Adherence to Oral Cancer Therapies: Nursing Interventions

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This article reviews nursing interventions to increase adherence to oral cancer therapies, such as patient and care-partner education, side-effect and medication management, and safety issues. Data sources included peer-reviewed nursing and medical literature, healthcare Web sites, and published monographs. Oncology nurses are uniquely positioned to promote patient adherence to oral cancer therapies by ensuring that patients understand the goals of treatment, promoting safe prescriptive practices, proactively managing treatment side effects, and identifying and resolving underlying barriers to adherence. When adherence is optimized, clinical outcomes are greatly improved. Primary responsibility for adherence to an oral cancer therapy regimen remains with the patient. Oncology nurses, as part of a healthcare team, can have a significant influence on patient adherence by providing thorough and timely patient and family education and by monitoring and managing side effects of treatment. Monitoring adherence to oral cancer therapies is not a recent phenomenon nor limited to oral cancer treatments but presents an increasing challenge as additional oral therapies enter the marketplace. Oncology nurses should develop and enhance strategies and materials for patient education on oral cancer therapies, improve side-effect management, assist with patient access to medications, and develop practice guidelines to ensure adherence and promote safety.

At a Glance

- Oral agents are becoming more common in cancer care, resulting in a need for nurse education.
- Although nurses are essential in teaching patients about IV chemotherapy, oral care education often is performed by physicians.
- Side effects and toxicities of oral therapies can be as difficult to manage as the effects of IV therapy.

Oncology nurses are an essential part of the oncology team when teaching patients about IV chemotherapy, often taking responsibility for most of the teaching, whereas physicians often teach patients about their oral therapies. Nurses need to become frontline teachers when patients start oral therapy regimens. Their skill at helping patients with side-effect management, procurement, handling medications at home, and follow-up care can help increase patient adherence to medication, thereby increasing the efficacy of drug therapy.

Patient Education on Oral Therapy

The growth of oral medications stems from research in the areas of extra- and intracellular signaling pathways. By interfering with or blocking these signals, targeted drugs have become standard agents in cancer therapy. Because the pathways are specific, inhibition occurs at certain sites within the cell, which may cause unique side effects (Goodin, 2007).

Side effects may differ, and patients take the medications at home; therefore, patient education should be thorough and complete. Teaching should occur at the appropriate time. When a patient is first diagnosed or learns of recurrent or progressive...
disease that requires treatment, he or she will be anxious, upset, or frightened; as a result, this visit may not be the best time for teaching about oral therapy (Moore, 2007). The stress of the new information precludes the ability to learn, grasp, and absorb teaching about any form of therapy, whether IV or oral. Ideally, patients should be scheduled for a follow-up visit with the physician or nurse to review the treatment plan, specifically oral regimens (Hartigan, 2003).

Other factors to consider with patient education include assessing the patient for any barriers to learning and identifying appropriate methods for the patient to learn (e.g., written, verbal, visual). Teaching should be tailored to each individual, avoiding scripted dialogue that could be given to every patient. Rapport is important for patients and their families to feel comfortable asking questions (Hartigan, 2003). If patients feel uncomfortable with their healthcare providers, the discomfort can impede their ability and willingness to learn (Osterberg & Blaschke, 2005). Teaching should include the patient as well as any family or care partners who are involved. Family or care partners may help monitor adherence and administer oral medications as well as assist with reporting side effects (Hartigan, 2003).

**Side Effects of Oral Cancer Therapies**

Side effects of oral cancer therapies may be different from drugs delivered via IV, but they have the same potential for severity, making patient education and monitoring equally important in both settings (see Table 1). Patients on all-oral therapy regimens may not visit the clinic as frequently as patients on IV regimens. All patients receiving cancer therapy need to know when, who, and how to call for healthcare support during and after clinic hours. Symptoms can quickly escalate at home, resulting in exacerbation of minor side effects into serious acute conditions that require admission to an inpatient unit for management. Good patient teaching and symptom triage prevent this.

