DDI-fficult Decisions: Navigating Drug Interactions in Oral Oncology Regimens

CE Presentation

02/12/2026 | Sandi Thein Sein, PharmD, PGY2 Oncology Pharmacy Resident, and Aurora St. Luke's Medical Center

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Disclosures

The planner(s) and speaker(s) have indicated that there are no relevant financial relationships with any ineligible companies to disclose.

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Learning Objectives

- Identify oral oncology agents with high drug-drug interaction (DDI) risks and describe the key pharmacokinetic and pharmacodynamic mechanisms that contribute to potential interaction.
- Explain how drug interactions involving CYP450 enzymes influence clinical outcomes.
- Describe the ways acid-suppressing agents interact with oral chemotherapy and summarize considerations for management.
- Explain how QT-prolongation agents interact with oral chemotherapy and outline key principles to monitor and prevent QTc prolongation.

Abbreviations

AML – Acute myeloid leukemia

BCL-2 - B-cell lymphoma 2

BCR-ABL - fusion of the Breakpoint Cluster Region gene (from chromosome 22) and the Abelson murine Leukemia gene (from chromosome 9)

BRAF - B-Raf proto-oncogene, serine/threonine kinase

BTK - Bruton's tyrosine kinase

CI – Confidence interval

CLL – Chronic lymphocytic leukemia

CRC – Colorectal cancer

EGFR - Epidermal growth factor receptor

FLT3 - Fms-like tyrosine kinase 3

H2RA – Histamine 2 receptor antagonist

HR – Hazard ratio

IV – intravenous

MEK - Mitogen-activated protein kinase kinase

mOS – Median overall survival

mPFS – Median progression-free survival

ORR – Overall response rate

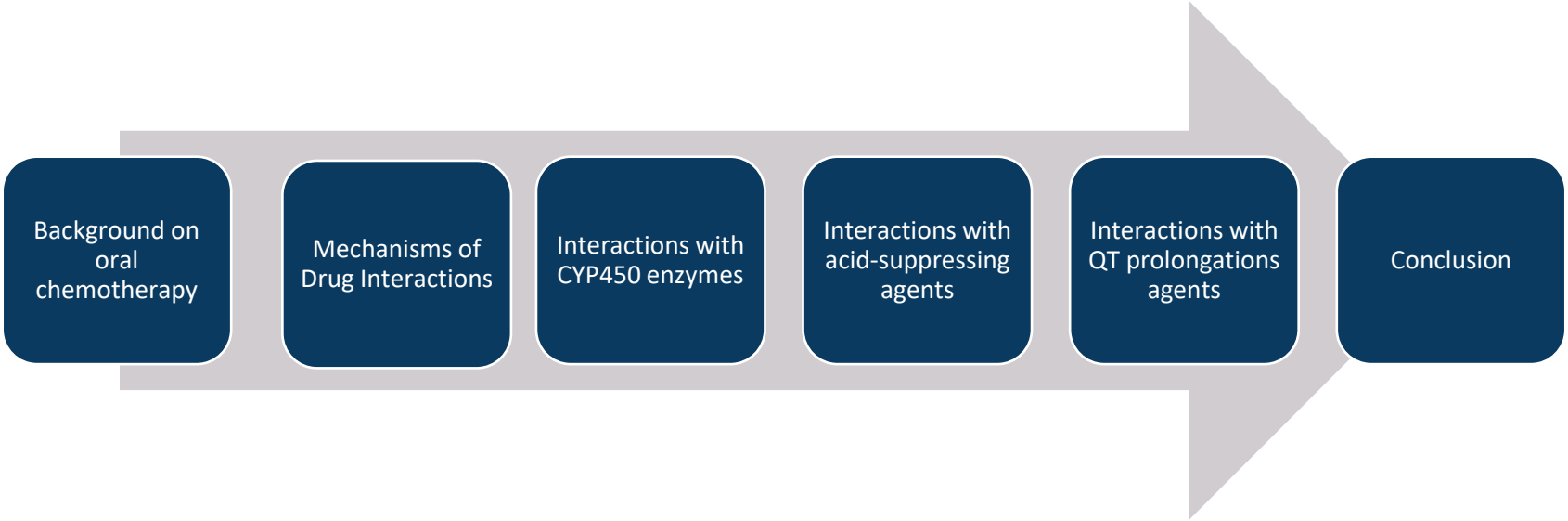
PPI – Proton pump inhibitor

SLL – Small lymphocytic lymphoma

TKI - Tyrosine Kinase Inhibitor

VEGF - Vascular endothelial growth factor

Roadmap


Background on oral chemotherapy
Mechanisms of Drug Interactions
Interactions with CYP450 enzymes
Interactions with acid-suppressing agents
Interactions with QT prolongations agents
Conclusion

Introduction

- Oral chemotherapy represents an important breakthrough in treatment options for people living with cancer
- Historically, chemotherapy was primarily administered IV in clinic or hospital settings, requiring frequent visits and travel
- Oral agents have demonstrated comparable efficacy to their IV counterparts
    - Can be administered at home, and reduce need for office visits
    - Avoids IV line placement, minimizing pain and discomfort

Source: Image generated by Copilot (Microsoft), Jan 2026.

Common Cancers Treated With Oral Chemotherapy

- Breast cancer
- Colorectal cancer
- Small cell lung cancer (SCLC)
- Non-small cell lung cancer (NSCLC)
- Lymphoma
- Leukemia
- Multiple myeloma (MM)

American Cancer Society. Getting Oral Chemotherapy. American Cancer Society. Updated May 15, 2025. Accessed December 26, 2025.

National Trends in Oral Chemotherapy Utilization

DIAGNOSIS	AVG. OO EXPENDITURES PP1	AVG. OO EXPENDITURES PP11	AVG. OO EXPENDITURES CHANGE	CONTRIBUTION OF OO TO TCOC CHANGE FROM PP1 - 11
Breast	$4,208	$7,869	87.0%	9.9%
Leukemia	$25,334	$41,128	62.3%	19.9%
CRC	$1,206	$2,158	78.9%	3.1%
Lung	$3,650	$3,625	-0.7%	-2.5%
Lymphoma	$4,193	$10,637	153.7%	13.0%
Myeloma	$25,109	$39,298	56.5%	6.7%
Prostate	$18,815	$20,114	6.9%	3.2%
Total	$8,291	$15,140	82.6%	10.8%

TCOC – Total cost of care
OO – Oral oncolytics
PP – Performance period

Jody S. Garey et al. The impact of oral oncology drugs in the era of value-based care. JCO Oncol Pract 20, 15-15(2024).

Oral Chemotherapy Agents

Source: Image generated by Copilot (Microsoft), Jan 2026.

Classification of Oral Chemotherapy Agents

Cytotoxic Agents

- Disrupting DNA synthesis, cell division, mitotic spindle formation
- Target rapidly dividing cells

Targeted Therapies

- Act on specific molecular pathways involved in cancer cell proliferation and survival
- May be present in normal tissue, but is overexpressed or mutated in the cancer

Hormonal Therapies

- Not chemotherapeutic in the classical sense
- Systemic treatment for hormone-sensitive cancers

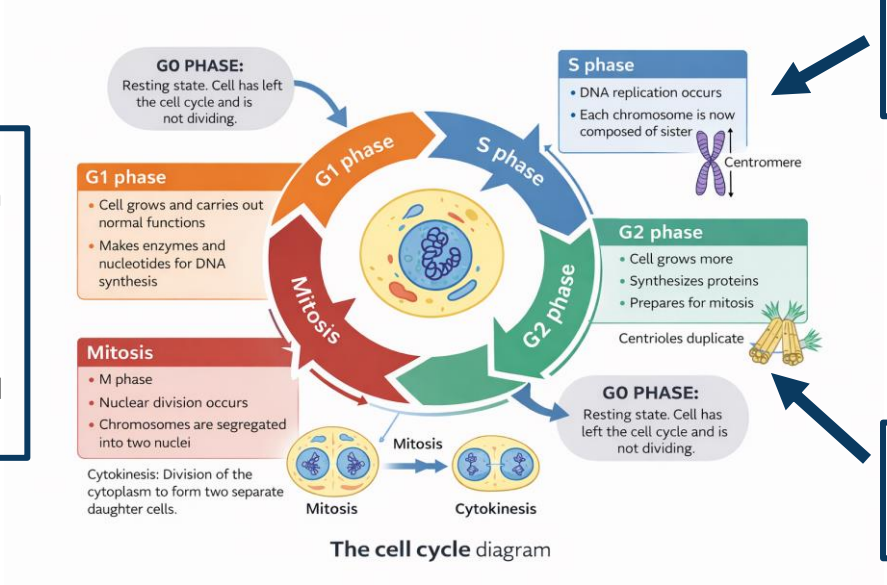
Oganezova T. Common Side Effects of Oral Chemotherapy and How to Manage Them. OncoDaily. Published July 4, 2025. Accessed December 26, 2025.

