Oral Chemotherapy: Drug-Drug Interactions (DDIs) & Clinical Pearls

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Pharmacist Objectives

- List common oral chemotherapy drug-drug interactions
- Explain recommendations for drug-drug interactions
- Describe oral chemotherapy clinical pearls
  - Storage and handling
  - Counseling
  - Side effects

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Technician Objectives

- List common oral chemotherapy drug-drug interactions
- Explain common drug-drug interactions
- Describe side effects of drug-drug interactions

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Disclosure

The speaker has no financial conflicts of interest to disclose.

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Oral Chemotherapy

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Resources

Organization	Guidelines or Guidance
American Society of Clinical Oncology (ASCO) Oncology Nursing Society (ONS)	Safety QOPI
American Society of Health Systems Pharmacists (ASHP)	Preventing Medication Errors
Hematology Oncology Pharmacists Association (HOPA) Oncology Nursing Society (ONS)	Best Practices for Oral Oncolytics Oral Chemotherapy Education Sheets
National Community Oncology Dispensing Association (NCODA) American Society of Clinical Oncology (ASCO)	Dispensing Standards

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Oral Chemotherapy: DDIs

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Drug-Drug Interactions

Kam, Teresa. Clinical Pearls: Significant Drug Interactions. 2 August 2014.

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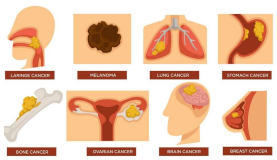
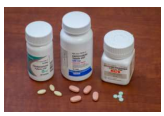
Risk Factors for DDIs





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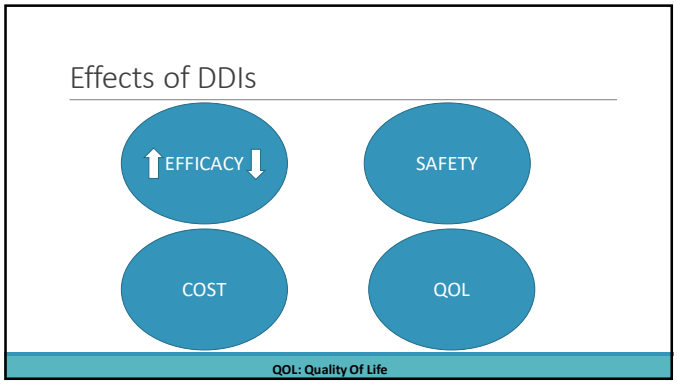
Effects of DDIs
EFFICACY
SAFETY
COST
QOL
QOL: Quality Of Life

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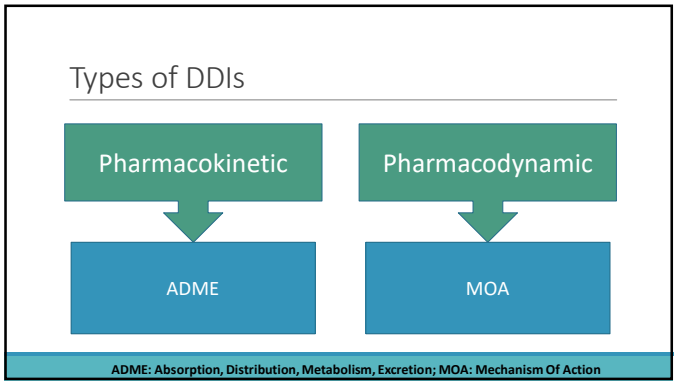
Types of DDIs
Pharmacokinetic
Pharmacodynamic
ADME
MOA
ADME: Absorption, Distribution, Metabolism, Excretion; MOA: Mechanism Of Action

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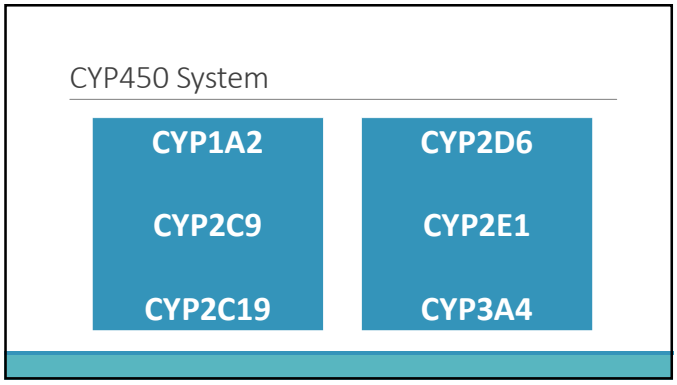
CYP450 System
CYP1A2
CYP2C9
CYP2C19
CYP2D6
CYP2E1
CYP3A4

