Adherence to oral cancer treatment:
What do we know and how can we use it?

Pamela K Ginex, EdD, RN, OCN
Nurse Researcher
Memorial Sloan Kettering Cancer Center

Laura Fennimore, DNP, RN
Director of Clinical Programs
UPMC Health Plan
“Drugs don’t work if people don’t take them.”

C. Everett Koop, Former US Surgeon General
Objectives

• Define medication non-adherence and contrast with the term medication compliance
• Describe the impact of non-adherence in health care
• Identify contributing factors and predictors of poor adherence to medication that impact successful treatment for chronic illness
• Describe innovative strategies to promote medication adherence
State of the problem

Patient scenario:

“MS, a patient with advanced breast cancer, participated in a clinical trial of an aromatase inhibitor. During the trial, her husband usually accompanied her on follow-up visits.

When MS was asked about medication usage since the previous visit, she invariably reported that she had taken her aromatase inhibitor as prescribed.

During one visit when her husband was not in the examination room, MS confessed to her nurse: ‘I just have to tell you the truth – Most of the time, I forget to take that pill.’”

(Palmieri, F.M., & Barton, D. L., 2007)
State of the problem

• For all medications:
  – **One third to one half** of all patients do not take medications as prescribed
  – Improving adherence to all medications can save as much as $300 billion in health care costs

• For oral cancer treatment:
  – **Rates of** adherence remain unknown but some studies in breast cancer have documented rates of 53-93% (Moore, 2010).
  – The number of agents and the number of patients taking these agents will only increase.
  – 50% of therapies in development are oral (Given, B.A., Spoelstra, S., & Grant, M., 2011).
  – Due to the gravity of a cancer diagnosis our **goal should be as close to 100%** adherence as possible.
Shift to oral cancer treatments

**Advantages**
- Patient convenience
- No need for IV access
- Can achieve sustained drug levels
- Minimal disruption in daily life
- Patient preference

**Disadvantages**
- Distances patient from provider
- Changes the way patients are monitored
- Safeguards for prescription or administration may be lacking
- Patients have more responsibility for their own care
Definitions

- Adherence/Compliance
  - Adherence is preferred but both terms are imperfect, and unfortunately, can stigmatize patients

- Definitions of adherence
  - World Health Organization
    - “the extent to which a patient’s behavior coincides with medical advice”
  - International Society for Pharmacoeconomics and Outcomes Research
    - “the degree or extent of conformity to the recommendation about day-to-day treatment by the provider with respect to the timing, dosage, frequency and duration of time from the initiation to discontinuation of therapy.”
  - Adherence is often defined to be taking 80% or more of a medication as prescribed
    - This is an arbitrary number
    - Adherence is impacted by multiple factors
Definitions

• Persistence
  – Duration of time a person takes medication, from **initiation to discontinuation**

• Overadherence
  – Defined as **taking more than the prescribed** amount of a medication
  – Reasons can include taking longer than prescribed or taking extra doses on a single day
  – One study found that overadherence was more likely than underadherence (20% compared to 13%)
  – More complex regimens were more likely to have overadherence

(Spoelstra et al, CJON 2013)
How do we measure adherence?

• No gold standard

• Most studies have used direct and indirect methods to measure adherence

• All methods have advantages and disadvantages
Direct measurement

- Directly observed (in person or remotely)
- Level of medication or metabolite in blood
- Level of biomarker in blood

Advantages – **most accurate** and objective

Disadvantages – patients can hide pills, impractical, variations in metabolism, expensive
Indirect measurement

- Patient self-report, questionnaires
- Pill counts
- Electronic pill caps
- Prescription bottle refills
- Physiologic markers (heart rate, BP)

**Advantages** – simple, inexpensive, some are objective

**Disadvantages** – susceptible to error, easily altered by patient, other factors can affect response
Why didn’t you take your meds today?

