Essentials of Oral Oncolytics: Developing a Nursing Reference

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Recognition of the increase in the amount of approved oral oncolytics has led to concerns for oncology nurses. Oncology nurses are challenged with the increased number of new oral drugs and the need for additional education to acquire drug knowledge. A sense of noninclusion with physician-to-patient communication may omit traditional nurse chemotherapy teaching. This frequently occurs in settings where oral oncolytics are not afforded the same procedures as infusion drugs, such as written informed consent and chemotherapy teaching by an experienced oncology clinician. Oral chemotherapy requires a significant amount of nursing time for patient education and counseling, particularly at initiation (Moody & Jackowski, 2010). Providing and reinforcing accurate, detailed patient education about oral chemotherapy, using terms appropriate for the patient’s understanding, may promote patient safety, optimal dosing, and adherence to the treatment plan (Hartigan, 2003). The authors of the current article assembled a resource of condensed information that is most critical to the oncology nurse (e.g., drug indications, dosing, dose modifications, common adverse events, warnings, necessary tests). The tool could be quickly accessed and reviewed by nurses prior to engaging in patient education, and it could reinforce and improve clinical knowledge related to a specific oncolytic. For comprehensive drug information, the nurse must still turn to the complete prescribing information.

The current literature has identified multiple barriers to patients and their caregivers in being willing and adhering to self-administration of their treatment (Griffin, 2003; Moore, 2007). Strategies to overcome these barriers must be developed at the initiation of oral agents to accomplish treatment goals, which include receiving maximum benefit of the oral oncolytic (Lester, 2012). The nursing education aspect in the prescribing of oral oncolytics may begin establishment of communication...
and supportive relationships between the patient and caregiver and the oncology nurse. Poor healthcare communication and lack of a patient and provider relationship have been identified as having a negative impact on oral adherence (Kardas, Lewek, & Matyjaszczyk, 2013).

The Oncology Nursing Society (ONS) Tools for Oral Adherence Toolkit was created to provide information and resources for nurses in the care of patients receiving oral oncolytic therapy. The toolkit includes 16 drugs and is a collection of strategies and resources compiled to facilitate oral adherence (Moore & Brandt, 2010). The problem of patient adherence in oral therapy has existed for decades. Because of the increased number of drugs being administered orally, the subject of patient self-administration in oncology requires prompt attention and planning. As the paradigm shifts from tightly monitored infusion chemotherapy to oral oncolytics, nurses will need to make practice changes to provide patients with the knowledge and support necessary for safe self-administration, side-effect monitoring and reporting, safe drug handling, and accurate dosing following medication-specific guidelines (Birner, 2003; Lester, 2012; Neuss et al., 2013; Osterberg & Blaschke, 2005). D’Amato (2008) noted that self-administration may increase the risk of medication error and potentially compromise the effectiveness of the anticancer therapy. In addition, the approval of more than 30 oral oncolytics during the past two decades has posed a challenge to oncology nurses to keep abreast of each new drug while determining how to successfully prepare the patient to self-administer oral oncolytics.

The authors of the current article created roundtable discussions to examine the increasing use of oral oncolytics and challenges with patient education. The purpose of initiating informal roundtable discussions with several groups of oncology nurses was to elicit ideas and opinions about the pervasiveness of the challenges to oral adherence for oncology nurses.

Methods

The authors conducted 17 educational inservice programs throughout the northeastern United States that were centered on the topic of challenges to oral adherence in oncology, with roundtable discussions prior to the educational program. These programs took place from September 2011 to February 2013. Participants included about 200 oncology nurses, infusion coordinators, advanced practice nurses involved in clinical care and in supervisory positions, practice managers, pharmacists, and pharmacy industry consultants. Practice institutions included freestanding, large, incorporated private hematology/oncology multisite practices, hospital-affiliated outpatient oncology clinics, inpatient oncology units, and major academic cancer centers from the Boston, Massachusetts, area.

Prior to the content presentation, participants were informally surveyed regarding their current policies and procedures for the education process for patients prescribed oral oncolytics, how confident they felt in providing patient teaching for oral oncolytics if it was their responsibility, and what resources they used for self-education and patient education. Other process-focused inquiries included what their documentation involved for several items, including consent, the teaching process, infusion chemotherapy orders (when the oral drug was part of a combination regimen), records of an oral drug, and follow-up phone calls related to monitoring oral adherence. The participants also were asked if their documentation was on paper, in an electronic health record, or a combination of both. Discussion was directed toward considering an optimal type of tool or resource to facilitate these processes.

