Nursing Considerations for Patients With Sarcoma on Pazopanib Therapy

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Background: Pazopanib was approved by the U.S. Food and Drug Administration for use in patients with soft tissue sarcoma (STS) in 2012. Because of the scarcity of effective treatments for advanced STS, pazopanib has become commonly prescribed.

Objectives: The purpose of this study was to assess the knowledge level of nurses regarding the safe administration of pazopanib, as well as management of its side effects. The study was also intended to examine the consistency of patient education about pazopanib.

Methods: A 12-question online survey was completed by six nurses working in the outpatient sarcoma department of a National Cancer Institute–designated comprehensive cancer center. The survey included questions about patient education, including side-effect management and medication safety.

Findings: The survey revealed that most nurses were consistent with best practices surrounding pazopanib teaching and side-effect management. However, many differences were observed, and patient education regarding drug interactions and the safe administration of pazopanib is lacking. Further standardization of nursing practice in this regard would greatly benefit patients taking pazopanib.

Pazopanib is an oral medication that was approved in April 2012 by the U.S. Food and Drug Administration (FDA) for the treatment of soft tissue sarcoma (STS) in patients who experienced disease progression with previous chemotherapy (National Cancer Institute [NCI], 2013). Because of the scarcity of effective treatments for advanced STS, pazopanib has become a commonly prescribed therapy in this patient population.

Background

As a multitargeted tyrosine kinase inhibitor (TKI), pazopanib targets the vascular endothelial growth factor (VEGF), platelet-derived growth factor, and c-kit. TKIs are targeted cancer treatments with a mechanism of action in competitive adenosine triphosphate inhibition at the catalytic binding site of tyrosine kinase (Hartmann, Haap, Kopp, & Lipp, 2009). VEGF inhibitors, including pazopanib, prevent angiogenesis by inhibiting VEGF receptors and limiting the vascular supply to the tumor, thereby stunting growth (GlaxoSmithKline, 2015).

Although pazopanib can be a safe and effective treatment for STS, patients who are prescribed the drug must be properly educated about it. Oncology nurses play a crucial role in patient education regarding the correct administration of pazopanib, as well as the management of its side effects. However, the rapid increase of pazopanib prescriptions for patients with STS has created an educational need among the nurses working with this population.

Pazopanib has been used as a treatment for patients with STS at Memorial Sloan Kettering Cancer Center (MSKCC) in New York, an NCI-designated comprehensive cancer center. To assess the strengths and weaknesses of patient education regarding the correct administration of pazopanib, as well as the management of its side effects. However, the rapid increase of pazopanib prescriptions for patients with STS has created an educational need among the nurses working with this population.

Methods

A 12-question online survey was designed by the current authors in response to conversations among nurses working
in the outpatient sarcoma department at MSKCC. Many nurses had expressed uncertainty about the best practices concerning patient education, including side-effect management, for patients newly prescribed pazopanib. The survey questions focused on areas that were thought to be of particular concern (i.e., the importance of taking the drug on an empty stomach, the frequency of interactions with other medications, the need to stop the medication prior to any invasive procedures, the risk of hepatoxicity, and the monitoring and reporting of common side effects).

Designed to identify discrepancies in patient education within the department, the survey was then distributed to outpatient sarcoma nurses at MSKCC. A link to the survey was emailed directly to each nurse; all six nurses who had been emailed the link completed the survey. Nurses received the initial email inviting them to fill out the survey on April 2, 2013, and they were given a deadline of April 23, 2013, to complete the survey. The survey consisted of 12 questions: five multiple choice, six yes or no, and one fill-in-the-blank.

When the survey closed, the current authors compiled the data and looked for areas in which staff education about the safe administration or side-effect management of pazopanib seemed to be warranted. Areas of patient education that appeared inconsistent based on the nurses’ responses were drug interactions, the importance of taking pazopanib on an empty stomach, and side-effect monitoring. The current authors then decided that developing a staff inservice to address the safe administration of pazopanib and management of its most common side effects was imperative.

