Increased Use of Oral Chemotherapy Drugs Spurs Increased Attention to Patient Compliance

Ensuring that patients with breast cancer are taking the oral aromatase inhibitors (AIs) prescribed as follow-up treatment to surgery is an ongoing concern for oncologists, who lose control of medication administration when it moves from the office or hospital setting to the patient's home. Patients with breast cancer who are receiving AIs are to take them for 5 years after initial treatment for optimal efficacy. Partridge et al¹ have demonstrated that initial research reveals "patients prefer oral to IV [intravenous] chemotherapy, so long as efficacy isn't compromised." Convenience is the main reason given for this preference.

Patient compliance is a major area of concern with oral medications. The reasons for noncompliance are as varied as the problems it can cause. The complexity of cancer drug regimens challenges patients, who do not always understand what missed doses, or worse yet, misunderstood package directions that lead to overdosing, can cause. Some oncology practices are trying interventions to improve the situation, with limited success.

With many more oral chemotherapy drugs in the pipeline, this is not an issue that is going to go away. A "Task Force Report on Oral Chemotherapy" recently released by The National Comprehensive Cancer Network (NCCN)² identifies a number of issues of concern related to oral drug management, including adherence, patient safety, adverse effect management, cost, communication, and medication errors.

Compliance Issues

Compliance is defined as, "implementation by the patient of the therapeutic plan that has been established."³ Adherence to any intervention over long periods is determined largely by an individual's perception of the risks, benefits, and costs of the intervention.¹ Adherence rates for many long-term drug therapies have been shown to be low, at around 40% to 50%. These low adherence rates have been associated with an increase in physician visits, higher hospitalization rates, and longer hospital stays.¹

In patients with cancer, noncompliance can have a negative affect on disease outcome. Why, then, do patients not comply? Certainly they want to protect their health. One of the most frequent reasons given is that they forget to take the medication. Some cannot afford it and do not know that they may be eligible for financial assistance. They may not want to experience the potential adverse effects, or they feel better and perceive that they no longer need the medication. They may find the instructions confusing, feel overwhelmed by the sheer

number of drugs they are taking and how to fit them all in during the day, or are experiencing adverse effects and do not know what to do or are too sick to do anything. Sometimes it may be something as simple as being unable to open the medication container or something as misleading as feeling that the medicine is not doing anything because they do not feel different.¹

Strategies for Improved Compliance With Oral Chemotherapy

Tennessee Oncology Establishes an Office-Based Pharmacy

Tennessee Oncology, a large Nashville-based practice with 50 physicians, has established its own pharmacy to make it easier for its patients to get their medications, which are not always readily available in commercial drugstores. When a retail pharmacist has to order the drug(s), it may cause a delay in the patient starting the medication.

Dr Jeffrey Patton

Dr Jeffrey Patton, who coordinated the project, says the reasons for developing the pharmacy were two-fold: the office pharmacy makes it convenient for patients to get their medications expediently, and it gives the practice a way to track patients' compliance with treatment. "This is a real opportunity for us to improve compliance and to open a dialogue with patients who aren't taking their pills," Dr Patton says.

Here is how it works. After seeing the doctor, the patient gives the prescription for the AI to the office staff member who faxes it to the pharmacy. The pharmacy fills the prescription(s) and mails it to the patient's home within 2 days. Prices are comparable with retail pharmacies. This process saves the patient time, money, and energy, and gets the patient started on medication(s) as quickly as possible. The staff processes 40 prescriptions a day.

When it is time for a refill, if the patient does not contact the pharmacy, the pharmacist alerts Tennessee Oncology. The physician then calls the patient to ask how he/she is doing and determines why the patient has stopped the medication. "Patients really seem to like that we call; it opens a dialogue," Dr Patton says. On the flip side, there are some patients who do not accurately follow directions and take more pills than prescribed, increasing the chances of adverse effects and

prescriptions running out early. In this case, the pharmacist would alert the physician.