Cytotoxic/Traditional Agents (Examples)

Cell-cycle Non-specific

Alkylating Agents

- **Cyclophosphamide** – used in breast cancer, lymphomas, and autoimmune malignancies
- **Temozolomide** – used primarily in glioblastoma and anaplastic astrocytoma



The cell cycle diagram

Capecitabine

- Used in colorectal, breast, gastric cancers

Etoposide

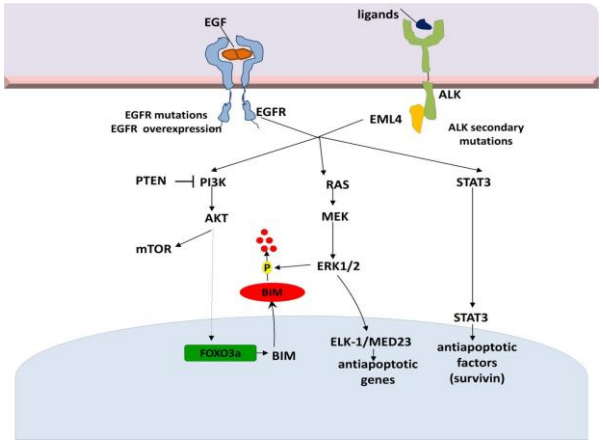
- Used for SCLC, testicular cancer

Katzung BG, Trevor AJ. Antineoplastic drugs. In: Basic & Clinical Pharmacology. 15th ed. McGraw Hill; 2021.

Source: Image generated by Copilot (Microsoft), Jan 2026.

Targeted Therapies (Examples)

Common Oral Chemotherapy Drug Classes	
Drug Class	**Medications**
BCR-ABL TKIs	Imatinib, dasatinib, ponatinib, nilotinib
Immunomodulatory drugs	Lenalidomide, pomalidomide
EGFR TKIs	Erlotinib, osimertinib
VEGF TKIs	Pazopanib, sorafenib
BRAF and MEK inhibitors	Dabrafenib, trametinib
FLT3 inhibitor	Midostaurin
BTK inhibitor	Ibrutinib
BCL-2 inhibitor	Venetoclax



Cascone VJ, et al. Evaluation of inpatient oral chemotherapy: an academic medical center experience. J Hematol Oncol Pharm. 2020.
Source: Image available from Cancer Biology & Medicine September 2014, 11 (3) 173-181 through CC BY 4.0 license

Hormonal Therapies

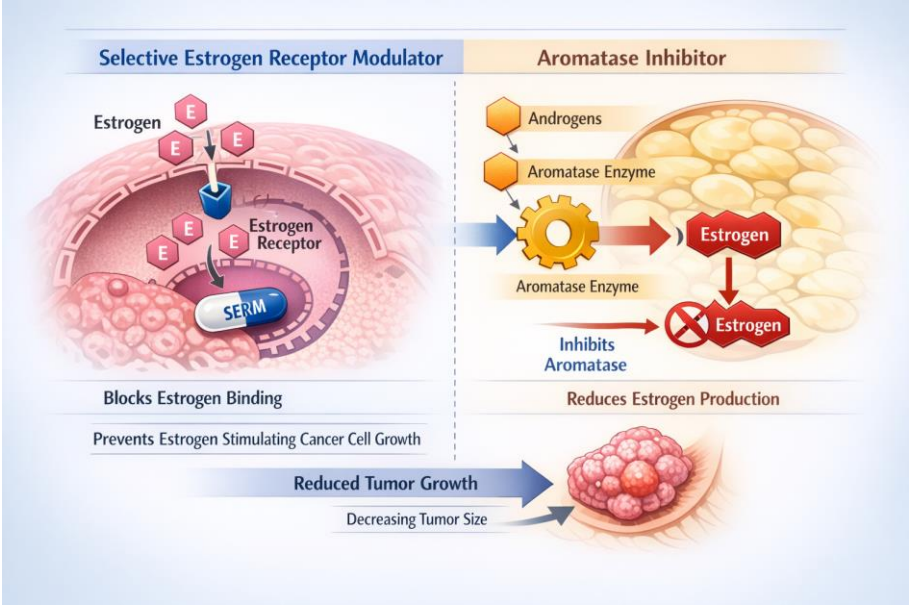
Mostly used in breast cancer with HR+

Selective estrogen receptor modulator (SERM)

- Tamoxifen

Aromatase inhibitors (AI)

- Letrozole
- Anastrozole
- Exemestane



Katzung BG, Trevor AJ. Antineoplastic drugs. In: Basic & Clinical Pharmacology. 15th ed. McGraw Hill; 2021.
Source: Image generated by Copilot (Microsoft), Jan 2026.

False Perceptions

- Oral chemotherapy agents are less dangerous than traditional IV chemotherapy
  - Can cause just as many dangerous side effects as chemotherapy given by other routes
  - Can have a higher risk for DDIs that can lead to toxicity or treatment failure
    - Absorption-related interactions
    - First pass metabolism
    - Negligence

Lohr LK, et al. Managing Drug Interactions With Oral Anticancer Treatments. J Adv Pract Oncol. 2023.
Source: Image available as open source from vectorstock.com

Risk Factors for DDI

Patient factors	Disease factors	Medication factors
• Polypharmacy • Advanced age • Adherence • OTC products, supplements, herbals	• Multiple comorbid conditions • Altered GI function • Malnutrition • Inflammation	• Narrow therapeutic index • CYP450 metabolism • Gastric pH • QT prolonging agents

Lohr LK, et al. Managing Drug Interactions With Oral Anticancer Treatments. J Adv Pract Oncol. 2023.
Marcath LA, et al. Drug-drug interactions in subjects enrolled in SWOG trials of oral chemotherapy. BMC Cancer. 2021;21(1):324. Published 2021 Mar 26.

Prevalence of DDIs

Study	Method	Objective	Results
Marcath et al., 2021	• N = 167 patients • DDIs were screened using protocol guidance, Lexicomp®, and pharmacist clinical judgment for clinical relevance	• Determined the prevalence of potential DDI involving oral anti-cancer trial agents in subjects enrolled in two SWOG clinical trials	• Using Lexicomp®, n = 48 (28.7%) had a DDI classified as moderate or worse • Pharmacist review indicated n = 12 (7.2%) had a clinically relevant interaction
Prely et al., 2022	• N = 294 patients • DDI using 4 interaction databases (Thériaque®, Drugs.com®, Hédrine, MSKCC)	• To assess DDI and HDI in outpatients taking oral anticancer drug	• Mean age = 67 years and • Median number of chronic drugs per patient = 8 • N= 267 patients (90.8%) had at least 1 DDI

Marcath LA, et al. Drug-drug interactions in subjects enrolled in SWOG trials of oral chemotherapy. BMC Cancer. 2021;21(1):324. Published 2021 Mar 26.
Prely H, et al. Real-life drug-drug and herb-drug interactions in outpatients taking oral anticancer drugs: comparison with databases. J Cancer Res Clin Oncol. 2022.

AMBORA Study

Objective

- To investigate the frequency, causes, and potential harm of medication errors in patients starting a new oral antitumor therapy

Method

- N = 202 patients
- Clinical pharmacologists/pharmacists performed advanced medication reviews for 12 weeks

Result

- Detected 1.7 medication errors per patient
- N = 83/202 (22.8%) drug-drug and drug-food interaction
  - N=63/83 (75.9%) were DDI classified as PK:
    - Inhibition or induction of CYP450 enzymes (36/65)
    - Reduced extent of absorption due to elevated gastric pH (14/65)
  - PD DDI: most frequent consequence QT prolongation (7/18)

Schlichtig K, et al. Medication Errors During Treatment with New Oral Anticancer Agents: Consequences for Clinical Practice Based on the AMBORA Study. Clin Pharmacol Ther. 2021;110(4):1075-1086.

Assessment Question 1

Which of the following factors can significantly influence the metabolism and absorption of oral anticancer agents?

