Role of the Nurse in Facilitating Adherence to Oral Therapies in Oncology Practice

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Medical Writer
Cheryl Zigrand
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The American Journal of Hematology/Oncology Editorial Board
Debu Tripathy, MD
Professor of Medicine and Chair
Department of Breast Medical Oncology
The University of Texas MD Anderson Cancer Center
Houston, TX
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Faculty
Carol Blecher, MS, RN, AOCN, APNC, CBCN
Advanced Practice Nurse/Clinical Educator
Trinitas Comprehensive Cancer Center/Trinitas Regional Medical Center
Elizabeth, NJ
Disclosure: *No relevant financial relationships with commercial interests to disclose.*

Amit A. Patel, MD
Attending Physician, Hudson Hematology/Oncology
Chief, Department of Hematology/Oncology, Barnabas Health - Jersey City Medical Center
Chairman, Barnabus Health - Jersey City Medical Center Cancer Center Committee
Chairman, Jersey Medical Center Institutional Review Board
Clinical Assistant Professor of Medicine, Jersey City Medical Center - Mt. Sinai School of Medicine
Assistant Professor of Medicine, St George's University School of Medicine
Clinical Assistant Professor of Medicine, New York Institute of Technology
Jersey City, NJ
Disclosure: *Speaker's bureau: Celgene*

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Overview
This activity is designed to inform healthcare professionals about issues related to adherence to oral oncology therapies.

Target Audience
This activity is directed toward hematologists, medical oncologists, nurses, and nurse practitioners who manage and treat patients with cancer. Transplantation specialists, radiation oncologists, pathologists, fellows, physician assistants, and other healthcare providers interested in the treatment of cancer are also invited to participate.

Learning Objectives
After participating in this CME activity, learners should be better prepared to:
- Appreciate the range of incidences of nonadherance to oral oncology therapies
- List some of the negative outcomes associated with poor adherence to oral anticancer therapies
- Identify some of the predictors of nonadherence to oral oncology therapies
- Identify and describe the roles of individuals needed as part of the multidisciplinary teams that support patients to obtain access to oral anticancer therapies

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Physicians' Education Resource, LLC
666 Plainsboro Road, Suite 356
Plainsboro, NJ 08536
Phone: (888) 949-0045
E-mail: info@gotoper.com

It goes without saying that in order for prescribed medication to be effective, the patient actually has to take it. With the recent increase in approved oral chemotherapy options, the majority of the onus falls on patients' shoulders to adhere to their prescribed treatment regimens. These oral agents have proven to be effective in clinical trials; however, these efficacy rates highly depend on patient compliance in real-world practice. Patients diagnosed with a malignancy usually demonstrate highly motivated behavior exhibiting high persistence and adherence in the clinical trial setting, at times even preferring oral therapies. Yet, data from the real-world setting tell a different story.[1,2]

To give one well-studied example from oncology, tamoxifen, which is recommended as an adjuvant therapy to be taken for a 5-year period, has been shown in randomized clinical trials to reduce recurrence and mortality in women with estrogen receptor–positive or progesterone receptor–positive early breast cancer.[3] However, these efficacy outcomes are largely contingent upon adherence to therapy. In clinical practice, one-third to one-half of women prescribed tamoxifen for 5 years do not adhere to the full regimen, and studies have shown that these women are now known to have an increased risk of mortality when compared with those who are adherent to therapy.[4-15] In addition, 19% to 28% of women prescribed adjuvant tamoxifen miss at least 1 out of 5 daily doses of medication, which equals an adherence level that is less than 80%, correlating to an increased risk of all-cause mortality.[6,11,15-18]

Oncology subspecialties, especially those involving chronic oral chemotherapy, have the potential to be affected by poor patient adherence rates. In a study of patients with chronic myelogenous leukemia, only 60% of patients with low adherence rates achieved a major cytogenetic response, while 90% of their highly adherent counterparts reached this marker of response. In the same study, the probability of achieving a major molecular response at 6 years declined from 94.5% to 28.4% in patients with higher than 90% adherence versus 90% or lower adherence to imatinib, respectively.[19]

Oncology nurses, specifically, are in a position to identify potential barriers to adherence to oral cancer therapies and to promote patient compliance.[20] *Carol Blecher, MS, RN, AOCN, CBCN, advanced practice nurse and clinical educator at the Trinitas Comprehensive Cancer Center in Elizabeth, New Jersey, provides her insights about how issues of adherence to therapy affect oncology, and, more specifically, the roles that nurses can play to identify and address these issues.*

Moderator: Do you feel that adherence is an issue in the oncology setting in particular that may be commonly overlooked? How can nurses have a positive impact on patient outcomes in recognizing and managing issues related to nonadherence?