It’s not just about forgetfulness. . .
Factors influencing adherence

- Patient factors
- Socioeconomic factors
- Clinician factors
- Therapy factors

Adherence
Factors influencing adherence

Patient and condition-related factors

- Cognitive impairment
- Co-morbidities (depression)
- Gender
- Psychological stress, anxiety, anger
- Other medications
- Beliefs about treatment and outcome
- Health literacy
- Confidence in ability to follow treatment regimen
- Substance abuse

Other Psychosocial Factors

- Ability to follow a prescribed regimen
- Communication with providers
- Patient satisfaction
- Health beliefs
- Adherence history
- Family stability and social support
Factors influencing adherence

Therapy-related factors
- Adverse events
- Length/complexity of treatment
- Pattern of dosing
- Side effects (actual or perceived)
- Refills
- Polypharmacy/drug interactions
- Label warnings

Dosing
Simple dosing helps but 10-40% of patients on a simple regimen have imperfect dosing.

Adherence is inversely proportional to frequency (QID dosing has average adherence rates of about 50%)
Complexity of treatment

BEACOPP

- Etoposide 100 mg/m² IVPB over 60 min Days 1 - 3* (May be given orally days 2 and 3)
- DOXOrubicin 25 mg/m² IVP Day 1
- Cyclophosphamide 650 mg/m² IVPB over 30 min Day 1
- VinCRISTine 1.4 mg/m² IVP Day 8
- Bleomycin 10 units/m² IVP Day 8
- Procarbazine 100 mg/m² PO Days 1 - 7
- Prednisone 40 mg/m² PO Days 1 - 14

Repeat every 21 days

Antiemetics

- Palonosetron 250 mcg IVPB ----
- Ondansetron ---- 8 mg PO
- Dexamethasone 12 mg IVPB ---- ----
- Ondansetron 8 mg PO/IV q8h PRN N/V PRN N/V PRN N/V
Factors influencing adherence

Socioeconomic-related factors

- Attitude towards treatment
- Cost of treatment
- Financial support
- Difficulty accessing pharmacy
- Distance to treatment center
- Social rank of illness
- Social support
- Cultural beliefs

What is the patient’s responsibility for co-insurance or co-payments?
Factors influencing adherence

Clinician-related factors
- After care management
- Communication skills
- Belief in treatment
- Provider/patient relationship
- Use of guidelines
- Provision of information
Question…….??.?

Why are some patients adherent to therapy despite many challenges while others struggle despite optimal circumstances?
Predictors of poor adherence

- Presence of psychological problems, particularly depression
- Cognitive impairment
- Inadequate follow up or discharge planning
- Side effects
- Patient lack of belief in treatment
- Poor provider-patient relationship
- Barriers to care or medications
- Missed appointments
- Complexity of treatment
- Cost of medication, copayments
What does all of this tell us?

There needs to be a nursing presence in all phases of oral cancer treatment.

We need to be PROACTIVE and not reactive

(Yagasaki & Komatsu, 2013)
Medication adherence across disease states

It’s important in every disease state….

• Remember previous medication adherence history impacts adherence to oral chemotherapy

CHECK medication adherence with other medications:

- Diabetes
- Asthma
- CAD / CHF
- Hypertension
- HIV / AIDS
HIV experience with adherence research

Why look at HIV adherence research?

• A significant amount of research has been conducted
  – Adherence is strongly related to the degree and durability of viral suppression
  – Adherence is associated with decreased rates of progression, hospitalization, and mortality
  – Poor adherence correlates with treatment failure and can limit options for future treatment due to cross-resistance
  – Viral load can be assessed as a marker for adherence

• Similar to oral cancer treatment in many ways
  – Complex regimens
  – Multiple side effects
  – High degree of toxicity
  – High pill burden
Barriers to adherence in patients with HIV

• **Sample:** 110 men and women from 4 US cities

• **Results:**
  
  – Numerous factors and multiple types of factors that seemed to effect adherence
  
  – Many issues affected medication adherence
  
  – Adherence was described as a dynamic phenomenon that changed over time, with changing beliefs, attitudes, emotions, and daily events as well as larger life experiences