The pharmacy has been in operation for a year, and Dr Patton soon will be reviewing the statistics. "This has been an improvement for us," he says. "And I'll be shocked if this contact with patients didn't improve compliance." He says he already knows that after 1 year, only 50% of patients taking AIs still are compliant. "This mirrors the compliance curve of antihypertensive drugs," he says.

The pharmacy is marginally profitable, but the practice expects it to be a revenue stream in the future, Dr Patton says. The most significant start-up cost was the pharmacy inventory. The pharmacy saves office staff time because the pharmacy handles tasks that a traditional retail pharmacy would not handle, and, therefore, would fall on the practice's staff. Each state has its own laws governing pharmacies that Dr Patton recommends others considering this business investigate during planning. The next step for Tennessee Oncology will be electronic prescribing.

Massachusetts Practice Implements New Process to Monitor Compliance

Commonwealth Hematology-Oncology in Massachusetts, the largest community-based, private cancer care group in New England, just launched a new oral compliance program including hormonal agents. Staff oncology nurse Jennifer Dookhran RN, BS, OCN, led the team in development of the process. It is a combination of in-person patient education, take-home packets of educational materials, and follow-up calls.

The take-home packet includes general instructions specific to the drug prescribed. It covers safe handling, medication storage, medication administration, disposal, and advice if adverse effects occur, including when to call the doctor's office. Personalized calendars are prepared to help patients remember when to take their medications.

Patients receive their prescription(s) from their physicians and then are brought to nursing for a teaching visit, similar to that given for intravenous therapy. Before this program, the nursing staff had little involvement with patients taking oral drugs. "Continuing our teaching with the oral therapies allows us to keep the communication open between the nurse and patient. We give patients the written information on the medication they are taking, explain dosing, potential side effects, when and how to take their medication and any other information, and give them our phone number and encourage them to call us if they have problems or questions," Dookhran says. Questions are answered in a more relaxed environment and patients know they can call this nurse whenever they have more questions. The nursing staff maintains a tracking sheet with set callback dates. For example, for AIs, 2 weeks after the start of the medication,

the nurse calls the patient to see how things are going. Remembering to take the medication regularly is often a concern. Dookhran brainstorms with the patient to think of ways the patient can remember to take her pills. She reminds patients to mark their calendars or suggests they try a pillbox. Patients are back in for an office visit in 1 month and again at 6 months and, of course, as needed in between those milestone visits.

If finances are a concern, Dookhran says she has coupons or free samples that can help, and there are prescription programs that can help low-income patients. "Nursing can work closely with our patient advocate to obtain coverage for the prescription," Dookhran says. "Patients are appreciative of this extra service. We've already had a couple of calls from patients, so it *is* working."

NCCN Releases Task Force Report on Oral Chemotherapy: Report Finds That Use of Oral Chemotherapy Agents Profoundly Affects All Aspects of Practice

Also concerned about the issues surrounding oral chemotherapy, the NCCN recently released a task force report on oral chemotherapy, which found that "The use of oral chemotherapeutic agents profoundly affects all aspects of oncology, including creating significant safety and adherence issues, shifting some traditional roles and responsibilities of oncologists, nurses, and pharmacists to patients and caregivers. The financing of chemotherapy also is affected."¹ The report was presented in a supplement to the March issue of NCCN's journal. To address these issues, NCCN convened a multidisciplinary task force comprising 16 oncologists, nurses, pharmacists, and payor representatives to discuss the impact of the increasing use of oral chemotherapy.

"This report is a comprehensive review of where we stand now," says Raymond Muller, MS, RPh, a pharmacist at Memorial Sloan-Kettering Cancer Center in New York City, who was an active NCCN Task Force participant. "Serving on the task force was a very good experience," he says. "This is the first time that this type of benchmarking has been done for oral chemotherapy. It is a very detailed report." Muller says the major benefit of oral chemotherapy for patients is the convenience aspect, but with that, comes many challenges. Adherence, adverse effect management, and ensuring that patients understand correct dosage are only a few of the issues, according to Muller.