**Nausea and Vomiting**

Nausea is common with many oral agents, and some patients may experience vomiting. Poor control of nausea and vomiting may make patients anxious about taking the next dose. Teaching patients about prevention of nausea with oral antiemetics prior to taking their oral therapy may prevent nonadherence. Patients should take most oral therapies with food to decrease gastrointestinal side effects unless contraindicated (e.g., erlotinib, lapatinib, sorafenib). If applicable, nausea may be minimized by taking the oral agent at night if once-daily dosing is prescribed. Patients also should be instructed on adequate hydration and the importance of eating regularly. Patients or care partners should contact the nurse if nausea or vomiting is causing decreased food or fluid intake or continues after 24 hours of antiemetic treatment (Murphy-Ende, 2006).

**Diarrhea**

Diarrhea is a common side effect of many oral agents. Patients should be instructed on the use of over-the-counter antidiarrheals such as loperamide, including dosing and clear instructions as to when the healthcare provider should be contacted.

### Table 1. Common Side Effects of Oral Cancer Therapies and Key Points for Patient Education

<table>
<thead>
<tr>
<th>SIDE EFFECT</th>
<th>DRUGS</th>
<th>PATIENT EDUCATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal values</td>
<td>Dasatinib, Imatinib, Erlotinib, Gefitinib, Lapatinib, Sorafenib, Sunitinib</td>
<td>Frequent laboratory tests, Replacement of minerals (may increase nonadherence), Monitor symptoms, Electrocardiograms if needed</td>
</tr>
<tr>
<td>Birth defects</td>
<td>Lenalidomide, Thalidomide</td>
<td>Programs or authorizations for administration, Special ordering requirements</td>
</tr>
<tr>
<td>Bone marrow suppression</td>
<td>Bexarotene, Dasatinib, Imatinib, Lenalidomide, Thalidomide</td>
<td>Frequent laboratory tests, Neutropenic precautions, Bleeding precautions, Transfusions for anemia</td>
</tr>
<tr>
<td>Cutaneous reactions</td>
<td></td>
<td>Use of emollients or creams, Antibiotic cream or oral steroids, Frequent skin checks and clinic visits, Medication break or dose reduction</td>
</tr>
<tr>
<td>Diarrhea</td>
<td></td>
<td>Use of loperamide, diphenoxylate hydrochloride or atropine sulfate, atropine, or tincture of opium, Increase fluid intake, Bland (low-residue diet) or BRAT (bananas, rice, applesauce, and toast) diet, IV fluid replacement in clinic Perineal and rectal hygiene</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td>Monitor weekly for six weeks from start of symptoms, Teach patients to monitor blood pressure at home, Add oral antihypertensives (e.g., thiazide diuretic, angiotensin-converting enzyme inhibitor, beta blocker, calcium channel blocker)</td>
</tr>
<tr>
<td>Nausea or vomiting</td>
<td></td>
<td>Take oral antiemetic 30 minutes prior to dose, Increase fluids, Monitor patient weight, Take medications with food</td>
</tr>
<tr>
<td>Thrombosis</td>
<td>Erlotinib, Lenalidomide, Thalidomide, Vorinostat</td>
<td>Increase activity (e.g., walking), Increase fluids and ensure adequate hydration, Elevate legs, Preventive low-dose aspirin or warfarin, Frequent monitoring</td>
</tr>
</tbody>
</table>

**Note.** Based on information from AstraZeneca, 2005; Bayer Healthcare Pharmaceuticals Inc., 2006; Bristol-Myers Squibb, 2006; Celgene Corporation, 2006a, 2006b; Genentech, Inc., 2005; GlaxoSmithKline, 2007; Held-Warmkessel, 2006; Ligand Pharmaceuticals, 2008; Merck & Co., Inc., 2008; Novartis Pharmaceuticals, 2006; Pfizer Inc., 2006; Roche Laboratories, 2006; Viale et al., 2005; Viele, 2007.
Other medications that can be used to treat diarrhea include diphenoxylate and atropine, fiber sources such as psyllium, subcutaneous atropine, tincture of opium, or octreotide (Lacy, Armstrong, Goldman, & Lance, 2006). Dietary instructions should include increased oral fluid replacement, use of the bland diet (soft foods with low seasoning such as mashed potatoes, cream of wheat, and rice), and use of the BRAT diet (bananas, rice, applesauce, and toast) (Held-Warmkessel, 2006; Viale, Fung, & Zitella, 2005). If diarrhea is not controlled, a call to the healthcare provider is needed to determine whether IV hydration in the clinic or hospital admission is required.