(Remien et al, 2002)
Barriers to adherence in patients with HIV

Major themes identified

• Belief and trust in treatment and health care providers
• Experiences of side effects and concerns about toxicity
• Self monitoring and taking personal control
• Regimen demands and planning
• Priorities, competing concerns and mood states
• Social support
• Future orientation

(Remien et al., 2002)
HIV patient support & education interventions

Factors that were associated with improved adherence

- Individual interventions
- Interventions that were longer in length
- Interventions that targeted practical medication management skills compared to those that targeted cognitive behavioral or motivational approaches

(Rueda et al., 2006)
Gross et al. (2013) studied Managed Problem Solving (MAPS) vs usual care

- MAPS – four in person and 12 weekly meetings over 3 months followed by monthly phone calls for 9 months
- The odds of being in a higher adherence category was 1.78 times greater for the patients who received MAPS than usual care
- The odds of having an undetectable HIV RNS level were 1.48 times greater for patients who received MAPS than usual care
- These results were sustained throughout the intervention (12 months)
- Involved minimal interaction with health care professionals
HIV patient support & education interventions

Simioni et al. (2010) – a nurse delivered intervention in China

- 70 patients in a randomized clinical trial
- Both arms received education, a pillbox, and support. The intervention arm included an electronic reminder, individual counseling or both

Results

- Adherence was high in all groups
- The intervention group reported better adherence, but the study was not powered to show statistical significance
Nurse counseling intervention

• **Telephone counseling** was given by a trained nurse to 98 participants
  – Patients received telephone counseling (median of 3 sessions)
  – Nurses assessed readiness for adherence, provided support to overcome barriers, and offered information based on participants questions

• **Results**
  – Counseling was associated with a high percentage of participants reaching target adherence levels

(Cook et al., 2009)
“Is there an APP for that?”

My Medications – AMA

Medication Guide – Google Play

Pillboxie – designed by RN
Mobile phone & text messaging interventions

2 studies from Kenya showed promise for text messaging interventions

- Lester (2010) – patients were randomly assigned to receive a brief text message weekly vs standard care
  - Patients who received the text message had a lower risk of nonadherence and a lower risk of virologic failure

- Pop-Eleches (2011) – patients were randomly assigned to short or long text messages either daily or weekly vs standard care
  - Patients who received any message had higher adherence although weekly messages were more effective
What can we learn from the HIV adherence work?

- Interventions providing education and support can be effective
- Technology can help to improve adherence and does not need to be frequent

We still need to know:

- Do the effects of the intervention remain after it is completed?
- Is support and education required continuously or are there times when support and education are more necessary?
What can oncology nurses do?

- Rethink how we practice
- Remember that **Education** and **Communication** are key
- Intervene
Rethink our practice patterns

• What are current practices in the US regarding care and safety of patients on oral cancer treatment?
  – Survey of 577 oncology nurses
    • 51% of nurses had specific policies, procedures and resources for patients on oral chemotherapy
    • Barriers included cost (81%) and adverse effects (27%)
    • Many practices had erratic procedures and inadequate communication

• Implications
  – Nurses should provide thorough education and repeated teaching to improve patient safety, adherence and self-monitoring for adverse effects

(Roop & Wu, ONF 2014)
Nursing Role

• Qualitative study of 18 oncology nurses
• “The need for a nursing presence” during oral chemotherapy treatment
• 4 themes emerged
  – Patient isolation in current practice
  – Involvement in entry
  – Proactive patient care
  – Coordination

• Proactive care leads to predictive care (prevention)
Practice culture

- What is the current MD/clinic/chemo unit flow and how should this change for patients on oral treatment?
- Do nurses always know who is on oral treatment?
- Uncertainty in roles/responsibilities
- Lack of consistent follow up
Involvement from the beginning

- Nurses should be involved early
- Nurses are more likely to consider the family/living situation more than other healthcare professionals
Proactive patient care

• Need to connect with the patient and family
• Develop a trustful relationship
• Work to decrease the fragmentation of care
Fragmentation of care

