

Keeping Pace with Oral Chemotherapy

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While the rising number of oral chemotherapies offers many cancer patients a more convenient and less invasive treatment option compared to infusion therapy delivered in a clinical setting, oral drugs also require a new model for patient education, monitoring, and support. Equally essential are additional levels of cooperation and integration among physicians, pharmacists, and other healthcare providers involved with the patient's overall care.

A Changing Landscape

Although some oral agents are prescribed as single agents, currently, most oral chemotherapy agents are used in combination with existing infusion regimens. To date, office- and hospital-administered chemotherapy infusions have not declined significantly, and experts suggest a market will exist for both oral and intravenous versions for many of the new drugs. For example, oral and intravenous agents are in development for the new histone deacetylase inhibitors class of drugs (e.g., vorinostat). For these agents, the choice between oral and intravenous administration may depend on physician and patient preferences and type of insurance coverage.¹ That said, nearly one-quarter of the antineoplastic drugs in the development pipeline are oral agents.²

This pipeline of oral agents is of great significance to oncologists, hospital administrators, and private practice physicians who prescribe oral chemotherapy in their offices. From a business standpoint, the infrastructure of oncology practice has long been based on the administration of infusional chemotherapy. Spatial configurations within cancer care facilities are also typically centered around a chemotherapy infusion area. In addition, oncologists in private practice are accustomed to deriving a substantial portion of their income from supplying and administering parenteral chemotherapy.¹ Consequently, the emergence of more and more oral chemotherapy regimens will require cancer care professionals to make a number of significant shifts.

Until recently, cancer care providers exhibited a considerable amount of control, including the certainty that the right drug is being administered in the right amount, via the right route, at the right time, and to the right patient—all of which is meticulously documented in the patient's records. In contrast, oral chemotherapy takes much of the control out of the clinicians' hands and places tremendous responsibility on the patient, raising a number of patient adherence and control issues.

To keep pace with the growing oral chemotherapy use, community cancer centers need to develop new infrastruc-

tures. Preferably, these changes would include a comprehensive system designed to select appropriate candidates for oral agents, along with a robust educational component to address safety and adherence practices, thus ensuring treatment efficacy.

The "Ideal" Oral Chemotherapy Patient

Ideal candidates for oral chemotherapy possess good communications skills (or have a responsible, committed family member who can communicate on behalf of the patient) and a demonstrated willingness and ability to comply with and adhere to physician and nursing instructions, along with the intellectual discipline and emotional wherewithal to commit fully to the program. Additionally, patient candidates should be assessed with regard to:

- Their understanding of the importance of their particular therapy to their disease
- Potential side effects due to the treatment
- How they will integrate the therapy into their schedule
- Whether they can swallow pills and/or liquids
- The number of medication doses normally missed on a weekly basis
- Where they obtain their medications
- How they pay for medications.³

The Cost of Treatment

Financial considerations figure prominently into the oral chemotherapy equation. The average charge for a 30-day supply of capecitabine (Xeloda[®]) exceeds \$2,000; the charge for a monthly supply of sunitinib (Sutent[®]) approaches \$7,000 (2006 dollars). While oral agents tend to be more costly, there is the potential for downstream cost-savings. For example, in the treatment of colon cancer, acquisition costs for capecitabine are higher than acquisition costs for 5-fluorouracil/leucovorin; however, one British study found less need to treat patients for adverse events, along with significant cost reductions with regard to patient time and medical resource utilization for the oral agent.⁴

In addition to a significant difference between the cost of oral chemotherapy and traditional infusion, patients obtaining a prescription for oral chemotherapy from a pharmacy are required to pay when the prescription is filled. Infusion patients, on the other hand, provide insurance information up front, receive treatment, and typically pay a balance due at some point once insurance claims are processed.

Clearly, potential candidates for oral chemotherapy need to be fully informed about the financial implications of starting and continuing these protocols. The optimal oral

Rewards, risks, and challenges for community cancer centers and cancer patients

chemotherapy program would then include financial counseling and social services, as well as provisions for helping patients navigate assistance organizations when the ability to pay for treatment is an issue.

The Convenience Factor

Given a choice between oral or parenteral chemotherapy, patients are often likely to have a preference for oral chemotherapy, primarily because of the convenience of being able to take their medications in the comfort of their own home. This choice is particularly true for patients receiving palliative treatment. At the same time, most patients are unwilling to sacrifice efficacy for convenience, according to a broadly referenced study regarding palliative oral chemotherapy.⁵ Other potential patient advantages for the use of oral chemotherapy include a sense of empowerment in managing their treatment, less frequent office visits, and less time spent waiting for intravenous setup and infusion.