A. CYP450 enzyme activity
B. Gastric pH alterations
C. Both A and B
D. None of the above

CYP450-Mediated Drug Interactions With Oral Chemotherapy

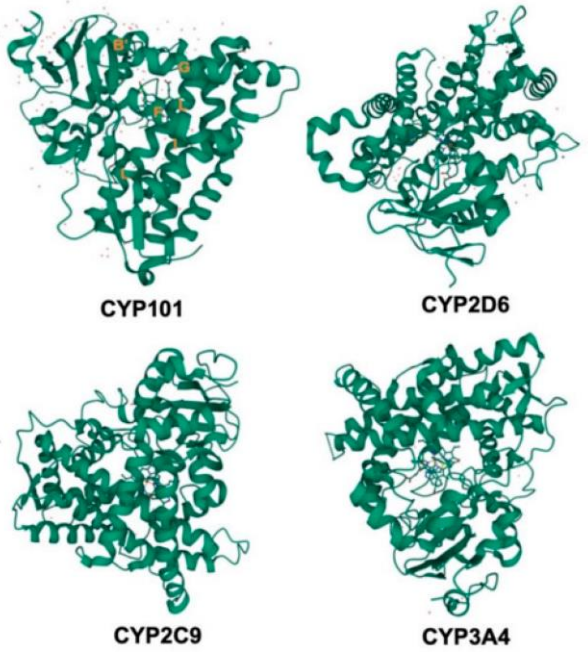
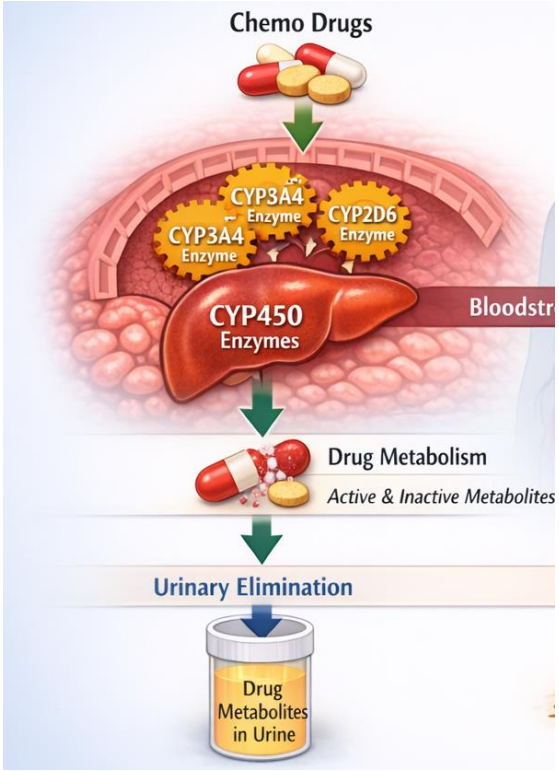


Image available as open access from Kondža M et al. Targeted but Troubling: CYP450 Inhibition by Kinase and PARP Inhibitors and Its Clinical Implications. Drugs and Drug Candidates. 2025; 4(2):24.

CYP450 Enzymes

- Many oral antineoplastic agents are hepatically metabolized through CYP3A4, CYP2D6, and CYP2C9 enzyme system



Lohr LK, et al. Managing Drug Interactions With Oral Anticancer Treatments. J Adv Pract Oncol. 2023.
Source: Image generated by Copilot (Microsoft), Jan 2026.

Oral Targeted Therapies

Target	Medication	Major Substrate	Major metabolic route
BCR-ABL	Imatinib, Dasatinib, Nilotinib, Ponatinib, Bosutinib	CYP3A4	CYP3A4
EGFR	Erlotinib, Gefitinib, Lapatinib	CYP3A4	CYP3A4
VEGF	Pazopanib, Sunitinib, Sorafenib	CYP3A4	CYP3A4
CDK4/6 inhibitors	Palbociclib, Ribociclib, Abemaciclib	CYP3A4	CYP3A4
PARP inhibitors	Olaparib, Rucaparib, Niraparib), Talazoparib	CYP3A4	CYP3A4
BCL-2 inhibitors	Venetoclax	CYP3A4	CYP3A4
FLT3 inhibitors	Midostaurin, Sorafenib, Gilteritinib	CYP3A4	CYP3A4
IDH1/IDH2 inhibitors	Ivosidenib, Enasidenib	CYP3A4	CYP3A4

Brüggemann RJ, et al. Management of drug-drug interactions of targeted therapies for haematological malignancies and triazole antifungal drugs. Lancet Haematol. 2022.

CYP3A4 Inhibitors/Inducers

	CYP3A4 Inhibitors	CYP3A4 Inducers
Effect on CYP344 substrate	↑ Drug exposure	↓ Drug exposure
PK	↑ C_{max}, ↑ AUC	↓ C_{max}, ↓ AUC
Clinical impact on oral chemotherapy	Increased toxicity	Decreased efficacy
CYP3A4 inhibitors/inducers are categorized by the strength of their enzyme inhibition/induction		

Lohr LK, et al. Managing Drug Interactions With Oral Anticancer Treatments. J Adv Pract Oncol. 2023.

CYP3A4 Inhibitors

CYP3A4 Inhibitors	Strength of Inhibitors	AUC	Potential intervention
Clarithromycin, idelalisib, itraconazole, ketoconazole, nefazodone, posaconazole, voriconazole, most protease inhibitors	Strong	Increase AUC of CYP3A4 substrates by ≥ fivefold	Dose reduction or Avoid or Monitor
Aprepitant, ciprofloxacin, crizotinib, cyclosporine, diltiazem, erythromycin, fluconazole, imatinib, verapamil	Moderate	Increase the AUC of CYP3A4 substrates by ≥ two- to < fivefold	

Lohr LK, et al. Managing Drug Interactions With Oral Anticancer Treatments. J Adv Pract Oncol. 2023.

CYP3A4 Inducers

CYP3A4 Inducers	Strength of Inducers	AUC	Potential intervention
Apalutamide, carbamazepine, enzalutamide, mitotane, phenytoin, rifampicin, St. John's wort	Strong	Decrease the AUC of CYP3A4 substrates by ≥ 80%	Increase the dose or Avoid or Monitor
Bosentan, efavirenz, etravirine, phenobarbital, and primidone	Moderate	Decrease the AUC of CYP3A4 substrates by ≥ 50% to < 80%	

Lohr LK, et al. Managing Drug Interactions With Oral Anticancer Treatments. J Adv Pract Oncol. 2023.

Venetoclax Management

Lexicomp®	Micromedex®
• Venetoclax/posaconazole • Risk rating: D (Consider therapy modification)	• Venetoclax/posaconazole • Severity: Contraindicated

Patient Management

- CLL or SLL
  - Contraindicated during the initiation and ramp-up phase of venetoclax
  - If unavoidable, following the ramp-up phase, reduce venetoclax to 70 mg daily
- AML
  - May be used during the initiation and ramp-up phase
  - Day 1: 10 mg, Day 2: 20 mg, Day 3: 50 mg, Day 4 and thereafter: 70 mg once daily
- Resume the previous venetoclax dose 2 to 3 days after posaconazole discontinuation

Venetoclax. Lexicomp Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. Accessed January 14, 2026.
MerativeTM Micromedex® Drug Interaction Checking (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/ (January 14, 2026).

Venetoclax Management

Package Insert

Coadministered drug	Initiation and Ramp-Up Phase		Steady Daily Dose (After Ramp-Up Phase)
Posaconazole	CLL/SLL	Contraindicated	Reduce dose to 70 mg
	AML	Day 1 – 10 mg Day 2 – 20 mg Day 3 – 50 mg Day 4 – 70 mg	
Other strong CYP3A inhibitor	CLL/SLL	Contraindicated	Reduce dose to 100 mg
	AML	Day 1 – 10 mg Day 2 – 20 mg Day 3 – 50 mg Day 4 – 100 mg	
Moderate CYP3A inhibitor	Reduce the dose by at least 50%		
Strong or Moderate CYP3A Inducers	Avoid use		

Venclexta (Venetoclax) [product labeling]. North Chicago, IL, USA: AbbVie Inc, November 2018.

Venetoclax Management

	Strong 3A4 Inhibitor	Moderate 3A4 inhibitor	Strong 3A4 inducer	Moderate 3A4 Inducer
Lohr LK, et al. (2023)	• Reduce dose by at least 75% if at steady daily dose • Concomitant use is contraindicated at initiation and during ramp-up phase	Reduce dose by at least 50%	Avoid concomitant use	Avoid concomitant use
Van Leeuwen et al. (2022)	• Avoid combination or decrease venetoclax dose • No action needed with fluconazole dosages of 150 mg single dose or 150 mg once a week		Avoid combination	

Lohr LK, et al. Managing Drug Interactions With Oral Anticancer Treatments. J Adv Pract Oncol. 2023.
van Leeuwen RWF, et al. Evidence- and consensus-based guidelines for drug-drug interactions with anticancer drugs; A practical and universal tool for management. Semin Oncol. 2022;49(2):119-129. doi:10.1053/j.seminoncol.2022.03.002

Venetoclax Management

Study	Method	Objective	Results
Diebold K et al., 2025	• N = 23 with posaconazole • N = 95 with voriconazole	• Evaluate outcomes of patients with newly diagnosed AML treated with HMA + VEN50 with either posaconazole or voriconazole	• Best ORR 60.8% with CR rate of 39.13% • VIALE-A: Best ORR was 66.4% with a CR rate of 36.7% • Reducing the venetoclax dose to 50 mg with either strong CYP3A4 inhibitor did not compromise on the efficacy of the combination

HMA - hypomethylating agent
VEN50 – venetoclax 50 mg

Diebold K, et al. Outcomes With Venetoclax 50 mg, Hypomethylating Agents, and Voriconazole or Posaconazole in Acute Myeloid Leukemia. EJHaem. 2025;6(3):e70049.

