

JADPRO

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Lectures

An APSHO
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Activity

JADPRO Regional Lectures

Hematologic Malignancies

Strategies for Adherence to Oral Therapeutics

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Faculty Financial Disclosures

- Ms. Kurtin has acted as a consultant for AbbVie, Bristol-Myers Squibb, Celgene, Genentech, Incyte, Janssen, and Takeda.
- Dr. Faiman has acted as a consultant, received honoraria from, and has served on the speakers bureau for Amgen, Bristol-Myers Squibb, Celgene, and Takeda.
- Ms. McNeill has served on the speakers bureau for Celgene, Pharmacyclics, Seattle Genetics, and Takeda.

Planning Committee Financial Disclosures

- Moshe C. Ornstein, MD, MA, Cleveland Clinic Taussig Cancer Institute (Reviewer) has nothing to disclose.
- Dorothy Caputo, MA, BSN, RN (Lead Nurse Planner) has nothing to disclose.
- Alana Brody, Lynn Rubin, and Patti McLafferty (Harborside Medical Education) have nothing to disclose.
- Sandy Leatherman, Annamarie Luccarelli, and Jessica Tamasi (APSHO) have nothing to disclose.
- Claudine Kiffer and Annie Yueh (Harborside Press) have nothing to disclose.

The hematologic malignancies educational activity is supported by educational funding donation provided by Amgen, Celgene Corporation and Pharmacyclics LLC, an AbbVie Company and Janssen Biotech, Inc., administered by Janssen Scientific Affairs, LLC.

Learning Objectives

- Identify strategies for encouraging patient adherence to oral therapeutics
- Discuss the pivotal role and necessary expertise of the AP as a vital part of the interprofessional oncology/hematology team

Case Studies

Patient A: 69-year-old male with mantle cell lymphoma

- PMH
 - COPD, CAD, HTN, Atrial fibrillation, BPH
- Lifestyle
 - 47 pack-year history of tobacco, quit 2 years ago, social alcohol use, does not exercise, plays golf 4-5 times per month
- Social history
 - Married x 45 years, lives with his wife, retired chemical engineer, no children
- Current medications
 - Montelukast, albuterol MDI prn, metoprolol, carvedilol, coumadin, tamulosin
- Insurance: Medicare with supplemental AARP

Patient B: 75-year-old female with mantle cell lymphoma

- PMH
 - Hypothyroid, rheumatoid arthritis, osteoporosis, macular degeneration
- Lifestyle
 - No tobacco history, infrequent alcohol use, participates in a walking club
- Social history
 - Widowed x 1 year; her husband was an army veteran, lives alone in a retirement community, 3 grown children and 6 grandchildren who live out of town, visual impairment limits other activities
- Current medications
 - Synthroid, ibuprofen or acetaminophen as needed, vitamin D, calcium
- Insurance: Medicare and Tricare for life

Oral Anti-Neoplastic Therapies for B-Cell Malignancies

Agent	Class	Indication
Chlorambucil	Alkylating agent	Newly diagnosed chronic lymphocytic leukemia (NDCLL)
Dexamethasone	Steroid	Multiple myeloma (MM) – multiple regimens
Ibrutinib	Bruton kinase inhibitor	NDCLL, relapsed/refractory CLL (RRCLL), mantle cell lymphoma (MCL)
Idelalisib	PI3 kinase inhibitor	RRCLL
Ixazomib	Proteasome inhibitor	Newly diagnosed MM (NDMM), relapsed/refractory MM (RRMM)
Lenalidomide	Immunomodulatory agent	NDMM, RRMM, maintenance post-hematopoietic stem cell transplantation (HSCT) in MM, CLL, non-Hodgkin lymphoma (NHL)
Melphalan	Alkylating agent	NDMM non-transplant eligible
Panobinostat	Histone deacetylase inhibitor	RRMM
Pomalidomide	Immunomodulatory agent	RRMM
Prednisone	Steroid	NHL
Thalidomide	Immunomodulatory agent	NDMM, RRMM
Venetoclax	BCL2 inhibitor	RRCLL

