When oral medications for the treatment of cancer became available, oncology providers and their patients were enthusiastic. The feeling was that finally there was a way for patients to preserve and control their personal time, by no longer needing to sit in an infusion chair for hours; instead, they could self-administer their medications by taking them in a pill form. This was exciting news, until the realization that oncologists no longer had a way of ensuring that their patients were actually taking their medications as prescribed.

This special feature provides insight into the primary barriers that cause patients not to comply with their medication schedule or not take their oral medications exactly as prescribed. Read about the importance of good communication between healthcare providers and their patients who are prescribed oral medications to take at home. Learn about the many barriers to patient adherence, and how to overcome these potential obstacles.

As oncology providers, in addition to managing the cancer, we must go beyond the patient’s physical health to also recognize and treat the patient’s emotional well-being, financial health, and psychological needs. These factors play an important role in whether patients consistently take their oral medications as prescribed. By reading this special issue, patients and their providers will gain a wealth of new knowledge that will help patients with multiple myeloma stay on track with their oral medications to improve the management of their disease.
Over the past 10 years, treatment options for patients with multiple myeloma have increased dramatically. These advances have resulted in improved survival rates for patients and an increased focus on the patient’s quality of life that have fueled the important development and use of oral treatments in recent years, a trend that is expected to continue. The oral therapies that are currently approved by the FDA for the treatment of patients with multiple myeloma include Thalomid (thalidomide), Revlimid (lenalidomide), Pomalyx (pomalidomide), and Farydak (panobinostat), and other drugs are still in development.

Oral therapies offer patients with multiple myeloma several benefits, such as the ease of administration and the convenience of taking the treatment at home, which translate to fewer visits to the care facility, less disruption to daily activities, and better overall quality of life.1 Being able to self-administer their oral medications also provides patients a positive sense of control and empowerment.1 However, the introduction of oral cancer drugs has also posed unique challenges compared with the office administration of traditional, infused, or injectable medications, and has altered the delivery of oncology services for patients with multiple myeloma.

This article outlines how these changes affect patients with multiple myeloma, and how they can work with their oncology care team to achieve the best treatment outcomes.

CHALLENGES ASSOCIATED WITH ORAL CANCER THERAPIES

Barriers to Medication Adherence

Foremost, oral cancer drugs for multiple myeloma have changed the roles and responsibilities of oncology providers, as well as for patients, in terms of the administration of medication (Figure).1

When providers are responsible for the administration of intravenous or injectable medications, the office setting allows for strict control of the dosages and ensures that patients receive their treatments as prescribed. However, with oral medications, the burden is shifted from the provider to the patient, who is now responsible for taking his or her medications as prescribed by the physician. The extent to which a patient follows the doctor’s prescribing instructions is called “adherence.”2

Adherence encompasses many aspects of medication intake, including whether the correct drug is taken, whether the right amount of the medication is taken, if the drug is taken at the prescribed time, whether and how often the patient follows the prescribing instructions, and whether the treatment

<table>
<thead>
<tr>
<th>FIGURE</th>
<th>Key Features of Using Infusions and Injectable Medications versus Oral Medications for Multiple Myeloma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infusions or injectable medications</td>
<td>Oral medications</td>
</tr>
<tr>
<td>The patient’s role is passive</td>
<td>The patient’s role is active</td>
</tr>
<tr>
<td>The patient is recipient of treatment</td>
<td>The patient self-administers the medication</td>
</tr>
<tr>
<td>The provider dictates the treatment</td>
<td>The provider collaborates with the patient about the treatment</td>
</tr>
<tr>
<td>The provider monitors and manages side effects</td>
<td>The patient is actively involved in early symptom recognition and management</td>
</tr>
<tr>
<td>Potential for medication nonadherence is low</td>
<td>Potential for medication nonadherence is high</td>
</tr>
<tr>
<td>The provider is responsible for medication procurement</td>
<td>The patient is responsible for medication procurement</td>
</tr>
</tbody>
</table>
is being taken for the prescribed length of time. Evidence from studies on chronic diseases shows that patients do not always take oral medications as prescribed. It has been reported that lack of medication adherence by patients ranges from approximately 20% up to 100%.

These percentages are disturbing, because a medication can only be effective if it is taken in the right amount and at the right time. Nonadherence to prescribed therapy has serious consequences and is a major contributor to reduced medication effectiveness, poor quality of life, more disease complications, increased hospitalizations, and worse overall patient outcomes. Therefore, for oral cancer therapies for multiple myeloma, following a physician’s prescribing instructions in terms of time and dose is of paramount importance to achieving the best results.

Although patients often intend to adhere to their oral medications, there are many reasons why they do not take them as prescribed. The side effects of the medication or complicated treatment regimens can cause lack of adherence to oral medications. Some patients skip doses or take smaller doses of their medication because they cannot afford it if they have no health insurance, or because of the high cost of the medication, or because they have limited access to healthcare facilities and/or to a pharmacy.

Other patients simply forget to take their medications because of older age or for other reasons, or because they take several medications for multiple myeloma or for coexisting conditions. The average medication adherence rate in older patients is estimated to be less than 45%. Some patients lack a support system either from family or a social support network, or they have inadequate supervision, which could contribute to their nonadherence. Moreover, patients receiving long-term treatment have nonadherence rates of about 50% and are more likely to be nonadherent to their medication.