Antidepressant Related CYP2D6 Inhibition

- Depression is more common in individuals with cancer compared to the general population
- Incidence of depression in patients with cancer is estimated to range from 8% to 24%
- Potential DDIs between anticancer agents and antidepressants via CYP2D6
- For example, Tamoxifen is metabolized by CYP2D6 to form active metabolites
    - Strong CYP2D6 inhibitors reduce tamoxifen activation and clinical efficacy

Britny G. Rogala et al. Oral Anticancer Therapy: Management of Drug Interactions. JOP 15, 81-90(2019).

Antidepressant-Induced CYP2D6 Inhibition and Effect on Tamoxifen Metabolism

Extent of CYP2D6 Inhibition	Antidepressant	Direction
Minimal	Venlafaxine (SNRI) Mirtazapine (Atypical) Trazodone (Atypical)	Safest choice
Mild	Citalopram (SSRI) Escitalopram (SSRI) Sertraline (SSRI)	Preferred alternative to minimal inhibitors
Moderate	Duloxetine (SNRI) Fluvoxamine (SSRI)	Use with caution after weighting risks and benefits
Severe	Paroxetine (SSRI) Fluoxetine (SSRI) Bupropion (NDRI)	Avoid with tamoxifen; switch to alternative

Britny G. Rogala et al. Oral Anticancer Therapy: Management of Drug Interactions. JOP 15, 81-90(2019).

Take Home Message

- CYP3A4
  - Check dose adjustment guidelines: adjust or avoid accordingly
- CYP2D6
  - Don’t stop antidepressant abruptly
  - Severe CYP2D6 inhibition -> Avoid
  - Mild/Moderate CYP2D6 inhibition -> use with caution or switch to safer alternatives
- Check multiple references, primary literature, and tertiary resources such as Lexicomp, Micromedex, package insert, etc.
- Dosing adjustments vary by CYP inhibitor/inducer strength
- Different oral antineoplastic agents may have different recommendations with the same CYP inhibitor/inducer

Britny G. Rogala et al. Oral Anticancer Therapy: Management of Drug Interactions. JOP 15, 81-90(2019).

Assessment Question 2

PL is a 68-year-old man with CLL is on venetoclax 400 mg daily and begins posaconazole for invasive fungal infection.

Which is the most appropriate management strategy?

A. Continue venetoclax at full dose with close monitoring

B. Reduce venetoclax dose

C. Hold posaconazole and switch to fluconazole

D. Discontinue venetoclax permanently

Assessment Question 3

BB is a 48 years old premenopausal woman with ER+ breast cancer is receiving Tamoxifen 20 mg once daily. She has a history of major depressive disorder and is currently on Paroxetine 20 mg daily. The pharmacist received a message from an RN asking whether paroxetine interacts with tamoxifen.

Which of the following is the most appropriate recommendation?

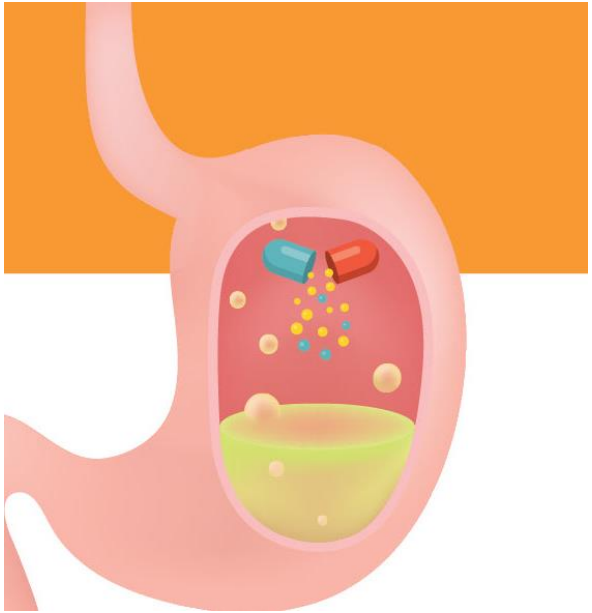
A. There is no interaction, so continue both medications

B. Titrate off paroxetine and switch to an antidepressant with minimal CYP2D6 inhibition, such as venlafaxine

C. Discontinue tamoxifen indefinitely

D. Increase tamoxifen dose to compensate for low clinical efficacy with paroxetine

Impact of Acid-Suppressing Therapy on Oral Chemotherapy



Source: Image available as public domain from Medlineplus.gov

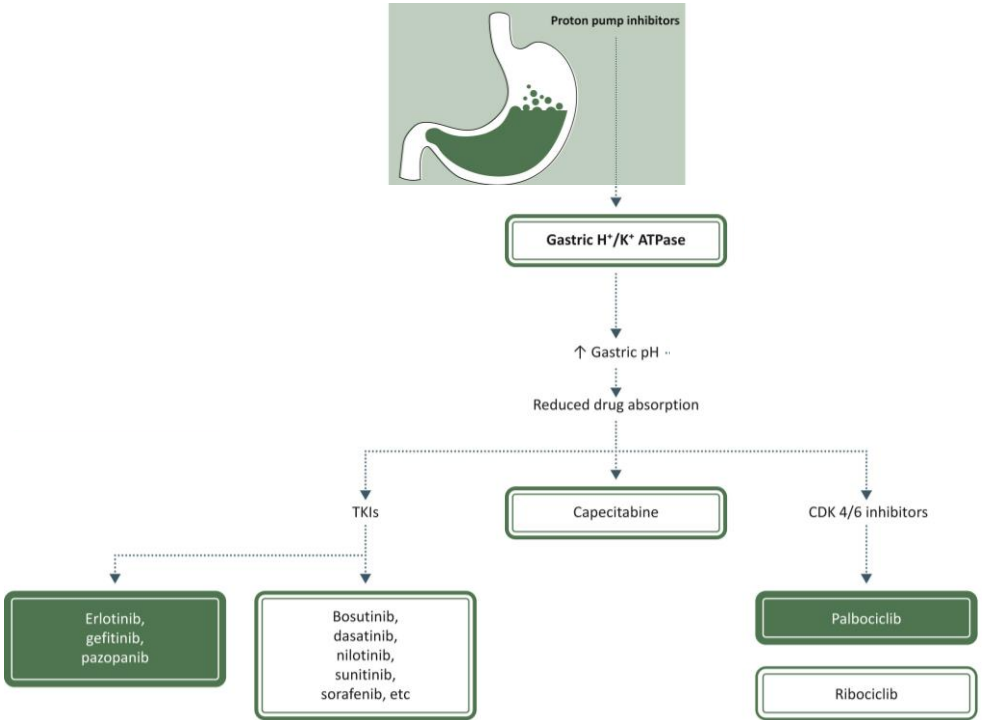
DDIs Related To Gastric Acid Suppression

- PPIs are some of the most frequently prescribed drugs in the world
- More than a quarter of cancer patients receiving oral antineoplastic treatment used PPIs
- Suppression of gastric acidity can decrease the absorption and therefore the efficacy of certain targeted therapies
- PPIs use in cancer patients is a significant concern due to possible DDI

Raoul JL, et al. Drug-drug interactions with proton pump inhibitors in cancer patients: an underrecognized cause of treatment failure. ESMO Open. 2023;8(1):100880.

Mechanism of DDIs of PPIs with Oral Chemotherapy

- TKIs and CDK4/6 inhibitors are weakly basic, and co-administration with a gastric acid-suppressive drug increasing the gastric pH decreases bioavailability
- Decrease in bioavailability can be significant and associated with decreased efficacy



Raoul JL, et al. Drug-drug interactions with proton pump inhibitors in cancer patients: an underrecognized cause of treatment failure. ESMO Open. 2023;8(1):100880.

PPIs and TKIs

Study	Method	Objective	Result
Sharma M et al. (2019)	• N = 12,538 • Retrospective study • Exposure period: at least 30 days of PPI use in the first 90 days from the start of TKI)	• OS and discontinuation of therapy in 90 days and 1 year after the end of the exposure period	• TKI-PPI use decreased survival in 90 days (HR, 1.16; 95% CI, 1.05-1.28) and in 1 year (HR, 1.10; 95% CI, 1.04-1.18) • TKI-PPI use is not associated with discontinuation of TKI
Lee CH et al. (2022)	• N = 4340 (gefitinib) • N = 1635 (erlotinib) • Retrospective study • Included patients receiving PPIs or H2RAs who had overlap with the duration of TKIs ≥ 20%	• OS association between PPIs or H2RAs and co-administered gefitinib or erlotinib	Gefitinib • mOS: 14.35 (PPI), 17.7 (H2RA), and 21.8 months (non-users), • P < 0.0001 Erlotinib • mOS: 17.0 (PPI), 20.1 (H2RA), and 23.9 months (non-users), • P < 0.0001

Sharma M, et al. The concomitant use of tyrosine kinase inhibitors and proton pump inhibitors: Prevalence, predictors, and impact on survival and discontinuation of therapy in older adults with cancer. Cancer. 2019.
Lee CH, et al. Proton pump inhibitors reduce the survival of advanced lung cancer patients with therapy of gefitinib or erlotinib. Sci Rep. 2022;12(1):7002. Published 2022 Apr 29.