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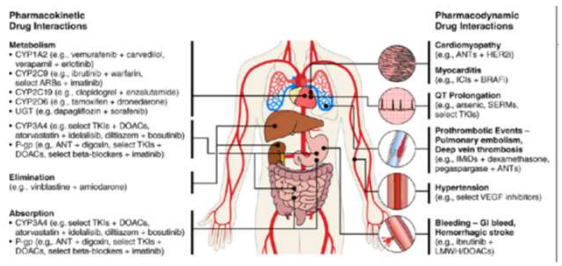

Beavers, Craig. Et al. Cardio-Oncology Drug Interactions: A Scientific Statement From the American Heart Association. 7 Mar 2022 https://doi.org/10.1161/CIR.0000000000001056Circulation. 2022;145:e811–e838

TKI: Tyrosine Kinase Inhibitors; DOACs: Direct Oral Anticoagulants; PGP: P-glycoprotein

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Common DDIs with Oral Chemotherapy

Class	Agents
Acid-Suppressor Drugs	PPIs vs H2RAs
Anticoagulant	Warfarin
Antibiotic/antifungal	Erythromycin

PPI: Proton pump inhibitor; H2RA: Histamine Type-2 Receptor Antagonists

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Audience Response Question

If chemotherapy is given with phenytoin, a CYP450 inducer, then:

A. The chemotherapy dose should be increased
B. The chemotherapy dose should be decreased
C. The phenytoin dose should be increased
D. The phenytoin dose should be decreased

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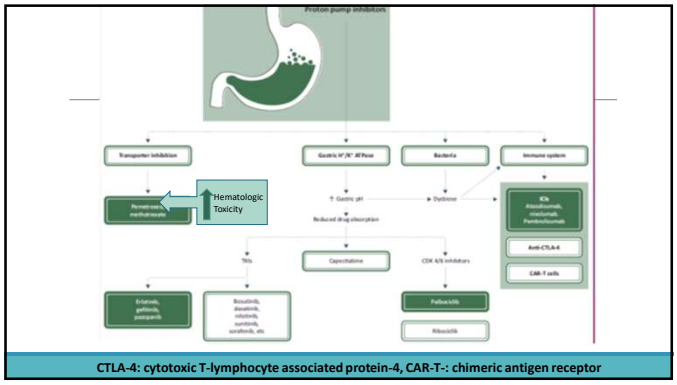

CTLA-4: cytotoxic T-lymphocyte associated protein-4, CAR-T-: chimeric antigen receptor

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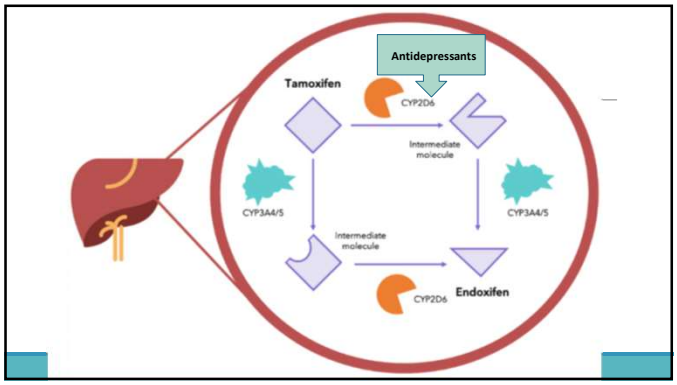

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QT Prolongation Drugs

CLASS EXAMPLE ONCOLOGY INDICATION(S)	DRUG(S)
Antineoplastic Agent Acute Promyelocytic Leukemia	Arsenic Trioxide
Antifungal Agents Antifungal prophylaxis in leukemias	Fluconazole, posaconazole, voriconazole
Fluoroquinolones Antibiotic prophylaxis in leukemias	Ciprofloxacin, levofloxacin, moxifloxacin
Macrolide antibiotics Prophylaxis/treatment	Azithromycin, clarithromycin, erythromycin
Tyrosine Kinase Inhibitors (TKIs) Various: NSCLC, CML, Renal, Melanoma, GYN, etc.	Crizotinib, lapatinib, nilotinib, sorafenib, sunitinib, pazopanib, vandetanib, vemurafenib
5HT3 antagonists Prevention/treatment of CINV	Ondansetron, palonosetron, granisetron, dolasetron