Ms Blecher: It is definitely an issue in oncology, as demonstrated by a few studies completed years ago with patients with breast cancer. What was actually found was that over the course of 5 years, many of the women stopped taking their tamoxifen. We know that if we don't achieve an 85% adherence rate, we run the risk of diminished response.

Nurses can definitely have an impact, as we know these problems exist. The Oncology Nursing Society has taken a look at this issue. Their "Putting Evidence Into Practice" team has reviewed many articles, mainly in the HIV treatment setting, as well as in cancer and other chronic diseases. This review revealed that nursing interventions can have a tremendous impact on patient outcomes, as nurses can be instrumental in helping patients adhere to therapy.

Moderator: Are there any predictors of nonadherence in oncology, and do some of them differ from what is seen in non-oncology treatment situations?

Ms Blecher: There are nonadherence issues with any pill. I think the biggest concern in the oncology setting is obtaining the medication. Unfortunately, patients cannot walk into their local pharmacy and hand in a prescription for a chemotherapy agent due to dispensing restrictions. Many of these medications must be obtained through specialty pharmacies and must be shipped to the patient. There are also specific insurance-related billing issues. Many local pharmacies are not trained to bill chemotherapy medications. These intricacies require a multidisciplinary team for access, involving social workers and access to financial support, in order for a patient to obtain a prescribed medication.

As an example, I recently had a patient whose monthly copay for lenalidomide was $3000. We had to do some research to figure out how to get financial assistance for the patient, demonstrating the major issue of cost. Other predictors of patient nonadherence include side effects and tolerability. For example, if patients get diarrhea, do they stop taking the drug immediately? Are they educated about the expected side effects, along with their signs and symptoms? And do they have a contact person to help determine the best way to manage these side effects?

Nurses can help prevent nonadherence by being aware of potential issues related to side effects. When the patient is started on a new medication, nurses can help reiterate the most common side effects that might cause patients concern if they are not given prior warning. It is important that patients are educated about the signs and symptoms of these side effects, and that they contact their healthcare team to find out how to proceed. In some cases, perhaps switching to a lower dosage can help prevent complete discontinuation of the medication. In others, there may be solutions available to manage the side effects so they are no longer bothersome. It is essential to ask the patient at each visit about side effects, probing further for specifics,

because side effects that have the opportunity to be adequately managed can help maintain a patient's medication adherence.

Moderator: Many times, at least in the non-oncology setting, such as with diabetes or hypertension, or any of the silent diseases, adherence can be a large problem because patients just don't see the need to take a medication. I think we're fortunate in oncology that, at least with some malignancies, treatment is becoming similar to other chronic medical illnesses. Do you feel that there is a risk of patients not adhering to therapy because their malignancy has become a chronic rather than an acute life-threatening condition, and therefore, they don't see it as an urgent enough issue to warrant adhering to their therapy?

Ms Blecher: Yes. When symptoms improve and patients feel better, they think they don't need to continue taking their medication. I've had patients very often ask me, "How long do I have to stay on this?" I look at them and say, "Forever or until the disease recurs." It's something that they're pretty much going to be on lifelong, but in that respect, it's similar to diabetes and hypertension because the patient feels okay and wonders, "Why am I taking this medicine?"

Moderator: And it's important to talk about efficacy and the fact that a lot of the supporting data depend on adherence to therapy.

Ms Blecher: Yes, we need to define *adherence*. A useful cutoff point for adherence is 85%, because we know that anything below that is a risk for treatment failure. This cutoff point has been cited in trials of imatinib in chronic myelogenous leukemia, which found that adherence levels below 85% were associated with loss of complete cytogenetic response, treatment failure, and inpatient hospitalizations.[21,22]

Moderator: What specific interventions are nurses in a great position to perform as a part of the multidisciplinary team to improve adherence?