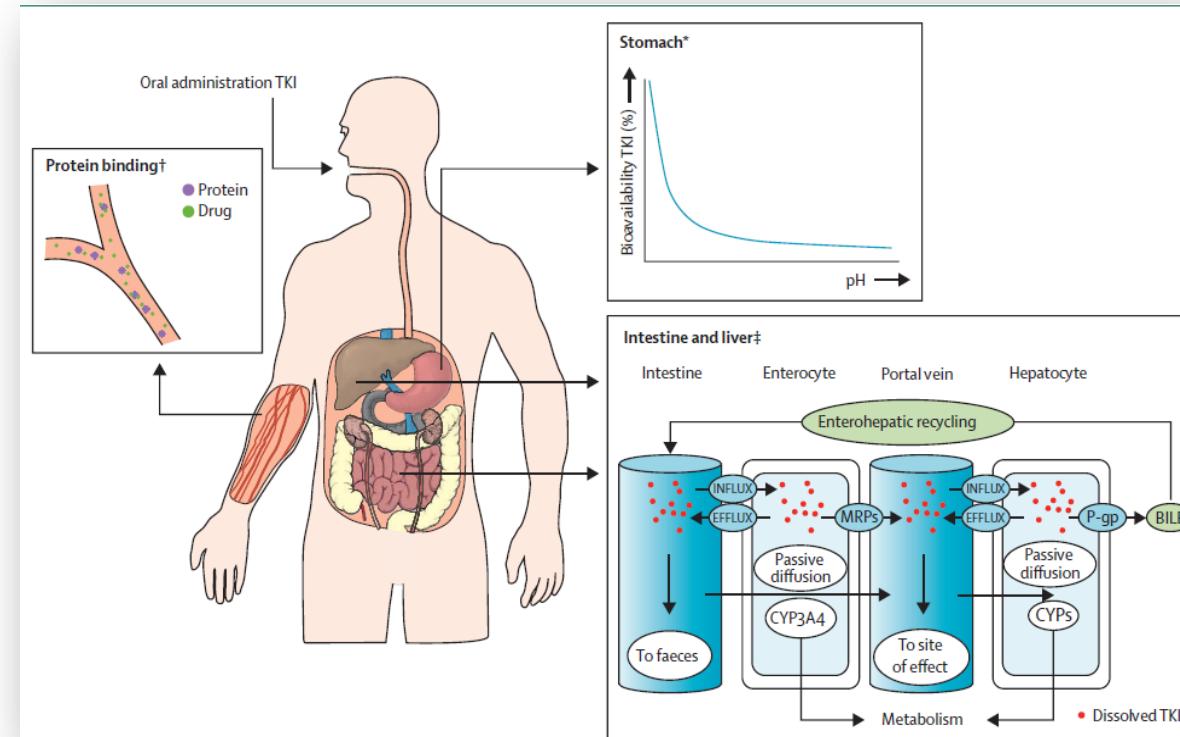
Things to Consider for Oral Anti-Neoplastic Agents

- Age-associated absorption, metabolism, and excretion
- Drug-drug and drug-food interactions
- Adherence, persistence, and treatment fatigue
- Access due to coverage for oral agents
- Lifestyle
- Comorbidities
- Polypharmacy
- Capability for health self-management

Oral Therapies: Major Sites of Pharmacokinetic Interactions

The ingestions, absorption, metabolism, and excretion of oral compounds require multiorgan function:

- Gastrointestinal tract
- Renal
- Hepatic
- Hematologic



Drug-Drug, Drug-Food Interactions

Absorption

- Oral bioavailability
- Food-drug interactions
- Stomach pH

Metabolism by the cytochrome P450 isozymes

- Pharmacodynamic interactions: synergistic, additive, or antagonistic

Most common things to avoid

- Grapefruit, Seville oranges, starfruit
- Azoles
- Proton pump inhibitors

Patient characteristics

- Elderly
- Hepatic impairment
- Ability to ingest oral formulations
- Renal clearance/excretion

Adherence and Persistence

- Adherence: Taking the drug as prescribed
 - Average rate of adherence to medication regimens in chronic illnesses is approximately 50%
- Persistence: The number of days or duration of time a patient is able to maintain adherence or continuation of therapy
 - On-time refills, the number of refills, and planned or unplanned gaps in therapy