• Nursing coordination during treatment

• Follow up

• Coordinate communication among healthcare providers

• Assess documentation, especially in the electronic medical record
Nursing process and adherence

• **Assessment**
  – Assess adherence at every visit

• **Planning**
  – Assessment challenges make planning difficult

• **Intervention**
  – Can be costly and time consuming
  – Incorporate small changes into your practice

• **Evaluation**
  – Is the plan working for the patient?
Education

• **Traditional counseling**
  – Healthcare provider is the expert
  – Assumes patient lacks knowledge
  – Tells patient what to do
  – Hopes patients follow directions
  – Goal is to motivate the patient
  – HCP persuades the patient to change behavior
  – HCP expects respect from the patient

• **Motivational interviewing**
  – HCP develops a partnership with the patient
  – Exchanges information to facilitate an informed decision
  – Patient has the right to decide own care
  – HCP and patient negotiate behavior and reach agreement
  – Goal is to access motivation and elicit patients’ commitment to change behavior
  – HCP understands and accepts patients’ action
  – HCP must earn respect from patient
Patient perceptions of education

- Women with breast cancer on hormonal agents
- Reasons for nonadherence
  - Side effects (69.8%)
  - Cost (20.8%)
  - Forgot (7.5%)
- Factors that would improve adherence
  - Knowing it would improve outcome
  - Better management of side effects
  - Reminded of the reasons to take medications as directed
  - Asking at every visit

Discussed the importance of adherence to oral medications (N=303)

- Occasionally (18.5%)
- Only once, before treatment (33.3%)
- Never (4%)
- At every office visit (44.2%)

(Kirk and Hudis, 2008)
Education

S – **simplify** the regimen

I – **impart** knowledge

M – **modify** patient beliefs and behavior

P – **provide** communication and trust

L – **leave** the bias

E – **evaluate** adherence
Education

• **Who and when?**
  – All patients on oral agents should see a nurse at start of treatment and in follow-up
  – MD and pharmacist should be involved
  – Building trust helps patients to be honest about missed or late doses
  – Caregiver should be included (for ALL patients)
  – Education should be ongoing and in multiple forms

• **Where?**
  – On going – in person and over the phone

• **What?**
  – Patients should know name (generic and brand), dose and schedule, how it’s taken (food, time), safety, side effects/symptom management.
Education

Sommers et al. (2012)

- Feasibility pilot of a face to face educational intervention, medication diary and nurse-initiated telephone call to support patients’ adherence and knowledge of oral chemotherapy

- 30 patients with gastrointestinal cancer
  - Patients demonstrated high adherence scores
  - The intervention was feasible and the scale used to measure adherence was easy to administer
Interventions

Communication strategies

• Ask the patient how they remember to take their medications
  – Avoid closed ended questions
  – “Do you have a way to remember to take your oral chemotherapy?”
  – “Everyone forgets to take their medication from time to time. When was the last time you forgot to take any of your medication?”

• If you know what the pill looks like, let them know
Interventions

• **Reminder triggers**
  - Pill diaries, pill boxes, calendar or spreadsheet, checklist
  - Postcard reminder for refills
  - Blister packs
  - Cell phones, alarms – message texting when doses are due

• **Teach back**
  - “I want to be sure that I explained your medication correctly. Can you tell me how you are going to take this medicine?”
  - “We covered a lot today about your treatment, and I want to make sure that I explained things clearly. So let’s review what we discussed. What are three strategies that will help you take your chemo correctly?”
  - “What are you going to do when you get home?”
Interventions

**Automated voice response system**
- 30 patients with solid tumors
- Received a Symptom Management Toolkit and weekly automated voice response calls
- If patients reported adherence less than 100% or symptoms of 4 or greater (on 0-10 scale) received a call from a nurse

**Outcomes:**
- 23.3% nonadherence rate (most common reason – forgetfulness)
- An association between symptom management and adherence was found
- Nurses should ask patients how they are taking their medications at each visit
  - Similar to smoking cessation, just asking will improve the outcome

(Decker et al., Cancer Nursing 2009)
Interventions

MASCC teaching tool (www.mascc.org)

• Develop in response to a nurse from Turkey who completed a study that showed nurses were lacking teaching tools and guidelines for oral cancer treatment.