**Findings**

The survey responses confirmed that many nurses working in the outpatient sarcoma department at MSKCC consistently adhere to best practices regarding pazopanib patient education. However, differences in patient education were also observed, and some areas of patient education were lacking.

**Drug Metabolism**

Responding to the current survey, four nurses said they informed patients about drug interactions with pazopanib. Pazopanib interacts with many commonly prescribed medications, and the interactions can have implications for effective dosing (either of the pazopanib or of the other medication in question), as well as risk for dangerous toxicities. Education about drug interactions should be included every time nurses teach patients about pazopanib to help patients avoid drug combinations that may be ineffective or simply unsafe.

Metabolism of pazopanib is performed by the hepatic system, mostly by the cytochrome P450 3A4 (CYP3A4) enzymes, so patients taking pazopanib must be told to avoid strong CYP3A4 inhibitors and inducers (GlaxoSmithKline, 2015). If a patient has to take a strong CYP3A4 inhibitor (e.g., clarithromycin), the prescriber may need to make a dose reduction of pazopanib. CYP3A4 inducers (e.g., dexamethasone) should be avoided because they can reduce concentrations of pazopanib (GlaxoSmithKline, 2015). Medication reconciliation is an important nursing consideration that allows nurses to identify potential drug interactions. Nurses should tell patients to alert their healthcare provider if medications are changing.

Patients’ liver function tests need to be monitored closely because of the hepatic metabolism of pazopanib. All six nurses who responded to the current survey reported that they include information about hepatic toxicity in their patient education. The provision of this vital information enables the patient to understand the rationale behind serial laboratory draws to monitor liver function. Patients are at high risk of elevated liver enzymes, and a baseline comprehensive metabolic panel should be obtained before beginning pazopanib. Hepatic impairment that is preexisting or caused by treatment may require dose modifications. The minimal renal metabolism of pazopanib means that patients with renal impairment are eligible to take the drug without requiring dose reductions.

**Drug Administration**

The adult dosing of pazopanib for the treatment of STS is 800 mg, or four tablets, to be taken daily on an empty stomach. Pazopanib should be taken either one hour before or two hours after a meal because of the drug’s increase in bioavailability with food (GlaxoSmithKline, 2015). If pazopanib is taken with food, increased absorption of the drug in the system may occur. However, only four nurses reported that they instructed patients to take pazopanib on an empty stomach. This lack of education on the part of nurses could result in serious adverse effects to the patient. To help patients avoid ingesting toxic levels of the drug, patients should be told to take the drug on an empty stomach and not to crush the tablet.

Nurses must also inform patients about when pazopanib should be held, or temporarily stopped. Because pazopanib inhibits angiogenesis, patients should hold the drug for seven days before surgery so they can experience optimal blood flow to the surgical site to help with wound healing. Patients should then resume the drug as per the instruction of their prescribing oncologist. All six respondents to the current survey indicated that they advise patients to call the office as needed to discuss surgery, including dental work, with their medical team, as well as to receive directions about taking pazopanib to optimize healing.

Results from the current survey suggest that patient education regarding how best to take pazopanib is inconsistent. This inconsistency in nursing practice reveals an area where a standardization of teaching should be implemented to increase safe administration of pazopanib. However, the survey also revealed that most nurses kept with best practice when teaching patients about holding the medication.

**Drug Side Effects**

The most common adverse reactions to pazopanib in patients with advanced STS are diarrhea, hypertension, and nausea and vomiting (GlaxoSmithKline, 2015). The current survey asked nurses how they monitor for side effects in patients starting pazopanib. All six indicated that they advised patients to call their oncologist’s office for new toxicities. Only two nurses specifically taught patients when to call their oncologist regarding diarrhea, nausea, and vomiting. Given that these side effects are common and have clear implications for patient hydration
status, electrolyte balance, and comfort, the current authors felt that clarification of their management was important to include in staff education.