To fully realize the “convenience” factor of oral chemotherapy, however, the patient needs to be on an exclusively oral regimen. Patients on regimens that combine oral and infusional therapy may actually find it more convenient to receive their entire regimen parenterally.¹ The paradox of convenience increases in complexity when considering a patient’s ability to manage the responsibility of an oral chemotherapy regimen over the long term. For example, frail individuals, those with little or no support systems at home, or patients integrating the management of oral chemotherapy while taking multiple non-cancer drug therapies, would likely experience greater challenges in managing oral chemotherapy regimens.

These factors, in addition to literature indicating that patients are inconsistent in adherence to oral medication regimens (e.g., not taking as prescribed, having financial constraints that result in failure to fill the prescription or taking less than the prescribed dosage, and inadequate reporting of side effects), create a new set of challenges for oncology providers.

Common Adherence Issues

With infusional therapy, providers know that the patient has received the correct treatment, allowing providers to accurately assess a patient’s progress and to write the next prescription with confidence. Conversely, with self-administered oral chemotherapy, the provider must rely on information reported from the patient as a basis for continued treatment orders. Inaccurate information from a patient could result in future treatment decisions being made in accordance with what a physician “believes” to have occurred during the prior course of treatment. To maintain dosing accuracy, providers *must* address patient adherence

through ongoing patient education and follow-up.

Studies show that medication adherence is related to a variety of socio-demographic characteristics, as well as the regimen type and specific characteristics of the illness. Still, predicting how these parameters interact with each other and determining how they can be used to predict adherence is difficult.⁶ Conventional behavioral models have also been applied to predictors of medication adherence. These include the Health Belief Model, which focuses on three key factors:

1. The individual’s own evaluation of his or her health condition (e.g., disease severity, perceived vulnerability or sensitivity to the disease state)
2. The individual’s personal risk versus benefit assessment of adherence to the prescribed medication
3. A stimulus or “cue to action” that is either internal or external, which prompts the individual to take the medication.⁷

Adherence can also be influenced by the “Hawthorne effect,” which asserts that there is potential for improved patient adherence based on the patient’s awareness of ongoing observation.⁶ At the same time, self-reporting from patients often shows a tendency to over-report adherence rates due to the patient’s desire to please healthcare providers.⁸

Consider also the various predictors of poor adherence. For example, patients who exhibit a presence of emotional and psychological issues, particularly depression, may be unable to adhere faithfully to an oral chemotherapy regimen. Other indications of adverse adherence include:

- Complex treatments
- Cognitive impairment
- Treatment of asymptomatic disease
- Inadequate follow-up or discharge planning
- Poor patient-provider relationships
- Missed appointments.

In addition, patients who lack realistic insight as to the severity of their illness or have little confidence in their treatment are likely to be unable to adhere to the regimen.

A Team Approach is Key

Given the intricacies of oral chemotherapy and in anticipation of the rapid growth in the number of oral agents in the not-so-distant future, the Trinitas Comprehensive Cancer Center in Elizabeth, N. J., took a proactive, team-focused approach and established protocols at a time when oral chemotherapies are still at a low volume. (Trinitas is one of eight hospital-based cancer centers in the Aptium Oncology network. Multidisciplinary collaboration; seamless coordination of patient information; care planning and care delivery; and a high level of supportive care services are all part of the Aptium model.) In addition to infrastructures,

Oral Anti-cancer Care Standards

At Trinitas Comprehensive Cancer Center, anti-cancer standardized interdepartmental procedures for physicians, nurses, and pharmacy assure adherence to protocols, patient safety, and quality of care. In brief, here's how our standards work in practice:

Step 1—The physician informs the nursing staff when an oral anti-cancer protocol is prescribed.

Step 2—The physician obtains the patient's informed consent using the chemotherapy and biotherapy consent form.

Step 10—The patient's medication is added to the chemotherapy and biotherapy section of the medication reconciliation sheet.



Step 11—Patients are instructed to bring their prescription bottles with them upon each visit to the cancer center.

Step 12—A note is placed in the follow up appointment screen (Oral Tx or P.O. Tx) as a trigger for reminding patients they should bring their prescription bottles and calendars with them when they are called and reminded of their appointment.

policies, and procedures promoting collaborative communications among physicians, nurses, and pharmacists, we developed an in-depth educational component that provides the linchpin for ensuring a successful and effective oral chemotherapy program.

Our program focuses on three key pillars—education, communication, and follow-up. These components allow our patients to take charge of their therapy and be active participants in the entire process, while still enabling physicians and nurses to maintain significant measures of control. (Oral chemotherapy essentially “transfers” control from physicians to patients, an issue that concerns many physicians.)