• This teaching tool has been prepared to assist health care providers in the assessment and education of patients receiving oral agents as treatment for their cancer.

• The goal is to ensure that patients know and understand their treatment and the importance of taking the pills/tablets as prescribed.
KEY ASSESSMENT QUESTIONS

1) What have you been told about this treatment plan with oral medications? *Verify that the patient knows that these oral agents are for cancer and are taken by mouth for their cancer.

2) What other medications or pills do you take by mouth? *If you have a list of medicines, go over the list with the patient.

3) Are you able to swallow pills or tablets? If no, explain.

4) Are you able to read the drug label/information?

5) Are you able to open your other medicine bottles or packages?

6) Have you taken other pills for your cancer? *Find out if there were any problems, for example, taking the medications or any adverse drug effects.

7) Are you experiencing any symptoms that would affect your ability to keep down the pills, for example nausea or vomiting?

8) How will you fill your prescription? *Delays in obtaining the pills may affect when the oral drugs are started.

9) Have you had any problems with your insurance that has interfered with obtaining your medications?

*Recommended information to assess is noted in italics

Special considerations when assessing patients receiving oral agents for cancer:

When teaching the patient, you may need to adapt your teaching to accommodate special considerations such as, age, feeding tube, vision problems/color blindness, dietary issues, mental problems (dementia, depression, cognitive impairments).
ONS adherence toolkit

• 12 tools for nurses
• Provides strategies and resources that nurses can use to facilitate adherence among patients with cancer related to:
  – Safety concerns: drug-drug and food-drug interactions, adverse effects
  – Pharmacy and reimbursement/financial resources
  – Monitoring of adherence
  – Motivational interviewing and counseling
  – Change theory and helping patients to change nonadherence into adherence.

Case study

Carla, a 67 year old woman, has been treated for colorectal cancer. She had a good response to first line therapy. After 5 years a routine CT found a local recurrence and liver metastasis. She was started on capecitabine, 2500mg/day (1500/1000). She also has diabetes, HTN, sleep problems and vision loss. She is on 5 other medications daily. She lives with her husband and grandchildren (6 and 8 years old).

• What should the nurse include in her teaching?
• What specific strategies would help Carla?
Case Study

Karin is a 49 year old female who was diagnosed with HER-2 positive breast cancer 8 months ago. She had a lumpectomy followed by adjuvant chemotherapy followed by radiation. She was then started on Herceptin.

She is a lawyer and lives with her husband and teenage son. She has a busy work schedule and takes no other medications. She has never eaten breakfast and is often at work by 8am and not home until 6 or 7pm.

On follow up she is found to have liver metastasis and is started on capecitabine and lapatinib. Her capecitabine is 4 pills in the am and 3 in the pm for 14 days on/7 days off. She is to take 5 lapatinib pills daily for 21 days.

- What factors about Karin and her treatment stand out?
- What strategies should the nurse consider when educating Karin about her treatment?
• Educational interventions show promise to increase adherence
• Technological based interventions also show promise to increase adherence
• Additional research (high quality RCT) are needed
• Nurses, in collaboration with other health care professionals, play a vital role in developing and implementing studies aimed at improving adherence
Summary

• Oral therapy for cancer treatment is here to stay and only going to increase as additional agents are developed
• Our practice settings need to change to accommodate a new treatment paradigm
• Nurses are the best advocates for patients on oral treatment regimens
• They can educate, manage symptoms, improve patient quality of life and help patients to stay on treatment
• We should have a significant presence in planning for patient care, research and guidelines related to oral cancer treatment
Questions, comments?  
Thanks!!

Our contact information:

- Pam Ginex, EdD, RN, OCN®  
  ginexp@mskcc.org

- Laura Fennimore, DNP, RN  
  fennimorela@upmc.edu