

under development. For agents such as these, the choice between oral and intravenous administration may depend on physician and patient preferences and type of insurance coverage.

Common Misconceptions About Oral Chemotherapy

As the previous discussion shows, oral chemotherapy suggests a number of benefits. However, growing experience in administering these therapies suggests that a cautious approach is warranted. Clinicians should also understand the common misconceptions that may be contributing inappropriately to the enthusiasm for oral chemotherapy.

Patient Preference

Patient preference for oral chemotherapy has been one of the main drivers for its current popularity. Oral administration would seem to avoid many of the more objectionable aspects of parenteral therapy: the office visit and associated inconvenience of transportation and parking, time spent waiting in the office, and time lost during intravenous set up and infusion.

In 1997 Liu et al.⁴ reported on the results of a questionnaire addressing patient preference for oral versus intravenous palliative chemotherapy. Preference for route of administration was evaluated against diminishing treatment response. Of 102 assessable patients, 92 preferred oral chemotherapy and 10 preferred intravenous therapy. Not unexpectedly, the major reason given for preferring oral chemotherapy was convenience. However, although patients expressed a clear preference for oral chemotherapy, they were unwilling to sacrifice efficacy for this preference.

Although these results seem to support convenience as a driving factor for patient preference, at least in the palliative setting, this survey may have presented oral chemotherapy in an overly simplistic fashion. For example, the convenience of oral chemotherapy will only be realized if the patient is on an exclusively oral regimen. Patients on combination regimens will need to make office infusion visits anyway; for these patients, it may actually be more convenient to receive the entire regimen parenterally. Capecitabine, for example, is an oral alternative to 5-fluorouracil (5FU) that is often administered with other parenteral agents.

Additionally, patients may not realize that choosing an oral therapy over an intravenous equivalent

will shift many of the responsibilities of managing the regimen and monitoring for doses and toxicity from the oncology team more directly to the patient. Although, some patients may appreciate a sense of empowerment from oral chemotherapy and get a sense of satisfaction from having direct responsibility for managing their chemotherapy, this same responsibility could become overwhelming, particularly for sick patients simultaneously dealing with complicated dosing regimens and schedules or for patients without reliable assistance from family or friends. The reliable administration of oral chemotherapy in the pediatric population is also challenging, even among well-intentioned families.⁵

These advantages and disadvantages of oral chemotherapy must be carefully discussed with the patient. Only well-motivated and health-literate patients and families may be able to manage complex oral chemotherapy regimens, and only patients with good oral food intake, good gut function, and minimal nausea and vomiting will be good potential candidates.

Fewer Side Effects and Easier Administration

Patient preference for oral chemotherapy may be based on the incorrect assumption that oral therapy is associated with minimal side effects; some patients may incorrectly assume that oral chemotherapy is not "real" chemotherapy and is more akin to taking a vitamin or antibiotic. This dangerous misconception may also be the rationale for the preference of oral chemotherapy in frail elderly patients.

Patients must understand that oral equivalents of cytotoxic therapies, such as capecitabine, have side effects that are similar to their parenteral counterparts (in this case, fluorouracil). The need to monitor for side effects and titrate dosages increases the complexity of oral chemotherapy regimens. For example, many oncologists can relate examples of patients who began to experience toxicity from capecitabine on a Friday but who did not consult a physician over the weekend. If these patients continue on the same dosage, either because they do not recognize the incipient side effects or because they do not want to compromise the effectiveness of their chemotherapy, they may have a life-threatening level of toxicity by Monday.

Furthermore, from the patient's perspective, an oral regimen may not be simple to administer. Instructions for capecitabine may include:

- Take with water within 30 minutes of a meal.
- If a dose is missed, do not take the drug when remembered and do not take a double dose.
- Stop taking capecitabine and contact the doctor if experiencing 4 or more bowel movements than usual per day, diarrhea at night, loss of appetite or large reduction in fluid intake, more than 1 vomiting episode in 24 hours, mouth sores, temperature greater than 100.5 °F, or pain, redness, or swelling of hands or feet that prevents normal activity.^o

Oral regimens must also be integrated with non-cancer drug therapies taken for comorbidities. Oral chemotherapy regimens may be particularly difficult to manage in assisted living situations where drugs are dispensed by staff with limited experience in monitoring the side effects of chemotherapy.

Furthermore, supportive care agents such as the 5-hydroxytryptamine₃ (5-HT₃) antagonist antiemetic drugs are best used parenterally and intermittently. Reimbursement for these agents on a daily oral basis is often limited when pharmacy benefit management programs base reimbursement on the FDA-labeled indications. When all these requirements are considered, a periodic office visit to receive chemotherapy may be more attractive to patients.

Another common perception is that oral drugs have a broader therapeutic index and thus are safer than parenteral drugs. The therapeutic index is based on the class of drug and its mechanism of action, not the route of administration. Thus, the therapeutic index of oral agents versus intravenous counterparts is generally the same. Nevertheless, clinicians should note that although biologic agents are not cytotoxic in nature, the adverse effects associated with them can still be significant. For example, the skin rash and diarrhea associated with epidermal growth factor inhibitors can be debilitating.

In summary, the assumption that all patients will prefer oral agents or that all patients are appropriate candidates for oral therapies is overly simplistic. Furthermore, that oral chemotherapy is routinely preferable for frail, elderly, and less motivated patients is also a commonly held misconception. Generally, highly motivated, capable patients who want and can actively participate in their care are better suited to assume the increased responsibility that comes with chronic home oral administration of chemotherapy.

Certainly, for some regimens, oral chemotherapy is the only alternative. However, the example of imatinib monotherapy, a simple regimen with minimal side effects, may be the exception rather than the rule. An entirely oral chemotherapy regimen may offer significant advantages over traditional infusion therapy in carefully selected patients, but patients must understand that the decision to use oral chemotherapy requires detailed consultation with the oncologist and oncology team, as well as ongoing support over the course of therapy.

Cost of Oral Chemotherapy: Offset by Decreased Need for Support Staff or Infusion Centers?

Some have argued that the high cost of oral chemotherapy drugs may be offset by the decreased need for ancillary services, particularly oncology nursing staff and infusion centers. Experience, however, has not uniformly borne this out. Oral chemotherapy requires a significant amount of nursing time for patient education when starting an oral chemotherapy regimen and extensive telephone consultation thereafter. Furthermore, in most practices, no time is built in for counseling patients on oral chemotherapy, and most offices do not have any dedicated space or personnel for this counseling. Thus, education and counseling have been improvised in hallways and other less private settings. Some oncologists offer written material, video material, or group educational sessions, but the bottom line is that the extensive and ongoing patient education required to ensure safe and effective oral chemotherapy is uncompensated and perhaps underappreciated. In contrast, prolonged infusion sessions provide many built-in opportunities for education.

Patient Selection Criteria for Oral Chemotherapy

Adherence

Although many patients may be eligible for oral chemotherapy, only a subset will both want to take oral agents and be considered appropriate candidates based on their ability to adhere to the regimen. One of the key factors in assessing candidacy for oral chemotherapy is adherence. Adherence can be a challenging commitment for many patients, and the decision to take oral chemotherapy must be based on a collaborative discussion between the patient and physician, with appropriate support from oncology staff.