It is so much more than simply taking medications

“Drugs don’t work in patients who don’t take them.”
~ C. Everett Koop, MD

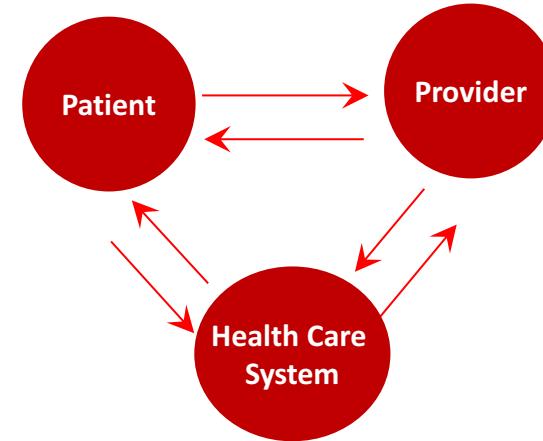
To be adherent, the patient must:

1. Fill the prescription
2. Consume it in a manner consistent with the prescription
3. Continue to take it unless directed otherwise by the healthcare provider
4. Keep follow-up appointments

Nonadherence is:

1. A multifaceted process
2. Linked to both intentional and unintentional factors
3. Not linked to any one type of disease

There is no typical patient profile for adherence.



Barriers to Adherence and Persistence

Personal

- Low health literacy
- Lifestyle: poor motivation, limited adaptation to healthy lifestyle
- Hopelessness
- History of nonadherence
- History of mental illness or substance abuse
- Cultural beliefs
- Competing comorbidities/polypharmacy
- Age
 - Peak at 70 y/o, then gradual declines in some patients due to age-related processes
 - Impaired executive function

Socioeconomic

- Limited financial or social resources:
 - Homelessness
 - Unstable housing
 - Uninsured
 - Lack of coverage for oral therapies
 - Copayment > \$90
- Lack of family/caregiver support
- Inconvenience

Barriers to Adherence and Persistence Related to Cancer Treatment

- Advanced disease or increased disease-related symptoms
- Episodic course of illness (periods of response and relapse)
- Lack of perceived benefit
- Patient-provider dynamics, lack of a sense of trust
- Perception of unacceptable treatment-related adverse events
- Perceived inability to effectively manage disease or treatment-related adverse events

No Typical Nonadherent Patient Type

- Adherence to prescription medications behavior is largely unrelated to self-care behaviors and lifestyle recommendations
- Well-trained athletes such as swimmers, marathon runners, and those who follow healthy diets, exercise, and abstain from alcohol may be nonadherent to medication
- People who are overweight, sedentary, or heavy smokers/drinkers may completely adhere to their medication



Common Myths: Forgetfulness

Survey of 20,000 patients identified key reasons for nonadherence:

1. Financial hardship (56%)
2. Side effects (46 %)
3. Concerns about medications (32%)
4. Lack of perceived need (25%)
5. Problems remembering to take medication (noted only for nonpersistence as the 7th reason) (12%)
6. Concern about medicines significantly predicts forgetfulness and carelessness in taking medication



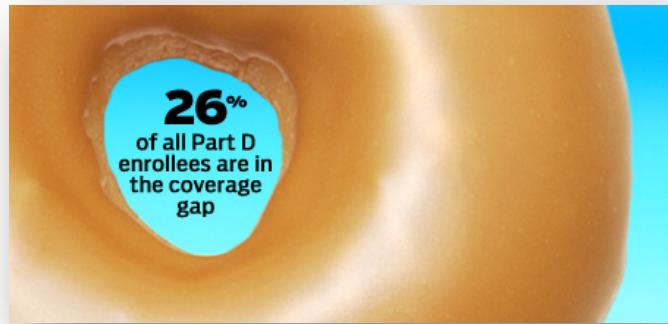
Lack of Coverage for Oral Agents: A Primary Factor in Adherence

Analysis of more than 10,000 pharmacy claims for oral anticancer drugs between 2007 and 2009

- 10% of patients abandoned their anticancer medicine
- 25% of patients had some delay in initiating another oncolytic
- 31% did not fill their initial prescription for oral anticancer medication (odds ratio 4.46, $p < .001$)
 - 25% of patients if the copayment amount was more than \$500
 - 6% of patients with cost-sharing of \$100 or less failed to fill their initial prescription

Other Factors Associated With Abandonment

Patients with 5 or more prescriptions have a 50% higher rate than for patients with no Rx processed within the past month (odds ratio 1.50; $P < .001$)



