomyolysis, and Severe Photosensitivity

- Vemurafenib dosed on different but usual schedule.

Package Insert Cotellic 11/2015

Breast Cancer Oral Treatments

- Capecitabine – Generic, multiple uses and schedules. Usually used in combination
- Lapatinib – HER2+ second line, used in combination with capecitabine and letrozole
- Palbociclib – Approved in February 2015

Lung Cancer Oral Treatments

- Afatinib – Approved July 2013. Similar to erlotinib.
- Cerritinib – Approved April 2014
- Crizotinib – Approved August 2011. Expanded to ROS-1+ this year
- Erlotinib – Approved November 2004
- Gefitinib – Approved May 2003 and July 2015
- Alactinib – Approved December 2015

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Melanoma Oral Treatments

- Vemurafenib – Approved August 2011
- Cobimetinib – Approved November 2015
- Dabrafenib – Approved May 2013
- Trametinib – Approved May 2013

Prostate Cancer Oral Treatment

- Abiraterone – Approved April 2011. Used in combination and alone. Improved treatment of prostate ca.

- Enzalutamide – Approved August 2012. Used much like abiraterone. Different pathway than old prostate cancer treatment.

Renal Cell Carcinoma Oral Treatment

- Sunitinib – Approved January 2006. Approved for Pancreatic ca in May 2011
- Pazopanib – Approved October 2009. Approved for soft tissue sarcoma in April 2012
- Sorafenib – Approved November 2007 and Thyroid ca in November 2013
- Everolimus – Approved 2009 and other indications
- Axitinib – Approved January 2012
- Cabozantinib – Approved April 2016

Other Oral Medications Approved Since 2015

• Lenvatinib	Thyroid Cancer
• Panobinostat	Multiple Myeloma
• Trifluridine & Tipiracil	Colorectal Camcer
• Osimertinib	NSCLC
• Venetoclax	CLL c 17p deletion

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Specialty Pharmacists

- Unlimited opportunities for pharmacist involvement
- Expansion of pharmacy services
  - Capture prescriptions that would normally go to the outside
  - Become a financial benefit for the hospital
- Many patients are discharged from the inpatient setting on oral chemotherapy
- Oncology trained pharmacists can be imbedded in ambulatory clinics in large medical centers to improve outcomes for oral medications

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Oral Chemotherapy Dosing and Monitoring

- Multiple tablet or capsules for each dose
  - Allow for variability of dose for toxicities
  - Always ask patient to repeat instructions
- Administration questions
  - Empty stomach?
  - How many times a day
  - Continuous or intermittent therapy
  - Toxicities that can be addressed before therapy is started
- Drug Interactions

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Inpatient Cancer Pharmacists

- Improve use of oral chemotherapy in the inpatient setting
- Provide discharge counseling for patients with EMR documentation
- Have drugs approved for ambulatory use for dispensing at discharge
- Guide patients to ambulatory pharmacies that are hospital imbedded

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Inpatient Cancer Pharmacist

- Provide REMS documentation for inpatient medications
- Ensure REMS documentation is complete for medication that cannot be dispensed from the hospital pharmacy
- Improve patient compliance by a provision of follow-up after care
- Decrease the time that cancer patients wait for expensive chemotherapy

Ambulatory Cancer Pharmacist

- Improve the process of starting patient on oral chemotherapy
- Prescreening patients that may receive oral chemotherapy
  - Start prior authorizations
  - Decrease waiting times
- Increase prescription fill rates at the hospital retail pharmacy
- Makes pharmacist a more integrated part of the team
- Provides a show place to show the benefit of pharmacists in the ambulatory arena and the financial benefit to the hospital

Ambulatory Cancer Pharmacist

- Provide similar laboratory and double check services that are utilized on parenteral chemotherapy
- Establish relationships with outside specialty pharmacies to improve patient care for your patients
- Provide financial and prior authorization for patients using pharmacy technicians
- Provide better patient counseling
- Provide continuous patient monitoring through phone calls and patient visits by the pharmacist

Oncology Specialty Pharmacist Benefits

- Decreased medication manipulation/documentation time used by physicians and nurses
- Improved medication reimbursement
- Improved workflows
- Develop oral medication protocols for the EMR or paper system
  - Help alert providers to to specific medication issues
  - Ensure appropriate laboratory monitoring
  - Reduce medication errors
- Improve patient adherence and potentially outcomes