Capecitabine

Study	Method	Objective	Result
van Doorn L et al. (2021)	• N = 22 • Randomized crossover study • Group 1: Capecitabine with esomeprazole • Group 2: capecitabine alone	Relative difference (RD) in exposure to capecitabine assessed by $AUC_{0\text{-inf}}$	• With PPI: 18.9% increase in $AUC_{0\text{-inf}}$ of capecitabine (95% CI -10.0% to 57.0%, P = 0.36) $T_{1/2}$ was significantly longer after esomeprazole (median 0.63 hours vs. 0.46 hours, P = 0.005) • Not negatively influenced by esomeprazole cotreatment
Lin WY et al. (2022)	• N = 8188 (16 studies) • Systematic review and meta-analysis • CRC patients receiving capecitabine-based or fluorouracil chemotherapy • Compared PPI users vs non-users	Evaluate whether concurrent PPI use negatively impacts OS and PFS in patients with CRC receiving chemotherapy	Capecitabine (Monotherapy) • Significantly higher disease progression rate (HR, 1.96; 95% CI, 1.21-3.16) compared to PPI non-users Capecitabine (Combination) • No significant difference in OS (HR 1.02; 95% CI 0.91–1.15) and PFS (HR 1.15; 95% CI 0.98–1.35) No difference in all-cause mortality in both group (HR, 1.31; 95% CI, 0.75 to 2.29)

van Doorn L, et al. Effect of the Proton Pump Inhibitor Esomeprazole on the Systemic Exposure of Capecitabine: Results of A Randomized Crossover Trial. Clin Pharmacol Ther. 2022.
Lin WY, et al. Do proton pump inhibitors affect the effectiveness of chemotherapy in colorectal cancer patients? A systematic review with meta-analysis. Front Pharmacol. 2022.

CDK 4/6 Inhibitors

Study	Method	Objective	Result
Lee J et al. (2023)	• N = 1310 • Retrospective cohort study • Patients with palbociclib and PPI overlapped by at least 33% (concomitant PPI group) vs. no PPI group	• Clinical outcomes (PFS and OS) of patients with advanced breast cancer who concomitantly use PPIs and palbociclib	• mPFS in the concomitant PPI group was shorter than no PPI group (25.3 vs 39.8 months; P < 0.001) • Concomitant use of PPI was also associated with shorter OS (HR, 2.71 [95% CI, 2.07-3.53]) • PPIs with palbociclib may hinder the complete therapeutic benefits of palbociclib

Lee J, et al. Concomitant Use of Proton Pump Inhibitors and Palbociclib Among Patients With Breast Cancer. JAMA Netw Open. 2023;6(7):e2324852.

CDK 4/6 Inhibitors

Study	Method	Objective	Result
Schieber T et al. (2023)	• N = 82 • Retrospective cohort study • Patients with palbociclib tablets with PPI (>50% duration of therapy) or without PPI	• PFS and OS	• mPFS 20.6 months w/o PPI (95% CI,16.07 – NA) vs 21.0 months w/ PPI (95% CI, 15.15 – NA), p = 0.95 • mOS was not reached in either arm • No difference in ADEs

- Palbociclib capsules have pH-dependent solubility, so acid-suppressive agents can significantly reduce absorption.
- Palbociclib tablet formulation has pH-independent absorption and doesn't demonstrate PPI interaction impact, making it preferable in patients who require acid-suppressing agents.

Schieber T, Steele S, Collins S, et al. Effect of Concurrent Proton Pump Inhibitors With Palbociclib Tablets for Metastatic Breast Cancer. Clin Breast Cancer. 2023;23(6):658-663. doi:10.1016/j.clbc.2023.05.009

Selpercatinib

Acid-Reducing Agents

- Concomitant use of selpercatinib with acid-reducing agents can decrease the plasma concentration of selpercatinib
- Avoid concomitant use of PPIs, H2RA, and antacids

If concomitant use cannot be avoided

- Take selpercatinib with food when coadministered with PPI
- Take selpercatinib 2 hours before or 10 hours after administration of an H2RA
- Take selpercatinib 2 hours before or 2 hours after administration of a locally-acting antacid

Retevmo (selpercatinib) [prescribing information]. Indianapolis, IN: Lilly USA LLC; November 2025.

Recommendation Use with PPIs

Contraindicated	Acalabrutinib, Bosutinib, Dasatinib, Erlotinib, Infigratinib, Methotrexate, Nilotinib, Palbociclib*, Pazopanib
Monitor	Capecitabine, Dacomitinib
Separate by 12 hours	Gefitinib

*capsule

Lohr LK, et al. Managing Drug Interactions With Oral Anticancer Treatments. J Adv Pract Oncol. 2023.

Recommendation Use with H2RAs

Contraindication	Dasatinib, Pazopanib
Take 2 hours before H2RA	Acalabrutinib, Bosutinib
Take 6 hours before or 10 hours after H2RA	Dacomitinib, Gefitinib
Take 2 hours before or 10 hours after H2RA	Erlotinib, Infigratinib, Neratinib, Nilotinib
Monitor	Methotrexate, Capecitabine

Lohr LK, et al. Managing Drug Interactions With Oral Anticancer Treatments. J Adv Pract Oncol. 2023.

Recommendation Use with Antacids

Separate by 2 - 3 hours	Acalabrutinib, Bosutinib, Dasatinib, Infigratinib, Neratinib, Nilotinib, Pexidartinib
Take 4-6 hours before or 6-10 hours after	Gefitinib, Sotorasib
Separate by several hours	Erlotinib, Pazopanib

Lohr LK, et al. Managing Drug Interactions With Oral Anticancer Treatments. J Adv Pract Oncol. 2023.

Take Home Message

- Avoid chronic PPI use when possible for dyspepsia or epigastric pain due to absorption-related interactions
- Long-acting PPIs are least preferred in patients receiving oral TKIs with pH-dependent absorption
- If acid suppression is necessary:
  - H2RA may be used with appropriate staggered dosing
  - Antacids are preferred with appropriate timing separation
- For some TKIs, even H2RA should be avoided

Raoul JL, Hansten PD. Proton pump inhibitors and cancer treatments: Emerging evidence against coadministration. Cancer Treat Rev. 2024;129:102794.
National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Chronic Myeloid Leukemia. Version 1.2026. NCCN; 2024. Accessed January 10, 2026.

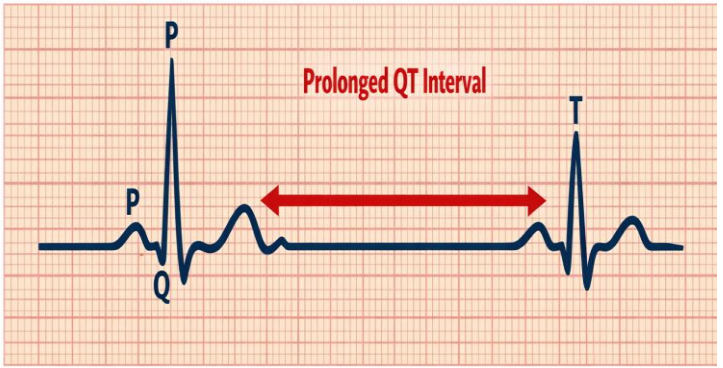
Assessment Question 4

CL is a 50 years old man with Ph+ CML is receiving Bosutinib 400 mg once daily. He has refractory GERD despite lifestyle modifications and antacid use. His PCP asks for a recommendation for acid-suppressive therapy.

Which strategy is most appropriate to minimize absorption-related complications and manage GERD?

A. Recommend omeprazole daily due to its superior in acid suppression
B. Recommend famotidine to take concurrently with bosutinib
C. Recommend taking famotidine 2 hours before bosutinib
D. Recommend increasing bosutinib to compensate for low absorption with omeprazole

QTc Prolongation Associated With Oral Chemotherapy Agents



Source: Image generated by Copilot (Microsoft), Jan 2026.

Prolongation of Cardiac QT Interval

- QT prolongation is also frequently encountered with oral antineoplastic agents
- QTc prolongation occurs in approximately 6% of patients with cancer before the initiation of therapy
- The incidence of QTc prolongation > 500 ms is more commonly reported with targeted therapy than with traditional therapy
- Reported incidence of arrhythmia or sudden cardiac death as a result of QTc prolongation is < 0.1%
- Over-reliance on the electronic QTc reported by ECG machine can lead to inaccurate values and adversely affect patient care

Kim, P, et al. How to Diagnose and Manage QT Prolongation in Cancer Patients. J Am Coll Cardiol CardioOnc. 2021.