Results

Oncology clinicians reported frustration, time constraints, and limited or no experience with these drugs as obstacles to providing optimum care. Other anxieties focused around patients receiving drug education only from physicians without nursing involvement. Nurse teaching may result in interactive nurse and patient communication and a positive nurse and patient relationship. Providing patients and caregivers with sufficient understanding to achieve safe, unsupervised self-administration of medications with potentially life-threatening side effects was described at these roundtables as critical to the nurse’s role as patient advocate.

The nurse’s role should include reviewing orders for accuracy, discussing with the patient how he or she took the drug during the last cycle and how it was tolerated, managing any side-effect issues, clarifying any misinformation or administration errors, and establishing that the patient has the required prescription and procurement routine in place. When given the educational resources and tools, nurse-provided education can improve the information that is given to patients and families.

When oral drugs are a component of cancer treatment, it adds another layer of responsibility for the oncology nurse. It requires additional time in patient education, assessment, documentation, and follow-up. The nurse may be required to spend time on the telephone with pharmacies, insurance companies, pharmaceutical reimbursement lines, social workers, in-office precertification specialists, and other supportive agencies to assist the patient in acquiring needed drugs (Hickey & Newton, 2012). Follow-up with the patient at home by telephone can also be time-consuming.

Determining a schedule for follow-up, monitoring oral oncolytics, and ensuring laboratory work is scheduled are important tasks. Nurses also need to assess how often the patient should be called versus seen in person. All of these factors require individual planning and clinician time to accomplish. Without useful tools to facilitate the workload, patient care may be compromised.

Several sources, including the ONS toolkit, provide useful information for the nursing role in oral oncolytics. The ONS toolkit contains easily accessible tools related to drug-drug interactions, administration directions (with or without food), safe handling, and common side effects. It includes useful information on assisting patients to overcome barriers to oral adherence, including emotional, psychosocial, and financial issues (Birner, 2003; D’Amato, 2008; Hartigan, 2003; Moore, 2007; Moore & Brandt, 2010; Neuss et al., 2013; Weingart et al., 2008). However, to the best of the authors’ knowledge, the available sources lack monitoring guidelines to follow patients while they are taking oral oncolytics.