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Starting Oncology Specialty Services

- Get clinic to demand services
- Look for ways to justify by targeting clinics with high oral chemotherapy utilization
- Built note templates in the EMR
- Create monitoring forms
- Provide antiemetic or antidiarrheal prescribing
- Get pharmacy technicians involved
- Formulate appeals letters

Future Pharmacy Directions

- Recording of patient outcomes that are measurable and show the value of the pharmacist in the clinic
- Improve pharmacy services for oral chemotherapy to the level most provide for I.V. chemotherapy
- Assist with the Quality Oncology Practice Initiative (QOPI) measures outlined by ASCO
- Assist with tumor genomics for evidence

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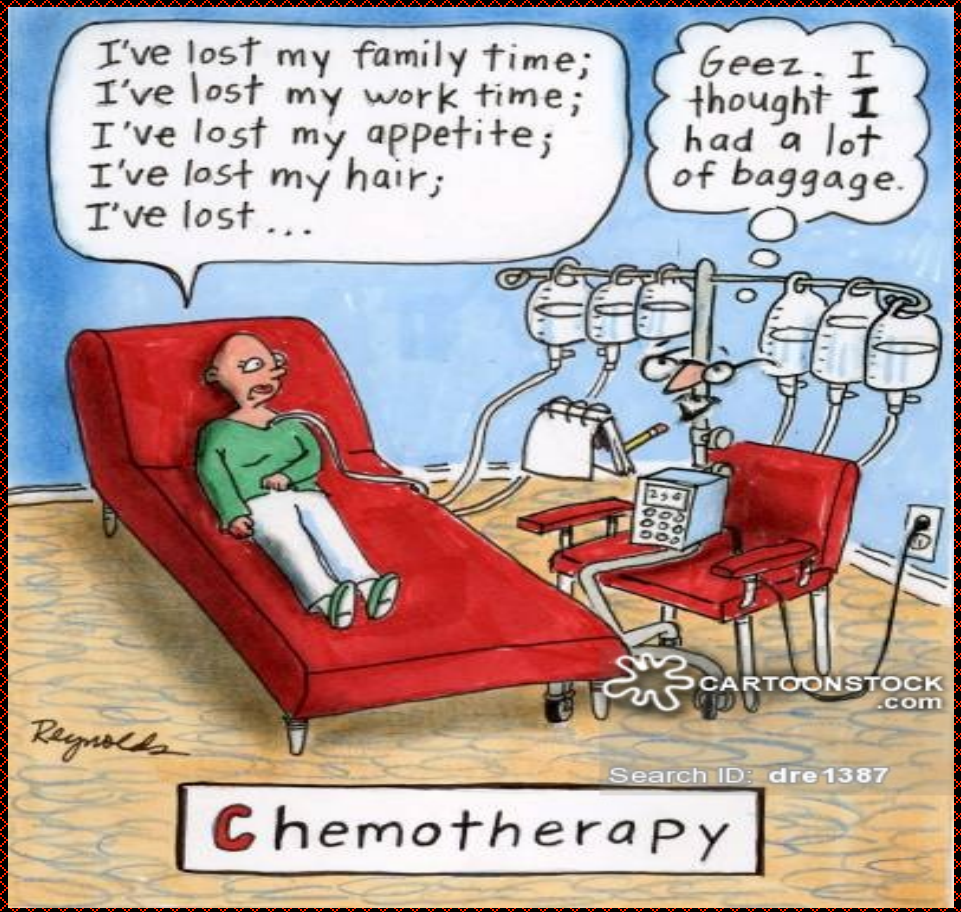
I've lost my family time;
I've lost my work time;
I've lost my appetite;
I've lost my hair;
I've lost ...
Geez. I thought I had a lot of baggage.
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Chemotherapy

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"I didn't take the pills you gave me. I couldn't get the child-proof cap off."

Tools to Stay Up-To-Date

- Drug approval list (FDA)
  - www.fda.gov/drugs/newsevents/ucm130961.htm
- APhA's DrugInfoLine
  - www.aphadruginfoline.com
- Hematology/Oncology Pharmacy Association
  - www.hoparx.org/

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Thank You