National Cancer Institute Common Terminology of Clinical Adverse Events (v5.0)

Grade 1	QTc 450 to 480 ms
Grade 2	QTc 481 to 500 ms
Grade 3	QTc >501 ms; >60 ms change from baseline
Grade 4	signs/symptoms of serious arrhythmia and TdP

QTc is generally defined as a QTc value > 450 ms in males and > 460 ms in females.

Kim, P, et al. How to Diagnose and Manage QT Prolongation in Cancer Patients. J Am Coll Cardiol CardioOnc. 2021.

QT Prolongation Diagnosis

Bazett Formula

- $QTcB = QT/RR^{1/2}$
- most useful for heart rates between 60 and 100 beats/min, with inaccuracies at slower (with overcorrection) and faster (with under correction) heart rates

Fridericia Formula

- $QTcF = QT/RR^{1/3}$
- More accurate values during tachycardia or bradycardia

Conclusion

- Have not been compared directly to determine which is most accurate for predicting TdP
- Generally recommended to use the QTcF when evaluating patients with cancer

Rao, V, et al. Clinical Approach to Cardiovascular Toxicity of Oral Antineoplastic Agents: JACC State-of-the-Art Review. JACC. 2021 Jun, 77 (21) 2693–2716.

Mechanisms of Drug-Induced QTc Prolongation

- Commonly, this is due to direct inhibition of the IKr potassium channels
  - Less common: effects on sodium channels or intracellular signaling pathways, such as the PI3K pathway
- Concomitant use of drugs that inhibit the metabolism of the cancer drugs can also prolong QTc (Ex: CYP3A4 inhibitors and CYP2D6 enzymes)
- Conditions that prevent elimination pathways of cancer drugs can prolong QTc (Ex: renal and liver failure)
- Potential for genetic predisposition to drug-induced QTc prolongation, although specific associations have not been established for cancer therapeutics

Rao, V, et al. Clinical Approach to Cardiovascular Toxicity of Oral Antineoplastic Agents: JACC State-of-the-Art Review. JACC. 2021 Jun, 77 (21) 2693–2716.
Kim, P, et al. How to Diagnose and Manage QT Prolongation in Cancer Patients. J Am Coll Cardiol CardioOnc. 2021.

Risk Factors for QT Prolongation

- Congenital long QT syndrome or QT ≥ 480 ms in females or 470 ms in males at baseline
- Congestive heart failure
- Bradyarrhythmia
- Electrolyte abnormalities
- Concomitant use of medications known to prolong the QT interval

Rao, V, et al. Clinical Approach to Cardiovascular Toxicity of Oral Antineoplastic Agents: JACC State-of-the-Art Review. JACC. 2021 Jun, 77 (21) 2693–2716.

QTc Prolongation Potential Cancer Drugs (Incidence of ADEs 1%-10%)

Classification	Drug	Indication
ALK	Crizotinib, Lorlatinib	NSCLC
BCR-ABL	Dasatinib, Nilotinib	CML, ALL
BRAF	Vemurafenib	Melanoma
FLT3	Midostaurin	AML, mast cell leukemia
VEGFR	Lenvatinib	Differentiated thyroid cancer, HCC, endometrial cancer, RCC
	Pazopanib	RCC, soft tissue sarcoma
	Vandetanib	Medullary thyroid cancer
Miscellaneous	Glasdegib, Ivosidenib	AML
	Ribociclib	Breast cancer
	Selpercatinib	BSCLC, thyroid cancer

Rao, V, et al. Clinical Approach to Cardiovascular Toxicity of Oral Antineoplastic Agents: JACC State-of-the-Art Review. JACC. 2021 Jun, 77 (21) 2693–2716.

Oral Chemotherapy Agents With Clinically Relevant QT-Prolonging Effects

Nilotinib

- **FDA BBW: QT prolongation and sudden cardiac death**
- Prior to starting: Monitor and correct electrolyte (K, Mg) and avoid use of concomitant drugs known to prolong QT interval, strong CYP3A4
  - If QTc > 480 ms: withhold medication, check electrolytes, and DDIs
- Monitoring: ECG at baseline, Day 8, then periodically, clinically indicated in those at risk for QT prolongation
- Alternatives: Dasatinib and bosutinib (2nd generation TKIs); imatinib (older patients with CV comorbidities)

Vandetanib

- Incidence of QT prolongation occurs 16% to 18%
- Weighted incidence of QT interval >500 ms at 2.6%
- $T_{1/2}$ is very long (19 days): recommended ECG at 2, 4, 8, 12 weeks after initiation of treatment and every 3 months
- Monitoring: electrolytes, Ca, TSH
- Not advice in patients with QTc > 480 ms; QTc > 500 ms during treatment -> stop the medication intil < 450 ms
- Alternatives: selpercatinib (less QT prolongation)

Coppola C, et al. Management of QT prolongation induced by anti-cancer drugs: Target therapy and old agents. Different algorithms for different drugs. Cancer Treat Rev. 2018.
National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Thyroid Canrcinoma. Version 1.2025. NCCN; 2025. Accessed January 23, 2026.
National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Chronic Myeloid Leukemia. Version 1.2026. NCCN; 2025. Accessed January 23, 2026.

Oral Chemotherapy Agents With Clinically Relevant QT-Prolonging Effects

Ribociclib

- MONALEESA-2 Trial: QT prolongation events were reversible by dose interruptions and reductions
- Recommended in patients with QTcF < 450 ms
  - Follow the dose adjustment guidelines if QTcF > 480 ms during treatment
- Prior to treatment and at the beginning of first 6 cycles: ECG at baseline, on day 14 of cycle 1 and at the beginning of cycle 2, serum electrolytes (including K, Mg, Ca, and PO_4)
- Avoid in patient with high risk for developing QTc prolongation (long QT syndrome, uncontrolled or significant cardiac diseases)
- Not recommended: use of ribociclib with any medications that is known to prolong QTc interval and strong CYP3A4 inhibitors
- Alternatives: Palbociclib, abemaciclib

Coppola C, et al. Management of QT prolongation induced by anti-cancer drugs: Target therapy and old agents. Different algorithms for different drugs. Cancer Treat Rev. 2018.
National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Breast cancer. Version 1.2026. NCCN; 2026. Accessed January 23, 2026.

Drugs to Avoid With QT-Prolonging Oral Antineoplastics

Anti-infective Agents	Antiemetics	Antidepressants	Antipsychotic Agents	Antiarrhythmic Agents	Other
Fluoroquinolones Macrolide Azole antifungals Antimalarials	Domperidone Droperidol Ondansetron	SSRIs SNRIs (Venlafaxine) TCAs	Clozapine Haloperidol Quetiapine Risperidone Ziprasidone	Amiodarone Dofetilide Dronedarone Ibutilide Procainamide Sotalol	Fosphenytoin Methadone Phenytoin

Oncological agents are essential and cannot be changed easily, alternative treatments that do not prolong the QT interval should be considered for other concurrent conditions.
If these agents are essential, then close monitoring for QT-interval prolongation is essential.

Rao, V, et al. Clinical Approach to Cardiovascular Toxicity of Oral Antineoplastic Agents: JACC State-of-the-Art Review. JACC. 2021 Jun, 77 (21) 2693–2716.

Ondansetron

- High IV ondansetron dose is associated with a higher risk of QTc prolongation
- Prospective observational study (ED, n = 22)
  - 4 mg IV ondansetron increased mean QTc by 20 ms from baseline (95% CI: 14–26 ms)
- Observational study in patients with cardiovascular disease:
  - Single 4 mg IV dose increased mean QTc by 19.3 ms
- QTc risk with ondansetron and oral chemotherapy is primarily additive; many oral anticancer agents independently prolong QT interval (Ex: TKI such as nilotinib, vandetanib, ribociclib)
- FDA recommendations:
  - Maximum single IV dose: 16 mg (to minimize QT prolongation risk)
  - Oral dosing may go up to 24 mg (maximum single dose/daily dose) for highly emetogenic chemotherapy

Moffett PM, et al. Intravenous Ondansetron and the QT Interval in Adult Emergency Department Patients: An Observational Study. Acad Emerg Med. 2016;23(1):102-105.
Hafermann MJ, et al. Drug Healthc Patient Saf. 2011;3:53-58.
National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Antiemesis. Version 2.2025. NCCN; 2025. Accessed January 23, 2026.