**Hypertension**

Blood pressure monitoring for hypertension is important in patients taking sorafenib or sunitinib (Bayer Healthcare Pharmaceuticals Inc., 2006; Pfizer Inc., 2006). At the start of treatment, blood pressure should be monitored at least weekly for six weeks (Onyx Pharmaceuticals, Inc., 2005). Clinic visits will allow for assessment of blood pressure, but patients can be instructed on monitoring blood pressure at home. If home blood pressure monitoring is a new skill, the patient and care partner should be asked to purchase a blood pressure monitor and bring it to the clinic for teaching. In addition, information on what blood pressure reading would prompt a call to the doctor or nurse should be conveyed. Patients who develop persistent hypertension should be started on antihypertensive medication by the oncology healthcare provider following the Joint National Commission guidelines (National Heart, Lung, and Blood Institute, 2003) or through referral to their internist or to a cardiologist. The most current Joint National Commission guidelines can be viewed at www.nhlbi.nih.gov/guidelines/hypertension/express.pdf. Patient adherence to oral antihypertensive medication should be assessed at regular intervals.

**Cutaneous Reactions**

A variety of cutaneous reactions such as skin rash, hand-foot skin reaction, and hand-foot syndrome (also called palmar-plantar erythrodysesthesia) can be seen with capecitabine, erlotinib, imatinib, gefitinib, and sorafenib (Viele, 2007). Patients experiencing rash while taking tyrosine kinase inhibitors may see the rash as a positive indicator that the drug is working and increase adherence or may decrease adherence because they consider the rash an unpleasant symptom. Patients need to be instructed adequately on the rash that occurs during the first cycles of targeted therapy treatment because it is very visible, often on the face, neck, and upper torso. The rash often is referred to as acniform, maculopapular, maculopustular, or follicular (Oishi, 2008). Although the rash is termed acniform by many practitioners, it is not acne and should not be treated as such. Rash occurs within the first two to three weeks of oral therapy treatment. Besides the rash, patients also may exhibit extremely dry skin and pruritus (OSI Pharmaceuticals, Inc., 2009). Instructing patients on care of the rash and frequent nursing assessment are imperative to prevent possible infections and nonadherence because of the rash’s visibility.

Treatment for the skin rash involves frequent assessments of the patient’s skin by the healthcare provider. Patients should notify the clinic at first signs of the rash so monitoring can begin. Teaching must include basic skin care such as washing with mild soap and water and recommended topical applications to help treat the rash (Eaby, Culken, & Lacouture, 2008). Treatment may include starting with a hydrocortisone ointment and moving on to clindamycin gel if the rash becomes pustular (OSI Pharmaceuticals, Inc., 2009). Systemic antibiotics such as minocycline or doxycycline may be warranted if lesions become more severe or drain. Treatment may be held or dosage adjustments made if the rash becomes severe enough to affect activities of daily living or the patient experiences infection or severe distress.

Hand-foot skin reactions with oral targeted agents differ from those seen with IV infusions such as 5-fluorouracil. The reactions often start with paresthesia of the fingers, palms, and padded areas of feet. The areas may resemble calluses that are very painful and may affect activities of daily living because of inability to walk. Treatment of the skin with over-the-counter salicylic acid or urea-containing lotions should be initiated at first sign of hand-foot reactions (Wood & Manchen, 2007). Frequent checks of hands and feet need to occur at home, and the hands and feet should be examined thoroughly at all clinic visits. Teach patients to avoid prolonged pressure to feet and hands, apply lotion liberally, and wear cotton gloves, socks, and appropriate shoes. If symptoms are severe or activities of daily living are affected, the package insert should be consulted for treatment interruption or dose modification.