Of particular significance to our program's development were the multiple risks and challenges already identified with increased use of oral anti-cancer therapies (e.g., dosing errors, drug interactions, non-adherence).⁹⁻¹¹ As a result, our project team first conducted an inclusive review of available literature, with the objective of designing processes that would help our program directly address these existing risks and challenges. Once the literature review was completed, we introduced concepts for the formalized program to our cancer center physicians, whose support and buy-in was paramount to successful implementation of the program.

Program Implementation

The next step was to kick off the program with a mandatory in-service for all clinical staff. In addition to reviewing current practices with oral agents, the in-service included a presentation of the research evidence that prompted the creation of a new model for oral chemotherapy delivery, as well as a presentation of the new program policies being instituted by the cancer center. One new tool: an Oral Anti-cancer Order Form developed by Trinitas pharmacists—who play an active role in treatment planning. Physicians use the order form to request oral agents and obtain chemotherapy and/or biotherapy consent for treatment. The order is then forwarded to the pharmacy, where the patient's current medications are reviewed for potential interactions. Once all approvals, assessments, and pre-authorizations are complete, an appointment is made for the patient to attend an education session. At this session the patient receives the prescription, information about the drug (including side effects and safe handling), and instructions on administration and adherence monitoring.

Our program is led by an advanced practice nurse (APN), who is immediately notified when a patient is prescribed an oral agent. At each physician follow-up appointment, an appointment is made for the patient to meet with the APN to monitor the patient's adherence and side effect management. Whenever possible, the APN includes the patient's family members and/or significant others in these appointments.

Promoting Patient Adherence

The APN ensures that patients receive instruction in safe handling procedures for their medication, as well as information about their specific diagnosis and the oral agent that has been prescribed for their treatment. Each patient is taken through a review of the medication's purpose, the number of pills to take, and when and how to take them. Key to the education process is helping patients understand how to identify, manage, and report side effects. Finally, each patient is given round-the-clock contact information for

our staff, ensuring that all patient questions receive prompt answers and any problems are reported as soon as possible.

To enhance patient understanding and adherence, we provide printed materials, individualized calendars, and, in some cases, pre-loaded pillboxes to assist patients in their medication use. Concurrently, our nurses provide weekly phone interventions for the first month, biweekly phone interventions for the second and third months, and monthly phone interventions thereafter.

Patients are told to bring their prescription bottles to every appointment. As part of our regular adherence evaluation and documentation, the prescription bottles are sent to the pharmacy for pill counts, a review of the patient's calendar, and monitoring of prescription renewals.

Communication is a key component of our program and we have taken steps to eliminate as many obstacles as possible, helping to ensure the success of each patient's treatment experience. For example, the cancer center uses a translation service to ensure effective communication with all non-English speaking patients. Trinitas also has measures in place to help patients circumvent financial barriers including an onsite financial counselor who meets with each cancer patient. And, because many patients have emotional, social, support, or transportation issues, our social worker helps assure patients that they have someone they



Step 3—Orders are written on an oral anti-cancer order sheet, which is sent to the pharmacy.

Step 4—The pharmacy screens for interactions with the patient's current medications.

Step 5—An appointment for an education visit is made for the patient.



Step 6—Patient is educated regarding medication, as well as safe handling procedures.

Step 9—The patient is provided with a calendar to mark off the doses as they are taken. Patients are also given pillboxes and printed material as appropriate during the education session.

Step 8—The patient is given the prescription and information about the prescription, which is documented in the teaching note.

Step 7—Pre-authorization is obtained as needed and the patient is referred for an assistance program if appropriate. Pre-authorization for cancer center monitoring of laboratory values is obtained, if appropriate.

Step 13—Prescription bottles are sent to the pharmacy for pill counts at each visit to assure patient adherence and as a trigger for re-education if necessary.



Step 14—The patient is called weekly during the first month of medication use to follow up and ensure adherence to protocol. During the second and third month, the patient is called every other week. After the third month, calls are made to the patient on a monthly basis between visits to promote adherence.

feel comfortable sharing issues with, and who can assist with a variety of referrals and resources.

Since the program's inception, the in-service has been incorporated into our new employee orientation. At the same time, a growing number of the cancer center's physicians are embracing the program. Finally, we are developing a program to educate local pharmacists regarding oral agents, toxicity profiles, and safe handling.

By combining safeguards, patient education strategies, intensive follow-up, and a system of effective checks and balances, Trinitas Comprehensive Cancer Center is taking innovative steps to maximize patient safety and oral chemotherapy treatment effectiveness, while keeping pace with the rapidly occurring changes in oncology practice.

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