Algorithm for QT-Interval Monitoring in Patients Receiving Oral Antineoplastic Agents

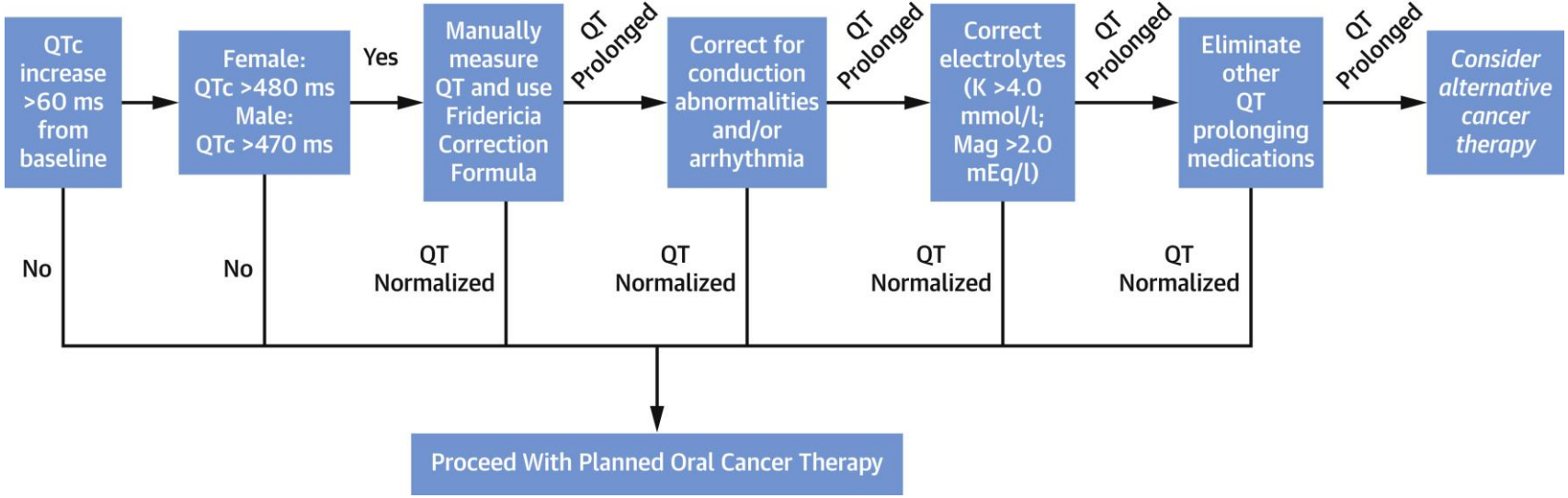


Image available as open access from Rao, V, et al. Clinical Approach to Cardiovascular Toxicity of Oral Antineoplastic Agents: JACC State-of-the-Art Review. JACC. 2021 Jun, 77 (21) 2693–2716.

Take Home Message

- The Fridericia (QTcF) formula is recommended when evaluating the QT interval in patients with cancer.
- Although several oral antineoplastic agents can prolong the QT interval, the risk of torsade de pointes is low.
- Lack of a standardized definition of QT prolongation for cancer therapeutics makes the implementation of screening and monitoring programs challenging.
- Recommend a baseline ECG, ECG at 14 days, and repeat ECG as clinically indicated in those at risk.
- Use of patch monitors, implantable loop recorders, and wearable devices, is becoming increasingly attractive to monitor for QT interval prolongation.
    - Studies in this population are lacking

Rao, V, et al. Clinical Approach to Cardiovascular Toxicity of Oral Antineoplastic Agents: JACC State-of-the-Art Review. JACC. 2021 Jun, 77 (21) 2693–2716.

Assessment Question 5

KC is a 60-year-old woman with HR+/HER2- metastatic breast cancer who is receiving ribociclib and letrozole. Her baseline ECG was 440 ms. She comes back to the clinic on Cycle 1 Day 14:

Cycle 1 Day 14 Labs	
QTcF	485 ms
K	3.4 mEq/L
Mg	1.8 mg/dL
Current medication	Ondansetron PRN

Which of the following is the best recommendation?

A. Continue ribociclib and repeat ECG in the next appointment

B. Hold ribociclib permanently

C. Reduce ribociclib dose 50%

D. Correct K and Mg, switch ondansetron to prochlorperazine, and hold ribociclib until QTcF improved

Dosage Adjustment and Management

Severity	Management
QTcF > 480 ms and ≤ 500 ms	Early breast cancer: **Hold ribociclib treatment until QTcF resolves to ≤ 480 ms**; resume at the same dose level. If QTcF ≥ 480 ms recurs, hold ribociclib until QTcF resolves to ≤ 480 ms and resume at the next lower dose level.
	Advanced or metastatic breast cancer: **Hold ribociclib until QTcF resolves to ≤ 480 ms**; resume at the next lower dose level. If QTcF ≥ 480 ms recurs, hold ribociclib until QTcF resolves to ≤ 480 ms and resume ae the next lower dose level.
QTcF > 500 ms	Hold ribociclib until QTcF resolves to ≤ 480 ms; resume ribociclib at the next lower dose level. If QTcF > 500 ms recurs, discontinue ribociclib.
QTcF > 500 ms or > 60 ms change from baseline and associated with Tdp, pVT, syncope, or s/s of arrhythmia	Permanently discontinue ribociclib.

Ribociclib. Lexicomp Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. Accessed February 1, 2026.

2018 HOPA Best Practices for the Management of Oral Oncolytic Therapy: Pharmacy Practice Standard

- Comprehensive review of new oral oncolytics using clinical data, guidelines, pathways, and financial considerations
- Assess patient-specific factors impacting drug selection and monitoring
- Conduct medication review for reconciliation and drug–drug interaction screening
- Collaborate with healthcare team to address concerns, confirm dosing/timing, and finalize monitoring plan

Mackler E, et al. 2018 Hematology/Oncology Pharmacist Association Best Practices for the Management of Oral Oncolytic Therapy: Pharmacy Practice Standard. J Oncol Pract. 2019;15(4):e346-e355.

Comparison of Nine Tools for Screening Drug-Drug Interactions of Oral Oncolytics

Objective

- Compare the abilities of nine DDI screening tools to detect clinically relevant interactions with oral oncolytics

Method

- Subscription-based tools (PEPID®, Micromedex®, Lexicomp®, Facts & Comparisons®) vs. free tools (Epocrates Free®, Medscape®, Drugs.com®, RxList®, WebMD®)
- Compared for their abilities to detect clinically relevant DDIs for 145 drug pairs including an oral oncology agent
- Descriptive statistics (sensitivity, specificity, PPV, NPV) were calculated for each tool and compared by free vs. subscription-based groups

Marcath LA, et al. Comparison of Nine Tools for Screening Drug-Drug Interactions of Oral Oncolytics. *J Oncol Pract*. 2018;14(6):e368-e374.

Comparison of Nine Tools for Screening Drug-Drug Interactions of Oral Oncolytics

Tool	Sensitivity (±SE)	Specificity (±SE)	PPV (±SE)	NPV (±SE)	Performance score (±SE)
Subscription					
Facts & Comparisons®	0.67 (0.044)	0.93 (0.046)	0.97 (0.018)	0.42 (0.061)	0.75 (0.13)
Lexicomp®	0.96 (0.019)	0.80 (0.073)	0.95 (0.021)	0.83 (0.070)	0.89 (0.041)
Micromedex®	0.86 (0.062)	0.87 (0.062)	0.96 (0.075)	0.62 (0.075)	0.83 (0.073)
PEPID®	0.90 (0.027)	0.53 (0.091)	0.88 (0.030)	0.59 (0.095)	0.73 (0.096)
Free					
Drugs.com®	0.93 (0.024)	0.73 (0.081)	0.93 (0.024)	0.73 (0.081)	0.83 (0.058)
Epocrates Free®	0.73 (0.041)	0.83 (0.068)	0.94 (0.024)	0.45 (0.066)	0.74 (0.10)
Medscape®	0.79 (0.038)	0.73 (0.081)	0.92 (0.027)	0.48 (0.074)	0.73 (0.092)
RxList®	0.65 (0.044)	0.83 (0.068)	0.94 (0.027)	0.38 (0.060)	0.70 (0.12)
WebMD®	0.79 (0.038)	0.77 (0.077)	0.93 (0.026)	0.49 (0.073)	0.67 (0.092)
P	0.0082	0.95	0.48	0.031	

PPV – Positive predictive value
NPV – Negative predictive value
SE – Standard error

Marcath LA, et al. Comparison of Nine Tools for Screening Drug-Drug Interactions of Oral Oncolytics. J Oncol Pract. 2018;14(6):e368-e374. doi:10.1200/JOP.18.00086

Conclusion

- Assess potential DDIs before initiating oral chemotherapy
- Obtain a complete medication history, including prescription and OTC agents
- Evaluate DDIs based on likelihood, severity, potential harm, and quality of evidence
- Proactive DDI management can reduce toxicity and enhance anticancer efficacy
- Strengthen DDI detection through protocols, pharmacist-led screening, and standardized tools