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Patient Case

VA is a 46 year old female with stage III breast cancer and presents to the clinic today for cycle 2 of 4 of AC (doxorubicin/cyclophosphamide). She mentions that she had nausea and vomiting 7 days after her cycle last time and the premedication's she received didn't seem to help. She has stage III breast cancer, epilepsy (tonic clonic seizures).

Medications:

Phenytoin 300mg po daily

Chemotherapy Regimen (every 2 weeks x 4 cycles, C2 to start tomorrow):

Doxorubicin (Adriamycin ®) 60mg/m^2 IV day 1 , Cyclophosphamide (Cytoxan ®) 600mg/m^2 IV day 1

Premedications (prior to each cycle):

Aprepitant (Emend ®) 125mg PO x 1 followed by aprepitant 80mg days 2 and 3, Palonosetron (Aloxi ®) 0.25mg IV x 1, Dexamethasone (Decadron ®)8mg IV x 1 followed by 8mg PO days 2, 3 and 4

Are there any drug drug interactions that would worsen her nausea and vomiting?

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Pharmacist's Role for DDIs

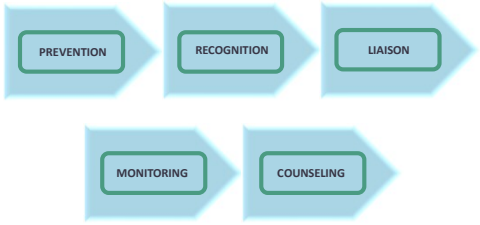

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Table 1. Example of Completed DIPS Form

DIPS QUESTIONS	Answer/ Score	Comments
1. Are there previous *credible* reports of this interaction in humans?	NA / 0	At the time of the report, 1 case report purporting an interaction and 1 report of 6 cases without an interaction had been published.[16,19] Neither report met the criteria for a credible report; both are disregarded as evidence in this case.
2. Is the observed interaction consistent with the known interactive properties of precipitant drug?	no / –1	Cyclosporine is a substrate for CYP3A4 and P-glycoprotein. Azithromycin is not known to inhibit CYP3A4 or P-glycoprotein.
3. Is the observed interaction consistent with the known interactive properties of object drug?	NA / 0	Since no known properties of azithromycin affect cyclosporine, the answer is NA.
4. Is the event consistent with the known or reasonable time course of the interaction (onset and/or offset)?	yes / 1	The time course of the change in cyclosporine concentrations would be consistent with a change in its elimination.
5. Did the interaction remit upon dechallenge of the precipitant drug with no change in the object drug? (If no dechallenge, use "Unknown or NA" and skip Question 6).	yes / 1	Stopping azithromycin did coincide with a fall in the concentration of cyclosporine.
6. Did the interaction reappear when the precipitant drug was readministered in the presence of continued use of object drug?	no / 0	No rechallenge was attempted.
7. Are there reasonable alternative causes for the event?	yes / –1	As noted by the authors, alternative reasons existed (eg, cytokine-induced inhibition of CYP3A4 metabolism) that could lead to reduced cyclosporine metabolism.
8. Was the object drug detected in the blood or other fluids in concentrations consistent with the proposed interaction?	yes / 1	Cyclosporine concentrations were measured and varied appropriately with the administration and discontinuation of azithromycin.
9. Was the drug interaction confirmed by any objective evidence consistent with the effects on the object drug (other than drug concentrations from question 8)?	NA / 0	There was no other evidence of the interaction except elevated cyclosporine concentrations.
10. Was the interaction greater when the precipitant drug dose was increased or less when the precipitant drug dose was decreased?	NA / 0	There was no change in the precipitant drug dose.

DIPS = Drug Interaction Probability Scale; NA = not applicable.

Horn JR, Hansten PD, Chan LN. Proposal for a new tool to evaluate drug interaction cases. Ann Pharmacother. 2007 Apr;41(4):674-80. doi: 10.1345/aph.1H423. Epub 2007 Mar 27. PMID: 17389673.