Ms Blecher: I think the nurse's role in education is huge and very important. Nurses direct patients toward where they need to go to get their medicine. They need to be knowledgeable about the medications, which is no easy task with all of the oral agents available now, and with more coming out all the time. It really requires nurses to keep up with the literature and know what's going on. Over the years, nursing has been one of the most trusted professions. We can build upon the patient's trust and work with them very closely in the area of oral agents.

Moderator: Are nurses who work with the administration of intravenous (IV) chemotherapy in a particularly opportune position in terms of establishing a relationship with patients that could allow them to identify situations that might lead to nonadherence?

Ms Blecher: I think they are, but once the patient starts on oral agents, they don't see the infusion nurses anymore. A special team works with the patient once they begin oral therapy. Now, I don't know about other practices, but my institution has nurses in our infusion area and nurses in our physician practice area. I think that the physician practice nurses need to be heavily involved with the patients' care. In some practices, they have 1 or 2 individuals who monitor these patients. I know of one particular institution where the nurse handles all of the oral chemotherapy in the practice and follows the patient. Here, I work with the physicians to divide up the work. I'll see the patient one week, and they see them another.

Moderator: How important is it to have pharmacy involvement in the patient's multidisciplinary healthcare team when oral therapies are prescribed?

Ms Blecher: In 2011 or 2012, a group was assembled to look at the multidisciplinary teams to determine who should be involved. We talked about starting the team with 3 individuals—the pharmacist, the nurse, and the social worker—as crucial members of the multidisciplinary team. My concern for many years has been that the pharmacy doesn't always know what other medications the patient is taking. As an example, I will send a prescription into a mail-order pharmacy, but most of them do not respond with a query about the other medications the patient is taking, even when the patient is enrolling with the pharmacy for the first time.

Another example is a patient whose insurance-approved mail-order pharmacy no longer handles lenalidomide. The patient's new pharmacy never asked what other medications the patient was taking. There may be interacting drugs. If I send in a prescription for capecitabine, the pharmacy might not know or ask whether the patient is also taking warfarin, which could cause an interaction. So we really need to promote pharmacy involvement. There is one specialty pharmacy that does ask us to send them a list of the patient's current medications, which I found irritating in the beginning. It's an extra step for me, but it's an appropriate step, and it is something that is needed.

Before getting to the point where the pharmacy can request information about other medications, though, nurses should carefully review with patients each and every medication they are taking. The more members of the patient's healthcare team who are aware of other medications, the more chances there will be to prevent potentially major toxicities in the form of drug-drug interactions.

What we try to do here is to have our pharmacists actively participate in the oral chemotherapy program. It's a bit problematic because they are so involved with the IV portion, but ideally, it would be nice to have that full circle. Pharmacies that are associated with the hospital can also be helpful. We're a hospital-based cancer center, so we have a pharmacy in the hospital that can directly access information about the patient's other medications.

Moderator: Do you or the physicians you work with ever hand out educational tools to patients as a means to promote adherence?

Ms Blecher: I personally give patients specific drug information regarding the agents they are taking, and I also prepare calendars for them to follow, at least in the very beginning. Some protocols are very complex; for example, some pills need to be taken with food,

and some without. I think calendars are very helpful reminders for those kinds of details. I have started emailing electronic versions of the calendars to either the patients or family members, so that the family members can help with the process.

Another thing we need to teach is safe handling. It's very important to know the social situation, who is in the home, whether there are young children, who is going to administer the medication, etc. I hand out chemotherapy gloves in case a family member needs to load the pill box.

Moderator: Are patients with malignancies that are more prevalent in elderly patients, such as chronic lymphocytic leukemia, and ones in which oral agents are used, more at risk potentially to be nonadherent?

Ms Blecher: Yes. Plus, the older population may be taking many other medications. Patients think, "I've got to take yet another pill, and I'm already taking this many pills," so we need to overcome this mindset. Of course, there may also be huge language barriers that we have to overcome and learn to work with.

Moderator: How has oncology treatment changed in ways that affect adherence?

Ms Blecher: In the past, we always gave chemotherapy in doctors' offices or in the hospital, whereas now there's a movement toward oral therapies, and that's when the issue of adherence comes into play.

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