References

1. American Cancer Society. Getting Oral Chemotherapy. American Cancer Society. Updated May 15, 2025. Accessed December 26, 2025.
2. Brüggemann RJ, Verheggen R, Boerrigter E, et al. Management of drug-drug interactions of targeted therapies for haematological malignancies and triazole antifungal drugs. Lancet Haematol. 2022;9(1):e58-e72. doi:10.1016/S2352-3026(21)00232-5
3. Cascone VJ, Hosmer KM, Mahmoudjafari Z, Henry DW, Grauer DW. Evaluation of inpatient oral chemotherapy: an academic medical center experience. J Hematol Oncol Pharm. 2020;10(6):359-363.
4. Coppola C, Rienzo A, Piscopo G, Barbieri A, Arra C, Maurea N. Management of QT prolongation induced by anti-cancer drugs: Target therapy and old agents. Different algorithms for different drugs. Cancer Treat Rev. 2018;63:135-143. doi:10.1016/j.ctrv.2017.11.009
5. Diebold K, Parker D, Worth S, et al. Outcomes With Venetoclax 50 mg, Hypomethylating Agents, and Voriconazole or Posaconazole in Acute Myeloid Leukemia. EJHaem. 2025;6(3):e70049.
6. Hafermann MJ, Namdar R, Seibold GE, Page RL 2nd. Effect of intravenous ondansetron on QT interval prolongation in patients with cardiovascular disease and additional risk factors for torsades: a prospective, observational study. Drug Healthc Patient Saf. 2011;3:53-58. doi:10.2147/DHPS.S25623
7. Jody S. Garey et al. The impact of oral oncology drugs in the era of value-based care. JCO Oncol Pract 20, 15-15(2024).
8. Katzung BG, Trevor AJ. Antineoplastic drugs. In: Basic & Clinical Pharmacology. 15th ed. McGraw-Hill; 2021.
9. Kim, P, Irizarry-Caro, J, Ramesh, T. et al. How to Diagnose and Manage QT Prolongation in Cancer Patients. J Am Coll Cardiol CardioOnc. 2021 Mar, 3 (1) 145–149.
10. Kondža M, Bukić J, Ćavar I, Tubić B. Targeted but Troubling: CYP450 Inhibition by Kinase and PARP Inhibitors and Its Clinical Implications. Drugs and Drug Candidates. 2025; 4(2):24. https://doi.org/10.3390/ddc4020024
11. Lee J, Kwon S, Kwon S, Jung H, Nam JH, Lee E. Concomitant Use of Proton Pump Inhibitors and Palbociclib Among Patients With Breast Cancer. JAMA Netw Open. 2023;6(7):e2324852. doi:10.1001/jamanetworkopen.2023.24852
12. Lee CH, Shen MC, Tsai MJ, et al. Proton pump inhibitors reduce the survival of advanced lung cancer patients with therapy of gefitinib or erlotinib. Sci Rep. 2022;12(1):7002. Published 2022 Apr 29. doi:10.1038/s41598-022-10938-x
13. Lohr LK, Blake KT, Chan CM, Sturm S, Walsh GT. Managing Drug Interactions With Oral Anticancer Treatments. J Adv Pract Oncol. 2023;14(5):419-438. doi:10.6004/jadpro.2023.14.5.7
14. Lin WY, Wang SS, Kang YN, et al. Do proton pump inhibitors affect the effectiveness of chemotherapy in colorectal cancer patients? A systematic review with meta-analysis. Front Pharmacol. 2022;13:1048980. Published 2022 Dec 12. doi:10.3389/fphar.2022.1048980
15. Mackler E, Segal EM, Muluneh B, Jeffers K, Carmichael J. 2018 Hematology/Oncology Pharmacist Association Best Practices for the Management of Oral Oncolytic Therapy: Pharmacy Practice Standard. J Oncol Pract. 2019;15(4):e346-e355. doi:10.1200/JOP.18.00581
16. Marcath LA, Finley CM, Wong SF, Hertz DL. Drug-drug interactions in subjects enrolled in SWOG trials of oral chemotherapy. BMC Cancer. 2021;21(1):324. Published 2021 Mar 26. doi:10.1186/s12885-021-08050-w
17. Marcath LA, Xi J, Hoylman EK, Kidwell KM, Kraft SL, Hertz DL. Comparison of Nine Tools for Screening Drug-Drug Interactions of Oral Oncolytics. J Oncol Pract. 2018;14(6):e368-e374. doi:10.1200/JOP.18.00086
18. Marcath LA, Finley CM, Wong SF, Hertz DL. Drug-drug interactions in subjects enrolled in SWOG trials of oral chemotherapy. BMC Cancer. 2021;21(1):324. Published 2021 Mar 26. doi:10.1186/s12885-021-08050-w
19. Marcath LA, Xi J, Hoylman EK, Kidwell KM, Kraft SL, Hertz DL. Comparison of Nine Tools for Screening Drug-Drug Interactions of Oral Oncolytics. J Oncol Pract. 2018;14(6):e368-e374. doi:10.1200/JOP.18.00086

References

20. Moffett PM, Cartwright L, Grossart EA, O'Keefe D, Kang CS. Intravenous Ondansetron and the QT Interval in Adult Emergency Department Patients: An Observational Study. Acad Emerg Med. 2016;23(1):102-105. doi:10.1111/acem.1283
21. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Chronic Myeloid Leukemia. Version 1.2026. NCCN; 2024. Accessed January 10, 2026.
22. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Thyroid Canrcinoma. Version 1.2025. NCCN; 2025. Accessed January 23, 2026.
23. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Chronic Myeloid Leukemia. Version 1.2026. NCCN; 2025. Accessed January 23, 2026.
24. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Breast cancer. Version 1.2026. NCCN; 2026. Accessed January 23, 2026.
25. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Antiemesis. Version 2.2025. NCCN; 2025. Accessed January 23, 2026.
26. Oganezova T. Common Side Effects of Oral Chemotherapy and How to Manage Them. OncoDaily. Published July 4, 2025. Accessed December 26, 2025.
27. Prely H, Herledan C, Caffin AG, et al. Real-life drug-drug and herb-drug interactions in outpatients taking oral anticancer drugs: comparison with databases. J Cancer Res Clin Oncol. 2022;148(3):707-718. doi:10.1007/s00432-021-03645-z
28. Raoul JL, Moreau-Bachelard C, Gilabert M, Edeline J, Frénel JS. Drug-drug interactions with proton pump inhibitors in cancer patients: an underrecognized cause of treatment failure. ESMO Open. 2023;8(1):100880. doi:10.1016/j.esmoop.2023.100880
29. Rao, V, Reeves, D, Chugh, A. et al. Clinical Approach to Cardiovascular Toxicity of Oral Antineoplastic Agents: JACC State-of-the-Art Review. JACC. 2021 Jun, 77 (21) 2693–2716.https://doi.org/10.1016/j.jacc.2021.04.009
30. Retevmo (selpercatinib) [prescribing information]. Indianapolis, IN: Lilly USA LLC; November 2025.
31. Rogala BG, Charpentier MM, Nguyen MK, Landolf KM, Hamad L, Gaertner KM. Oral Anticancer Therapy: Management of Drug Interactions. J Oncol Pract. 2019;15(2):81-90. doi:10.1200/JOP.18.00483
32. Schieber T, Steele S, Collins S, et al. Effect of Concurrent Proton Pump Inhibitors With Palbociclib Tablets for Metastatic Breast Cancer. Clin Breast Cancer. 2023;23(6):658-663. doi:10.1016/j.clbc.2023.05.009
33. Schlichtig K, Dürr P, Dörje F, Fromm MF. Medication Errors During Treatment with New Oral Anticancer Agents: Consequences for Clinical Practice Based on the AMBORA Study. Clin Pharmacol Ther. 2021;110(4):1075-1086. doi:10.1002/cpt.233
34. Sharma M, Holmes HM, Mehta HB, et al. The concomitant use of tyrosine kinase inhibitors and proton pump inhibitors: Prevalence, predictors, and impact on survival and discontinuation of therapy in older adults with cancer. Cancer. 2019;125(7):1155-1162. doi:10.1002/cncr.31917
35. van Leeuwen RWF, le Comte M, Reyners AKL, et al. Evidence- and consensus-based guidelines for drug-drug interactions with anticancer drugs; A practical and universal tool for management. Semin Oncol. 2022;49(2):119-129. doi:10.1053/j.seminoncol.2022.03.002
36. van Doorn L, Heersche N, de Man FM, et al. Effect of the Proton Pump Inhibitor Esomeprazole on the Systemic Exposure of Capecitabine: Results of A Randomized Crossover Trial. Clin Pharmacol Ther. 2022;111(2):455-460. doi:10.1002/cpt.2444
37. Venetoclax. Lexicomp Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. Accessed January 14, 2026.
38. Venclexta (Venetoclax) [product labeling]. North Chicago, IL, USA: AbbVie Inc, November 2018.
39. Ribociclib. Lexicomp Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. Accessed February 1, 2026.

Questions?

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