Medicare coverage ($P < .05$)

- ~ 50% of all cancer patients have Medicare
- Patients with Medicare coverage had higher rates of abandonment (16%) vs commercial patients (9%)



Lower income ($P < .05$)

Income $< \$40,000$ = 20% more likely to abandon vs those with income $> \$75,000$ ($P = .058$)

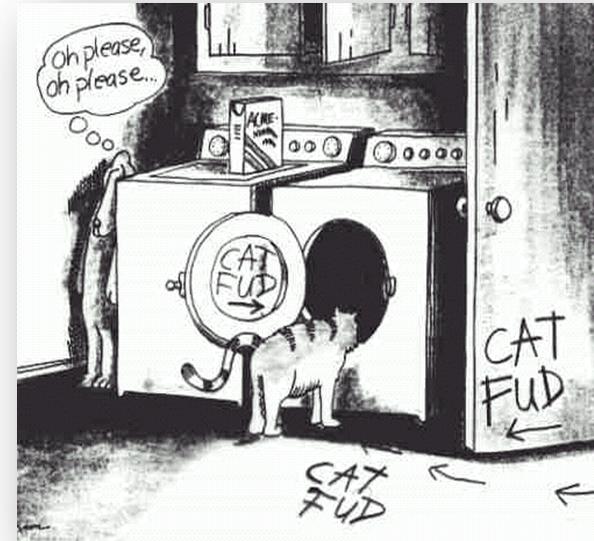
Strategies to Support Patients and Caregivers

- Empower with knowledge and resources
 - Including e-health technologies such as text messaging and calendar reminders
- Shared decision-making and effective communication strategies
- Engage caregivers in the treatment and education process
- Optimize treatment; prevent and/or reduce the severity of adverse events
- Simplify the treatment regimen
- Engage members of the interprofessional
- Use available assistance programs

Krueger, KP et al. *Adv Ther* 2015;22:313-56; Mallick R, et al. *Curr Med Res Opin* 2013;29:1701-8; Haynes RB, et al. *JAMA* 2002;288:2880-3000; Accordino MK, et al. *Am Soc Clin Oncol Educ Book* 2013;271-6; Kurtin SE, et al. *J Adv Pract Oncol* 2016;7(Suppl).

Effective Communication of Treatment Plan

- Patients must be able to understand how to take their medications in order to adhere...
- However, simple instructions do not guarantee improved understanding or that people will want to follow them



Reinforcement of learning is critical to successful self-management

Effective Communication of Treatment Plan

Complexity is not the key issue: It's how well the treatment fits into the individual patient's routine



- Food-drug interactions
- Daily activities: enjoyment or employment
- Perceived benefit
- Individual health beliefs



Reinforcement of learning is critical to successful self-management

CANCER DIAGNOSIS

Patient starts medication based on best recall
Recall for instructions provided may not be accurate
Patient may take wrong dose or follow wrong routine

Physician-patient consultation
Prescription written for oral chemotherapy

Prescription given to patient
Patient with a new diagnosis or recent change in therapy may be overwhelmed
Delay in processing Rx, delay in treatment

Patient picks up prescription
May have large copay or out-of-pocket costs
Delay in starting treatment

Patient takes Rx to pharmacy
Activates prior authorization process
Delay in starting treatment

Adherence Communication

- Healthcare providers assume patients are adherent
 - In one study, 89% of surveyed physicians believed the majority of their patients (> 75%) adhered to their medical recommendations
 - In a second study, 74% of physicians perceived their patients to be highly adherent
- Patients do not communicate openly with their providers
 - Among 1,100 adult patients
 - 68% said they would never communicate to their provider that they did not want a drug
 - 83% said they would never communicate to their provider that they did not plan on buying the drug

Key Elements of an Oral Therapies Program

- Designated staff and defined process for patient consultation and enrollment
 - Identify all patients on oral oncolytic
 - Provide structured education and counseling
 - Referral to appropriate resources
 - Interprofessional involvement
- Collaboration with specialty pharmacies
- Use of assistance programs

Conclusions

- A growing number of patients with cancer are being prescribed oral anticancer medicines
- All practices should develop an oral therapy program
- Strategies
 - Tailored interventions
 - Frequency of visits
 - Prevention of adverse events
 - Use of assistance programs