Hand-foot syndrome or palmar-plantar erythrodysesthesia is a common side effect of capecitabine, an oral 5-fluorouracil prodrug. Early signs of palmar-plantar erythrodysesthesia include erythema of the palms of the hands and soles of the feet and pain and swelling as it progresses (Wilkes & Doyle, 2005). Later stages of this adverse effect can include skin fissures or desquamation of the skin. Interventions for palmar-plantar erythrodysesthesia include liberal use of lubricating skin lotions and avoiding heat or trauma to the hands or feet. Dose interruption and modification to manage palmar-plantar erythrodysesthesia should be made according to manufacturer guidelines (Roche Laboratories, 2006; Viale et al., 2005).

**Myelosuppression**

As with IV chemotherapy, some oral agents also can cause grade 3–4 myelosuppression. Patients will need education on normal laboratory values and the significance of neutropenia and thrombocytopenia. Standard neutropenic precautions such as handwashing and monitoring the body temperature, with instructions to call the doctor or nurse for a temperature of 100.5°F or higher, should be discussed with the patient and included in written instructions to be kept at home (Lynch & Rogers, 2006). Bleeding precautions are important if thrombocytopenia is an expected side effect. Healthcare providers should educate patients on the symptoms of anemia such as dizziness, fatigue, shortness of breath, headache, or tachycardia so that patients understand and report them. Regular laboratory monitoring is required and patient teaching should include the importance of obtaining requested tests. Tests can be arranged at the clinic at a scheduled appointment, where the physician or nurse may review laboratories and triage patients if they are symptomatic. Patients also may be assessed at a clinic close to home.

Adequate nursing assessment, ongoing patient education, and proactive symptom management contribute to optimal adherence. Patients should feel that their symptoms are important and...
someone is listening to them. Nonadherence may be avoided by frequent patient assessments, careful side-effect management, and access to healthcare providers when patients need them, even when the clinic is closed. Provide patients with phone numbers for the healthcare clinic and instruct patients to post the numbers in readily available places. Patients should carry information cards identifying their medications and healthcare providers’ names and phone numbers in case of emergency.

**Monitoring Adherence**

Pill counts are a suggested mechanism of following patient adherence (Viele, 2007). However, patients can manipulate pill counts easily. Patients generally do not purposefully fabricate medication records but want to show the physician or nurse that they are being “good” patients (Hartigan, 2003; Partridge, Avorn, Wang, & Winer, 2002). If patients know that a pill count is going to occur, they may remove the number of pills (without taking them) so that the pill count appears correct.

Using the microelectronic monitoring system (MEMS), an electronic top that can record the time a bottle is opened (Hartigan, 2003), is another strategy. Patients can manipulate this by opening the bottle and not taking the medication or by taking too much. To date, most MEMSs are used in clinical trial settings and the observation of patients on trial may influence adherence rates (Partridge et al., 2002). MEMS is expensive and involves support equipment such as a computer to evaluate results.

Prescription refill monitoring is another mechanism to monitor adherence. A study by Nilsson et al. (2006) evaluated 300 copies of refill prescriptions for oral cancer drugs in Swedish pharmacies. Nilsson et al. (2006) found that 141 prescriptions were for cancer drugs, with many being hormones or hormone antagonists. Results showed that 20 prescriptions (14%) had a refill adherence lower than 80% and 56% reflected satisfactory refill adherence; no specific drugs were found to have more adherence issues. The results were equivalent to adherence rates in patients on other types of drugs. The process of refill monitoring is costly and time consuming, and patients may use more than one pharmacy to fill their prescriptions, making tracking refills difficult and inaccurate. Some medications may require use of a specialty pharmacy, which may impede refill monitoring.

