Identified Complications of Extended International Travel for Patients Receiving Oral Anticancer Drugs

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Healthcare has become increasingly costly with the advent of advanced technologies, and the field of oncology has not been spared from issues related to cost. The use of oral anticancer drugs has dramatically increased over the past several years, highlighting the need for medication cost reforms, and ways to manage patients with cancer effectively in an ambulatory setting. Patients receiving intravenous anticancer agents have always been closely monitored for safety, efficacy, and adherence in a supervised setting; however, these processes often do not exist for patients receiving oral medications.

Oral anticancer regimens require patients to take a more active role in monitoring for toxicity and adherence to therapy. The medical oncology team provides the patient with guidance to optimize therapy, minimize the risk for adverse events, and attempt to prevent secondary toxicities. It is imperative that patients taking oral anticancer drugs understand the serious risks and high probability of toxicity associated with their use, along with the need for supportive care measures to manage such toxicities.

For example, oral maintenance medications for different disease states may not require frequent blood monitoring. In comparison, the majority of oral anticancer drugs are accompanied by specific recommendations for monitoring for serious and/or potentially fatal adverse events. The label of pazopanib (Votrient) carries a box warning for hepatotoxicity, which requires monitoring liver function tests at baseline, at weeks 3, 5, 7, and 9, at months 3 and 4, and then periodically. This requirement imposes significant clinic visit burden on patients, and if the patient fails to complete the necessary blood work, the oncologist may decide to interrupt the therapy, which is no longer safe without current liver function information. The case report provided in this article is a good example of these dilemmas.

Medication therapy management provided by pharmacists is very effective in influencing patient adherence to therapeutic regimens and ensuring that all necessary monitoring is completed within an appropriate period of time. Success of oral anticancer medication therapy management by oncology pharmacists has been documented by pharmacists at the Princess Margaret Cancer Centre, Toronto, Canada. They reported a 94.7% satisfaction rating of the clinical pharmacy services among 113 patients in their ambulatory chemotherapy unit. However, discussing challenges during follow-up with patients who travel internationally for extended periods has rarely been addressed in the literature.

With every patient, providers should be cautious when prescribing oral anticancer drugs. If patients have difficulties remaining adherent to therapy, reporting adverse events, or attending follow-up visits, they may not be good candidates for oral therapy. An additional layer of complexity arises when a patient travels extensively or primarily lives outside of the United States. An evaluation and discussion of the various effects on the patient, the provider, and the pharmacy of a patient who is on extended international travel while taking oral anticancer medications should attempt to address a critical area of unmet need in oncology care.

The cost of foreign travel has decreased significantly in recent years, making global treks available to the masses. People now have the means to travel routinely across the world, which may include strategic visits to countries with better healthcare than the healthcare in the patient’s country. However, foreign travel is not without risks.

At the University of Massachusetts Memorial Medical Center, we have a fairly diverse patient population, including patients who travel from the United States around the world for extended periods (eg, for business, to visit family) and are unavailable for medication refills, for communication with their healthcare team, and for

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We have had patients in our clinic who came to the United States and travel from all over the world to see a physician at our institution for assessment of their cancer diagnosis, to receive a prescription for oral chemotherapy, or to obtain the medication.

Before the onset of oral oncolytics, if patients were receiving high-risk medications, such as intravenous chemotherapy, foreign travel would be discouraged, because the patient might have missed life-prolonging or even life-saving treatment. With the growing popularity of oral anticancer agents, however, patients are able to receive treatment away from the clinic or the hospital.

Without frequently scheduled routine visits, the lines of communication between patients and their healthcare team can be easily severed. If patients are living in a foreign country, necessary toxicity checks, laboratory monitoring, or follow-up imaging may not be possible, which can present an ethical dilemma for the healthcare team.4,5 As a healthcare team, we cannot in good conscience allow patients who are leaving the United States to receive treatment unsupervised, especially in the very early stages of therapy, but we also know that the standard of care in the United States may not be available to these patients should they have to receive treatment in a developing country.

Language barriers can also present a roadblock to optimal care for patients traveling to the United States for treatment. Translated instructions can potentially lead to misinterpretations, especially if a certified medical translator is unavailable. Interpreters may have difficulty finding specific words for some terms in particular languages, which could lead to confusion or errors in patient medication management. Nonverbal social cues also vary between cultures, and may result in unforeseen misunderstandings between provider and patient. These verbal and nonverbal language barriers may stay unresolved for people from cultures where it is considered rude to question a person of authority, such as a physician.