Some oral drugs may be used as maintenance therapy after initial treatment, with longer intervals between follow-up...
<table>
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<tr>
<th>Indication</th>
<th>Manufacturer Recommendations</th>
<th>Initial Dosing and Dose Adjustments</th>
<th>Precautions, Warnings, and AEs</th>
<th>Additional Clinical Information</th>
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<tr>
<td>Afatinib (Gilotrif&lt;sup&gt;®&lt;/sup&gt;)</td>
<td><strong>Pretesting:</strong> LFTs</td>
<td>Initial: 40 mg once daily one hour before or two hours after a meal. Continue until disease progression or until no longer tolerated. Do not take a missed dose within 12 hours of the next dose. <strong>Hold</strong> for any grade 3 or higher toxicity, grade 2 or higher diarrhea for two consecutive days while on antidiarrheals, grade 2 or higher cutaneous reactions for more than seven days, grade 2 or higher renal dysfunction, or worsening liver function. <strong>Discontinue use</strong> if symptomatic left ventricular dysfunction occurs, or if a severe or intolerable adverse reaction occurs on a dose of 20 mg per day.</td>
<td>Most common (20% or greater) AEs: Diarrhea, rash, dermatitis acneliform, stomatitis, paronychia, dry skin, decreased appetite, and pruritus. Uncommon AEs: Severe bullous, blistering, and exfoliating lesions (0.15%), interstitial lung disease (1.5%), fatal hepatic impairment (0.18%), and keratitis (0.8%)</td>
<td>Can cause embryofetal toxicity; advise females of potential hazard, to use highly effective contraception, and to cease breast feeding. If on P-gp inhibitors, reduce by 10 mg per day if not tolerated. Increase to previous dose after discontinued use of P-gp inhibitors.</td>
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<td>Axitinib (Inlyta&lt;sup&gt;®&lt;/sup&gt;)</td>
<td><strong>Pretesting:</strong> Thyroid function, proteinuria, alanine transaminase, aspartate transaminase, bilirubin, blood pressure</td>
<td>Initial: 5 mg twice daily 12 hours apart, with or without food and swallowed whole with a glass of water. Dose increases from 5 mg to 7 mg to 10 mg twice daily depending on tolerance. Dose can be interrupted or decreased to 3 mg or 2 mg for intolerance. <strong>Reduce dose</strong> by about half in patients with baseline moderate hepatic impairment and if a strong CYP3A4 inhibitor is required. Reduce dose for persistent hypertension despite use of antihypertensive medications or in case of severe proteinuria.</td>
<td>Most common (20% or greater) AEs: Diarrhea, hypertension, fatigue, decreased appetite, nausea, dysphonia, hand-foot syndrome, weight loss, vomiting, ashenia, and constipation. Other AEs: Arterial and venous thromboembolism, hypothyroidism, RPLS, elevated LFTs, and proteinuria.</td>
<td>Blood pressure should be well-controlled prior to initiating axitinib. Patients should be monitored for hypertension and treated as needed with standard antihypertensive therapy. Avoid strong CYP3A4/5 inhibitors and inducers. Fetal harm can occur. Women must be advised not to become pregnant or breast feed. Discontinue use at least 24 hours prior to scheduled surgery.</td>
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<td>Bexarotene (Targretin&lt;sup&gt;®&lt;/sup&gt;)</td>
<td><strong>Pretesting:</strong> Pregnancy test (in women of child-bearing potential) one week prior, fasting blood lipids, fasting triglycerides (maintain below 400 mg/dl), LFTs, bilirubin, ECG, chemistry panel, WBC.</td>
<td>Initial: 300 mg/m&lt;sup&gt;2&lt;/sup&gt; per day. Capsules should be taken as a single oral daily dose with a meal. <strong>Reduce dose</strong> to 200 mg/m&lt;sup&gt;2&lt;/sup&gt; per day then to 100 mg/m&lt;sup&gt;2&lt;/sup&gt; per day if necessary, based on toxicity. Doses may also be suspended. Doses can be increased if toxicity is controlled. <strong>Increase dose</strong> to 400 mg/m&lt;sup&gt;2&lt;/sup&gt; per day, with careful monitoring, if no tumor response occurs after eight weeks and if initial dose was well tolerated.</td>
<td>Most common AEs: Lipid abnormalities, hypothyroidism, headache, ashenia, rash, leukopenia, anemia, nausea, infection, peripheral edema, abdominal pain, and dry skin. <strong>Warnings:</strong> Use caution in patients with a known hypersensitivity to retinoids; can enhance the action of diabetic agents, resulting in hypoglycemia; can reduce plasma concentrations of other substrated metabolized by CYP3A4 if used concomitantly; pharmacokinetics may be altered in renal insufficiency.</td>
<td>Do not use in women who are pregnant or plan to become pregnant. Bexarotene is similar to vitamin A; patients should limit vitamin A supplements because of potential additive toxic effects. Advise patients to minimize exposure to sunlight and artificial ultraviolet light. Concomitant administration of gemfibrozil with bexarotene is not recommended.</td>
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**Note.** Based on information from Boehringer Ingelheim Pharmaceuticals, Inc., 2014; Eisai, Inc., 2010; Pfizer Labs, 2014.

AE—adverse effect; ECG—electrocardiogram; EGFR—epidermal growth factor receptor; FDA—U.S. Food and Drug Administration; GI—gastrointestinal; LFT—liver function test; NSCLC—non-small cell lung cancer; P-gp—permeability glycoprotein; RPLS—reversible posterior leukoencephalopathy syndrome; WBC—white blood cell count.
appointments, which contrasts with the close monitoring required when starting active treatment. Active therapy, such as with imatinib (a tyrosine kinase inhibitor for chronic myelogenous leukemia), requires complete blood counts weekly for the first month, biweekly for the second month, and periodically thereafter (Novartis, 2014). Careful monitoring is required initially because of the potential for high incidence of side effects (more than 30% of patients in clinical trials), including fluid retention, nausea, muscle cramping, diarrhea, rash, and abdominal pain (Novartis, 2014). The full prescribing information does not specify how often to evaluate patients for these side effects because each patient must be evaluated individually. As noted by the surveyed nurses, variation exists between drugs regarding laboratory monitoring, side effects, and toxicity warnings, and variation also exists between prescribers regarding how often they want to have patients evaluated. This requires each practice to develop guidelines for each drug and allow flexibility for each patient in his or her specific treatment plan. The American Society of Clinical Oncology/ONS Chemotherapy Administration Safety Standards note that documentation should include, “For oral chemotherapy, the frequency of office visits and monitoring that is appropriate for the individual and the antineoplastic agent and is defined in the treatment plan” (Neuss et al., 2013, p. 8s). Having the essential oral oncolytic information in a brief and concise format would save time by not requiring nurses to read through the full prescribing information, and that saved time could be better spent teaching the patient.