Diarrhea: Diarrhea is commonly mild to moderate in severity. Nurses should advise patients of the best ways to manage mild diarrhea, as well as to call their oncologist if moderate to severe diarrhea occurs so it can be managed appropriately. Results of the current survey revealed that only two nurses were teaching patients to call their oncologist for management of diarrhea. The remaining four nurses said they also included patient education regarding the reporting of side effects to their oncologist; however, such instruction is too vague and may result in patients failing to report this common toxicity and receive appropriate care.

Grade 1 (mild) diarrhea is four stools per day over baseline, grade 2 (moderate) is four to six stools per day over baseline, and grade 3 (severe) is more than seven stools per day over baseline, incontinence, hospitalization indicated, or limiting self-care activities of daily living. To standardize care, nurses should teach patients to contact their provider if they experience more than four stools over baseline. Management of acute diarrhea includes treatment of dehydration with oral rehydration therapy and nutrition (World Gastroenterology Organisation, 2008). Pharmacologic treatments include antimitoty medications, antisecretory agents, absorbents, and antimicrobials.

Hypertension: All VEGF inhibitors, including pazopanib, can cause hypertension. VEGF inhibitors can cause a decrease in the number of capillaries and arterioles, which is associated with hypertension. They also can cause arterial stiffness, as well as decrease nitric oxide and prostacyclin production, which increases vascular resistance (Escalante & Zalpour, 2011).

In a phase III clinical trial by van der Graaf et al. (2012) of pazopanib versus placebo involving a total of 372 patients with STS, grade 3 hypertension (systolic blood pressure [SBP] of 160 or greater; diastolic blood pressure [DBP] of 100 or greater) was reported in 41% (n = 99) of patients in the pazopanib arm and in 7% (n = 8) of patients in the placebo arm. In cases of grade 3 hypertension, patients require medical intervention either through additional antihypertensive drugs or increased doses of antihypertensive drugs the patient already takes, or both (van der Graaf et al., 2012).

Candidates for treatment with pazopanib should be screened by their nurses for prehypertension (SBP of 120–139; DBP of 80–89) and undiagnosed hypertension. Patients’ blood pressures should be well controlled before initiating treatment with pazopanib (Escalante & Zalpour, 2011). Hypertension from pazopanib usually appears early in the course of treatment, with 40% of cases appearing by day 9, and 90% of cases appearing within the first 18 weeks (GlaxoSmithKline, 2015). A baseline blood pressure should be recorded prior to initiation of therapy, and patients should monitor their blood pressure frequently at home, particularly during the beginning of therapy.

When teaching patients about pazopanib, five of the nurse respondents in the current study said they advised patients to monitor their blood pressure daily, and one reported telling patients to monitor their blood pressure “multiple times a week.” Despite the disparity, either of these practices is sufficient. Patients taking pazopanib should be instructed to monitor their blood pressure within one week after starting pazopanib and frequently thereafter (GlaxoSmithKline, 2015). Although the survey did not find that nurses were teaching patients about the need to monitor their blood pressure with the same frequency, it did determine that all six nurses were within the guidelines recommended by the manufacturers of pazopanib.

The frequency with which patients should monitor their blood pressure is individual to each patient; however, nurses should encourage greater frequency for patients with a history of hypertension, poor hypertensive control, and the presence of other comorbidities, particularly those of the cardiovascular system (Escalante & Zalpour, 2011).

In patients with hypertension not responding to antihypertensive drugs, a dose reduction of pazopanib should be considered. A patient may require multiple hypertensive drugs to bring his or her blood pressure down to an acceptable level. In cases of severe hypertension or hypertension that is not responsive to treatment with medication, pazopanib may have to be discontinued (GlaxoSmithKline, 2015). To ensure patient safety, nurses must provide clear instructions to patients starting pazopanib about monitoring for hypertension, as well as the importance of reporting increases in blood pressure.