We have had cases were physicians believed that patients were taking a particular oral agent at home, but the patients admitted to the pharmacist that they never actually intended to take it; they just did not want to disappoint the physician. This communication breakdown between provider and patient because of cultural differences or language barriers may result in treatment delay and in other adverse events, as in our experience.

Multitude issues can arise in the pharmacy when patients who take oral anticancer medications live in or travel to different countries. Patients who travel to the United States from other countries may not have US insurance coverage, or may have trouble obtaining it. We have had patients in our clinic who came to the United States on temporary visas and were diagnosed with cancer during their trip. They were not healthy enough to travel home for treatment, and they did not believe that they would receive the same level of treatment there; therefore, we had to help them apply for emergency MassHealth coverage.

Other common issues for patients who travel for long periods are complications related to prescription refills. Some ways that we try to address these potential issues is by asking questions during our first conversations with our patients who fill their prescriptions at our UMass Memorial Specialty Pharmacy, or those who are seen in our clinic but use an outside pharmacy. These questions include, how will they obtain their refills? Will they be home in time to refill their medication? Can they pick up their medication in person, or should it be shipped to them within the United States? Will they be traveling outside of the United States? If so, is the physician aware of their planned travel?

Because we cannot ship drugs internationally, we ask patients if they have a family member who can send the medication to them. However, we avoid this practice whenever possible, because we lose the ability to monitor the medication’s storage and handling in transit. Patients may also have trouble obtaining follow-up blood monitoring or staging imaging.

These are examples of questions and scenarios that we believe healthcare professionals should evaluate when deciding how to proceed in this situation. Chemotherapy medications are hazardous and require handling precautions that patients may not be aware of before speaking with a pharmacist or with other healthcare providers.

When counseling patients on chemotherapy medications, we usually advise them to avoid starting any new medications without first consulting their oncologist or pharmacist. This becomes difficult when patients are staying in another country for extended periods, because they may have access to different herbal or over-the-counter medications that are not accessible in the United States. This can become an issue when patients do not inform their oncologist or pharmacist, or if they cannot get in contact with them to discuss initiating a new medication.

Therefore, we typically ask our patients to call us on our clinic cell phone if they have questions about starting new medications. Patients have called us from Florida, as well as Africa, and we have been able to prevent medication errors. However, this can occasionally be difficult, because there may not be any data on certain over-the-counter drugs or herbas that are not available in the United States, or the medications may not be easily translated into English, so the oncologist or pharmacist may not have enough evidence-based...
information to know whether it is safe for the patient to take a new drug.

Patients with cancer face many challenges and barriers to treatment, whether their international travel is into or out of the United States for an extended period of time. The healthcare team encounters a different set of challenges when treating these patients, to ensure that patient safety is consistently the primary driver of care. Fully informed decisions about patient care in oncology necessitate a patient-centered approach; knowledge of the patient’s citizenship, travel plans, and communication needs during treatment with oral chemotherapy medications is essential to making the most ethical treatment decision.

Case Report

A male patient aged 57 years was presented to the emergency department with worsening right chest pain and self-reported metastatic renal-cell carcinoma, approximately 2 years post right nephrectomy (the original diagnosis date was unknown, but the patient stated that it was within the past 10 years). The patient had medical records with him from Brazil, written in Portuguese.

The treatment plan was to rebiopsy, conduct a whole-body scan, and perform a computerized tomography scan of the abdomen and pelvis. However, the patient was lost to follow-up for 3 months, because of a reported emergency in Brazil. He then presented with new diagnostic images from Brazil, showing a new metastatic lesion.

We completed the rebiopsy and imaging series, which confirmed the diagnosis of metastatic renal-cell carcinoma. The patient stated that his physician in Brazil instructed him to ask about PD-1 therapy in the United States.

The oncologist decided to have the patient start pazopanib therapy, and the patient agreed to stay in the United States during treatment, so that he could be properly followed and monitored for adverse events. After receipt of the medication, however, a pharmacist attempted to reach the patient by phone several times to counsel him about this oral anticancer drug, with no success.

Eventually, a friend answered the phone and said that the patient was back in Brazil, with no known return date. The pharmacist reported this information to the patient’s oncologist, who made the decision to not treat the patient again, because the risks outweighed the benefits of continuing to prescribe pazopanib without required laboratory monitoring.

Author Disclosure Statement

Dr Whitman, Dr Sendrowski, Ms Longo, and Ms Bernas have no conflicts of interest to report.

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