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Oral Chemotherapy: Clinical Pearls

Prescribing | Dispensing | Education
Monitoring | Practice Management | Adherence

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PRESCRIBING

THE ROLE OF A PHARMACIST
❖ Developing templates, protocols, formulary, guidelines
❖ Selecting the appropriate patient: financial, access
❖ Indication per cancer, PMH, DDIs, labs
❖ Precision medicine, clinical cancer pathways

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DISPENSING

THE ROLE OF A PHARMACIST
➢ Specialty Pharmacy Benefits
➢ Robust communication with provider and patient
➢ Prior authorization and special programs
➢ Coordination amongst all parties involved

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EDUCATION

THE ROLE OF A PHARMACIST
○ Verbal and written
○ Expectations for handling, costs, AE (>30%) and administration
○ At initiation and throughout treatment
○ Follow up calls every 2 weeks

AE: Adverse Effects

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MONITORING

THE ROLE OF A PHARMACIST
✓ Symptom management
✓ Collaborative practice agreements
✓ Labs, tests, supportive care medications

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PRACTICE MANAGEMENT

THE ROLE OF A PHARMACIST
❑ Telepharmacy/virtual visits
❑ Tracking patient behavior
❑ Financial justification

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ADHERENCE

THE ROLE OF A PHARMACIST	
❑ Patient diaries	❑ Medication calendars
❑ Monitoring plasma levels	❑ Incorporation in daily routine
❑ Cell phone alarms	❑ Storing in accessible location

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STORAGE AND HANDLING

*OCA= Oral Chemotherapy Agent

- Store medications as instructed by the pharmacist, in a dry location, away from light. Although most OCAs are stored at room temperature, some may require refrigeration.
- Keep OCAs out of reach of children and pets.
- Leave OCAs in the provided packaging until ready to be taken.
- Wash hands with soap and water prior to taking the dose.
- Caretakers should put on gloves to avoid touching the medication (gloves are not necessary for the patient).
- Administer the medicine immediately by mouth with water.
- Remove gloves and do not use them for anything else. Throw gloves and medicine cup into the household trash container.
- Wash hands with soap and water.
- If a daily pill box or pill reminder is used, a separate one should be used for OCAs. Do not mix other medications into the box with chemotherapy. The person filling the box or reminder should wear gloves (gloves are not necessary for the patient). When empty, the box or reminder should be washed with soap and water before refilling. Wash hands with soap and water after the task is complete, whether or not gloves are worn.
- Do not throw away OCAs in the trash and do not flush down the sink or toilet. Talk to your care provider or pharmacist about proper disposal of OCAs.
- When traveling, OCAs should be put in a sealed plastic bag. Ask the pharmacist if any additional travel precautions are required.

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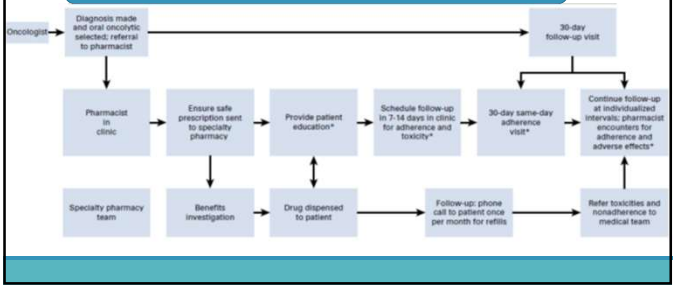
ORAL ONCOLYTIC MANAGEMENT



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Audience Response Question

Pharmacists can assist with oral oncolytic management by:

A. Prescribing
B. Dispensing
C. Education
D. All of the above

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Training

The National Community Oncology Dispensing Association

- Best practices for dispensing
- Training for all parties involved
- Processes to ensure follow ups are being done
- Continuing education
- Standardized approach

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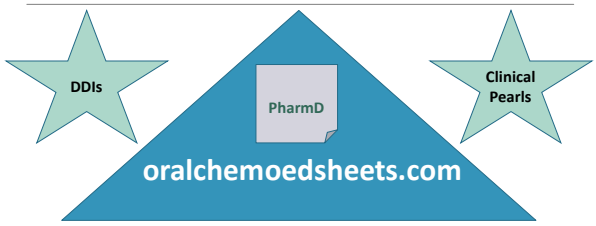
Conclusion



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