Nausea and vomiting: In a clinical trial of 240 patients with STS, pazopanib caused nausea 56% of the time; only 22% of patients on the placebo arm experienced nausea. Of those patients with STS, just 3% experienced grade 3 nausea (i.e., requiring IV fluid, tube feedings, or total parenteral nutrition) (GlaxoSmithKline, 2015). Nausea is listed as the fourth most common side effect of pazopanib behind diarrhea, fatigue, and hair color changes among patients with renal cell carcinoma, for whom pazopanib has been approved by the FDA since 2009; however, rates of nausea among patients with STS are considerably higher (GlaxoSmithKline, 2015). Most patients who take pazopanib can expect to experience nausea, but the risk for emesis is lower—33% as compared to 11% for the placebo group (GlaxoSmithKline, 2015).

Despite the frequency with which patients experience nausea and vomiting, the National Comprehensive Cancer Network (2015) classifies pazopanib's emetogenic potential as minimal to low risk. This classification may be based on the population of patients with renal cell carcinoma; the rate of nausea associated with pazopanib in this population was 26% versus 9% for members of the placebo group. Likewise, the prevalence of vomiting was 21% versus 8% for members of the placebo group (GlaxoSmithKline, 2015).

Given the prevalence of nausea with pazopanib in the population of patients with STS, nurses must prepare patients for this side effect. In their responses to the current survey, only two nurses indicated that they advised patients to report nausea to their oncologist. Whether or not this omission in patient education stems from a perceived lesser risk of nausea associated with pazopanib than actually exists in the population of patients with STS is unknown. Regardless, pazopanib patient education should include the dose and schedule of any prescribed antiemetics, dietary recommendations for managing nausea, and information about any pharmaceutical techniques (e.g., meditation, acupressure) that may help the patient manage nausea that persists. Patients should be told to contact their oncologist or nurse if nausea is not well controlled.
An online survey completed by six oncology nurses at an NCI-designated comprehensive cancer center highlighted discrepancies in patient education regarding medication management for the oral tablet pazopanib. These differences were of concern to the current authors and showed that a need existed for nurse training through a staff inservice. The resulting inservice had 100% attendance and featured a presentation about the common side effects of pazopanib, as well as the treatment of those side effects. In addition, a dialogue was opened to establish a standardized patient education program throughout the oncology service, instead of teaching based on individual physician preference. The follow-up plan is to create and distribute a postinservice survey to determine if the information shared at the inservice was effective, and also to continue the dialogue with hospital administration regarding the standardization of patient education.

### Implications for Practice and Conclusions

Pazopanib is a viable treatment option for patients with STS. To ensure adherence to the drug and better management of its side effects, patients who are prescribed pazopanib must receive a thorough education about it in the clinic setting; they can also be referred by their healthcare provider to the medication guide on the pazopanib package insert.

Through the survey regarding pazopanib patient education and best practices, nurses working in the outpatient sarcoma department at MSKCC were able to gain a better understanding of the existing similarities and variations in practice among other nurses, as well as identify areas in which further staff education would be beneficial. Increased standardization of nursing practice regarding pazopanib patient education would greatly benefit patients prescribed pazopanib for the treatment of STS.

The current survey highlighted the need to keep nurses abreast of new medications made available for patients with STS. With many new oncology drugs receiving FDA approval, nurses must stay current in their understanding of these drugs and their potential side effects. An inservice for nurses after a drug is approved by the FDA is an excellent way to keep a nursing staff educated, as well as open up a discussion about new medications. The idea of surveying nurses to identify gaps in knowledge about a specific drug, then providing an inservice based on results of the survey, is a useful one that can be translated across all oncology specialties at various institutions. The ultimate hope is that nurses reading the current article can identify areas within their own practice in which they lack knowledge, then work toward bringing better medication education to their patients.

### References