A medication diary or calendar may help patients increase or maintain adherence (Moore, 2007). Patients can write in their diaries when they take doses, how many pills are taken, and any associated side effects. Medication diaries may be furnished by the pharmaceutical manufacturer. If the calendar is made in the clinic by the healthcare team, it should include the name of medication, how many pills per dose, how many doses per day, and times to take the medication (see Figure 1). Patients then can mark off each time medication is taken. Other medications, such as antiemetics, also can be placed on the calendar. Patients often need to be highly motivated to use a patient diary. Patients should bring the calendar or diary with them to each office visit for review by the oncology nurse or physician. If doses are missed, patients are to write that on the calendar or diary. Using a calendar or diary also can help the nurse identify cyclical or temporal patterns to certain side effects so that proactive interventions can be instituted.

**Safety**

When writing prescriptions, healthcare providers should take measures to ensure patient safety. Oral therapy prescriptions should be held to the same standards as IV chemotherapy orders, including signatures to confirm use of a double-check system. Full patient name, allergies, date of birth, body surface area, diagnosis, cycle number, dosage calculation, and a double check by another provider are needed on the prescription (Bartel, 2007). Pharmacists can provide valuable assistance with drug-drug interactions, particularly if patients use the same pharmacy for most of their regular prescriptions. In the clinic, review of medication lists with each clinic visit can minimize drug-drug reactions.

Medication histories should include prescription as well as nonprescription over-the-counter medications. Asking patients about herbal and vitamin supplements also is important. Interactions may occur with over-the-counter medications and oral agents. Antacids may cause an increased toxicity of 5-fluorouracil by reducing its elimination (Goodin, 2007) or interfere with the enteric coating of tamoxifen (Viele, 2007). St. John’s wort herbal remedy may decrease concentrations of certain oral agents such as sorafenib (Wood & Manchen, 2007).

Many oral agents are metabolized by the cytochrome P enzymes located in the liver. If oral agents are taken with other drugs that may be considered inhibitors, then increases in blood concentrations of the oral agents may occur (Goodin, 2007), which can lead to increased toxicity and need for dosage adjustments. Alternately, medications considered to be inducers of the cytochrome P pathway can cause reduction in blood concentrations of the oral agents, thereby reducing efficacy (Wood & Manchen, 2007).

Teaching patients about oral therapy should include how they should be stored, whether refrigeration is required, and whether they should be kept from light. Patients or their care partners

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**Figure 1. Sample Schedule for Patients on All-Oral Chemotherapy Regimen of Capecitabine and Lapatinib**

<table>
<thead>
<tr>
<th>Regimen Day</th>
<th>Xeloda AM and PM, Tykerb at bedtime</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-14</td>
<td>Day 1: ______ through Day 14: ______</td>
</tr>
<tr>
<td>15-21</td>
<td>Tykerb at bedtime Day 15: ______ through Day 21: ______</td>
</tr>
<tr>
<td>22-26</td>
<td>Xeloda AM and PM, Tykerb at bedtime Day 22: ______ through Day 26: ______</td>
</tr>
</tbody>
</table>

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**Table 1: Sample Schedule for Patients on All-Oral Chemotherapy Regimen of Capecitabine and Lapatinib**
can be given a medication cup to put their pills in at administration time to minimize handling of medications. If medication falls on the floor, it should be picked up with gloves or paper towels and disposed of properly, preferably in a biohazard container (Bartel, 2007; Winkeljohn, 2007). Medication should not be flushed down the toilet or a drain because of environmental concerns. If capsules break open, patients or care partners should be cautious not to inhale or touch the contents. Patients and care partners should always wash their hands after taking or administering medications. Extreme care should be taken to keep the medications out of reach of children. At the end of treatment, patients and their families should be encouraged to bring their unused medications to the clinic for proper disposal (Goodin, 2007).