The report covers the drivers of oral chemotherapy, common misconceptions, patient selection criteria, safety issues, and factors affecting oncology practice, distribution, financing, and trends in oral chemotherapy. In discussing the drivers of oral chemotherapy, the authors talk about the fact that oncology practice infrastructure has been based on the

parenteral administration of chemotherapy. The authors write, "Oncology office visits and the configuration of office space have been centered on chemotherapy infusion, and oncologists derive a substantial portion of their income from supplying and administering parenteral chemotherapy. Oral chemotherapy is changing this model."²

Contributing to this paradigm shift is the fact that pharmaceutical companies are investing heavily in developing new oral drugs, as well as oral counterparts to existing cytotoxic therapies. The report asserts that the introduction of Medicare Part D is a strong incentive to these companies, given that Medicare Part D provides coverage for oral chemotherapy for the first time.²

Patient preference is cited in the report as "one of the main drivers for its [oral chemotherapy's] current popularity," explaining that some patients prefer oral agents because of the convenience of being able to take them at home, which saves the drive to and from the physician's office and the infusion time. Patients receiving combination regimens of oral and parenteral drugs will not realize the same benefits; "... for these patients, it may actually be more convenient to receive the entire regimen parenterally."²

Adherence

The section of the report on patient selection points out that, although many patients may want to take oral agents, only a subset of patients can be considered appropriate candidates for them. Adherence is one of the key factors in assessing candidacy for oral chemotherapy.² The decision, say the authors, must be based on a collaborative discussion between the physician and patient, with appropriate support from the oncology staff. Adherence to chronic medication generally is fair to poor, according to the authors, who go on to say that there really is no "well-established mechanism to prospectively assess adherence."² Monitoring adherence also is crucial, according to the task force report. It helps the physician to determine treatment effectiveness, toxicity, and safety. The report categorizes the methods into direct and indirect. (See text box.)

Conclusion

With pharmaceutical companies allocating millions of dollars to developing oral agents and numerous oral chemotherapy agents, both new and old, in the development pipeline, health care professionals must deal with the many issues associated with oral regimens. Select patients who qualify for oral agents often prefer them for the convenience they offer as long as efficacy is not adversely affected. With administration in the hands of patients and caregivers, oral agents present new

Methods of Monitoring Adherence

Direct Methods

- Directly observe therapy (easy with parenteral administration in the office; not so with oral medications the patient takes at home)
- Pharmacokinetic measurement (patient can manipulate results by becoming adherent immediately before the physician visit)

Indirect Methods

- Patient self-report (not always accurate because of poor patient memory or reluctance to report nonadherence)
- Patient diaries
- Pill counts (does not mean the patient took them according to dosing schedule)
- Rates of prescription refills (does not mean that patient took them according to dosing schedule)
- Electronic medication monitors (ie, intelligent tablet bottle)

Note: The authors for the NCCN report write, "Regardless of the technique used to assess adherence, clinicians must realize that lack of adherence typically reflects the complexity of the regimen rather than willful or manipulative behavior from the patient."²

challenges for the health care team and inject new people into the chemotherapy administration model. Adherence is one of the main issues associated with oral chemotherapy, and monitoring adherence has become a huge part of the picture. Physician practices are trying to address this issue by developing new methods of monitoring patient adherence via office pharmacies and new patient education and documentation systems. The ultimate goal is patient safety, adherence to their regimens at proper dosages, and adequate adverse effect management. The newly released *NCCN Task Force Report on Oral Chemotherapy* gives practitioners an excellent overview of the issues, serves as a benchmark of current practice, and points to the challenges oncologists and their teams will face as oral chemotherapy plays an increasingly more important role in cancer care.

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