**Discussion**

**Motives for Tool Development**

Nonadherence is a prevalent problem in the administration of oral oncolytics. Oncology clinicians generally assume that patients with cancer will adhere to treatment recommendations because of the seriousness of a cancer diagnosis; however, reports in the literature have demonstrated adherence levels as low as 20% (Moore & Brandt, 2010). This project was undertaken to identify challenges described by oncology nurses related to interacting confidently, consistently, knowledgably, and effectively with patients taking oral oncolytics. The project resulted in the development of a new tool, the Essentials of Oral Oncolytics Guide (EOOG) (see Table 1). This tool provides useful information about currently available oral oncolytics (described as “targeted” or “novel”) in a simple format, focusing on and summarizing essential aspects of each drug. Its purpose is to serve as a resource for oncology nurses and other oncology clinicians involved in the care of patients who self-administer oral oncolytics. To receive a copy of the EOOG in its entirety for use by oncology clinicians, email the authors of the current article.

**Determining Tool Content**

The categories selected for inclusion in the tool were based on the input of nurses who reported how limited their time was. Nurses often must search through multiple resources and lengthy documents to locate essential information. The EOOG details elements of each oncolytic that quickly offers the indication(s) and recommended testing before starting and while monitoring the patient on the drug. It also specifies dosing and dose adjustments and describes adverse events and warnings or precautions, with any black box warnings identified. The authors aggregated these sections described as essential or need-to-know by the discussions with nurses. Hormonal agents (e.g., tamoxifen) and older oral chemotherapy drugs (e.g., cyclophosphamide) have been deliberately excluded from the tool to limit the number of agents and the size. Keeping the information as abbreviated as possible makes the tool more useful, particularly for telephone triage. Should the nurse be unfamiliar with the caller’s particular oncolytic, as was often the reported case, crucial information could be rapidly accessed using the tool. Although several abbreviations are within the text, most are medical abbreviations that healthcare practitioners should know. In addition, the drug names (generic and brand) are listed to allow the user to quickly access the manufacturers’ website for more comprehensive data, including patient education resources and the entire prescribing information.

**Future Considerations**

As the number of oral oncolytics continues to increase at an accelerated rate, oncology nurses will be challenged with keeping abreast of multiple new drugs as well as side-effect profiles, dosing, appropriate pretesting, follow-up, costs, insurance coverage, and indications for use. Many sources exist where nurses can search for information, from published texts to journal articles and online sites, that searching and summarizing can be overwhelming and time-consuming. Participants in the roundtables endorsed that a brief, concise chart like the EOOG would be a valuable asset in practice. Additional information and updates will be necessary on a continual basis for the tool to remain current and be of value as a rapid reference for oral oncolytics. The authors of the current article intend to make additions and changes at least annually.

**Implications for Nursing and Conclusion**

The EOOG will need to be measured for usefulness in clinical settings. Nurses who use this tool should consider reporting their experiences with it. The authors plan to continually add to the EOOG. Nurses and other oncology clinicians could contribute to enhancing this tool for the clinical setting in several ways. They could use it for reference when assigned to telephone triage. Nurses could then assess the benefits and detriments and edit the tool for practice use. Nurses could keep the file of the tool

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### Implications for Practice

- Enhance knowledge of specific oral oncolytics for the improvement of patient outcomes.
- Decrease amount of time used to determine required clinical tests for patients starting or continuing oral oncolytics by using a condensed resource.
- Provide consistent, evidence-based information when teaching about oral oncolytics.
on computer desktops for easy access. Recording how often a pilot group of nurses use the EOOG and noting their satisfaction with the tool to confirm or refute its usefulness would be useful. Nurses could use the EOOG as an improvement exercise to monitor whether appropriate testing is done prior to start of oral oncolytic treatment. Putting this type of tool into practice can add another instrument to supplement the ONS toolkit and support efforts to improve patient care in the area of oral oncolytics.

References