Access to Oral Cancer Therapies

Patients undergoing cancer treatment may be uninsured or lack adequate pharmaceutical coverage on their health insurance policies. Oncology nurses are essential in helping these patients find access to medications. Patient assistance programs are available for those with low income and high medical costs or those without health insurance. In addition, several nonprofit organizations provide financial assistance with drug costs or copayments (see Figure 2). Nurses can help patients access these programs by assisting with paperwork, providing confirmation of diagnosis or prior authorizations as needed by the insurance company. Nurses may need to help patients find alternative pharmacies (e.g., mail-order pharmacies) that may offer lower prices or copayments. Because of issues with delay in filling prescriptions, the oncology clinic staff may benefit from familiarizing themselves with local pharmacies that carry certain oral cancer therapies to better inform patients. Patients should be advised to contact the nurse if the pharmacy cannot fill the prescription within 24 hours.

Oncology nurses should familiarize themselves with resources available to help patients with financial or procurement issues. National and local agencies can be contacted by the patient or the nurse to start the appropriate paperwork. Oncology nurses should keep lists of drug assistance programs that can be given to the patient or be contacted by the office to start the process of assistance.

Conclusion

Adherence to oral cancer therapies is far from optimal, and oncology nurses are charged with developing programs, instruments, and interventions that can improve outcomes. Many new antineoplastic agents in development are oral therapies, and additional studies specific to the new agents are needed to track accurate adherence rates. Nurses may be instrumental in gathering data or developing a research protocol to measure adherence. Oncology clinics can develop programs to help monitor adherence such as identification of staff nurses to be responsible for the oral therapy programs. The nurse can instruct patients in oral therapy and triage patients on a regular basis to monitor adherence and toxicities. Identification of a single nurse may help promote trust with patients and provide them with a single point of contact with the oncology office. The same nurse also could have patients call in to the clinic once they get their prescriptions to review what is written on the bottles and instructions they have received.

Nurses can develop patient educational materials and activities at offices and clinics. Activities may include providing written information in the waiting area (Partridge, Ades, Spicer, Englander, & Wickerham, 2007). A patient newsletter can be developed that reviews the cancer under treatment and the oral medication to treat the cancer (e.g., renal cell cancer and sunitinib). Education classes on oral therapies can be held at scheduled intervals in the clinic, taught by either an oncology nurse or physician (Partridge et al., 2007). If available, oncology clinics can use either an oncology pharmacist or pharmacy technician to do much of this patient teaching. The pharmacist or technician also can review medication lists to evaluate for drug-drug interactions. If time allows, pharmacy personnel can help determine insurance coverage or copayment and assist with drug procurement or patient assistance programs.

Most pharmaceutical manufacturers have patient assistance programs (PAPs) that provide free drugs or reduced cost for their individual medications. In addition to pharmaceutical programs, the following Web sites may provide assistance for patients unable to afford medication or copayment.

Association of Community Cancer Centers (www.acc-cancer.org/cancer_care/patients/patients-hotlines.asp) publishes a listing of reimbursement assistance programs for oncology-related services.

NeedyMeds (www.needymeds.org) is a clearinghouse for medication and low-cost medical care PAPs. NeedyMeds does not provide assistance directly but offers links and information to a variety of PAPs.

The Partnership for Prescription Assistance (www.pparx.org) combines U.S. pharmaceutical companies, doctors, other healthcare providers, patient advocacy organizations, and community groups to help qualifying patients who lack prescription coverage get medicines through appropriate public or private programs. Many patients will receive medication for free or almost free. The organization’s mission is to increase awareness of PAPs and boost enrollment of eligible patients. The Web site offers a single point of access to about 475 public PAPs, including more than 180 programs offered by pharmaceutical companies.

The Patient Advocate Foundation Co-Pay Relief Program (www .copays.org) provides direct financial support to insured patients, including Medicare Part D beneficiaries who qualify financially and medically to access pharmaceutical copayment assistance. The program offers personal service to all patients through call counselors who guide patients through the enrollment process.

RxAssist (www.rxassist.org) offers a comprehensive database of PAPs and practical tools, news, and articles for healthcare professionals and patients. The site includes Web pages relevant to healthcare professionals and patients.

Figure 2. Patient Assistance Resources

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