In some cases, patients’ beliefs and perceptions about their disease and treatment lead to nonadherence. Some patients do not fully understand the risks for disease progression when a medication is not taken as prescribed, and they may not comprehend the severity of their disease and the need for medications to control their disease. Some patients may have the misconception that missing a few doses now and then will not impact their disease. Patients may not see value in their medication’s ability to control their disease, or the medication’s side effects may prompt some patients to stop taking it. Some patients may become more complacent with their medication schedule when they erroneously equate disease without symptoms with cure. Studies have shown that the greatest nonadherence occurs when patients are symptom-free.

Side-Effect Management

Another concern that emerges with oral oncolytic therapy is that providers are unable to closely monitor their patients’ side effects, because oral drugs are taken outside of the office setting. Therefore, the onus is on patients to report any side effects that they may be experiencing in a timely manner. In addition, the lack of regular interaction between the patient and the provider when receiving infusions or injectables may cause patients to alter the dose of an oral medication or skip it entirely, because they are unable to tolerate the side effects at the prescribed dose and they do not inform their provider. Such behavior can have harmful consequences that will affect the patient’s safety.

Financial Difficulties

Medication affordability, insurance coverage, medication costs, and timely acquisition of medication can contribute to compliance concerns regarding oral medications. Many oral drugs are expensive and are often subject to higher patient cost-sharing than intravenous therapies; this can translate to high copays and coinsurance. Patients who are under financial strain may be more inclined to skip or reduce their medication dosing. In the absence of regular face-to-face interactions with their
provider, patients may hesitate to inform their cancer care team if they face such financial difficulties.

**Drug Acquisition Difficulties**

Patients receiving oral therapies are responsible for obtaining their medications, whereas the oncology care team is involved in procuring infusion and injectable medications, and patients may not be willing or equipped to handle this. Some oral medications are only available from specialty pharmacies or have other distribution limitations, which could cause delays in obtaining or refilling a prescription. One survey reported that more than 25% of patients did not get their prescription filled because they thought it was unnecessary, which could be attributable to a lack of awareness of the negative effects of nonadherence. However, when faced with such medication acquisition difficulties, patients may not readily approach their oncology care team for help. Such issues are less likely to occur when patients have frequent office visits with their oncologist.

**PARTNERSHIP BETWEEN THE PATIENT AND THE ONCOLOGY CARE TEAM**

The shift in the roles and responsibilities associated with oral therapies also changes the dynamics of the relationship between the patient and the oncology care team (which may include physicians, oncology nurses, nurse navigators, and pharmacists, as noted in the Figure).

Patients are more passive recipients of treatment from the oncology care team when they receive an infusion or injectable in the office. By contrast, patients receiving self-administered oral cancer medications are required to take a more active role in their care. It is important for patients to understand that although the delivery of care has changed, this does not translate to being isolated in their struggles. The oncology care team, particularly oncology nurses and nurse navigators, play an important role in assisting patients with any challenges they face.

To achieve the best treatment outcomes, patients must engage in a partnership with their oncology care team and must develop a sense of ownership. To make the partnership work effectively, communication between patients and their oncology care team and patient education are critical.

The oncology care team assists in providing the necessary education, tools, and resources needed to overcome treatment challenges, including those related to medication adherence, side-effect management, as well as financial and acquisition difficulties. For their part, patients must be empowered through the resources provided to surmount any challenges they may face. The oncology care team and the patient must collaborate to create an individual treatment plan that fits the patient’s needs, daily routine, and lifestyle.

**PATIENT EDUCATION**

After an oral medicine is prescribed, the patient must be educated on its key information, including what the risks and benefits are, why it is being prescribed, when it should be taken, how much should be taken and for how long, and what could happen if the drug is not taken as prescribed. Patients with multiple myeloma may experience medication-related side effects during treatment, and it is important that patients are not caught off guard when side effects occur. Patients must be aware of the drug’s most common side effects, how to prevent these side effects, information on any food or drug interactions that may cause other side effects, and how and when to contact their provider.

For the overall success of an oral treatment, such information must be provided to patients by their care team, and patients must be proactive and actively request information or clarifications on any uncertainties they may have about their medication, side effects, or treatment plan. It is important that patients recognize side effects when they experience them and inform their oncology care team immediately so that these can be managed without reducing the medication dose or stopping the treatment.

The oncology care team and the patient must
work together to identify individual barriers to medication adherence and must address them with adherence aids, reminders, and behavioral changes.\(^1,6\) To improve adherence, patients can use reminder aids, such as medication calendars or schedules that help patients take their medication on the exact days and times they need to, or pillbox organizers.\(^6\) Other helpful tools include setting a reminder alert on a cell phone, watch, or timer; using a pocket pillbox that vibrates; or using a smartphone medication reminder app.\(^6\)

Patients should be encouraged to maintain accurate medication diaries to track their medication adherence so that patterns of nonadherence can be identified and addressed.\(^1\) Specialty pharmacies often use postcard reminders, calendars, diaries, and dosing sheets to promote timely refills.\(^6\)

For patients who have financial difficulties and cannot afford their medication, oncology nurse navigators can direct them to financial assistance resources.\(^1\) Many drug companies, nonprofit organizations, and government agencies offer patient assistance programs that provide free or low-cost medications to patients who are unable to afford their medication, or for those who need help with their copays, deductibles, reimbursement, or insurance premiums.

CONCLUSION

With the continuing transition toward oral medications for multiple myeloma, it is imperative that patients and their oncology care team recognize that their responsibilities have changed, and they all embrace their new roles. In the context of patients facing the increased responsibility of maintaining their own healthcare, patient engagement in a partnership with the oncology care team is the cornerstone of achieving optimal outcomes with oral treatments. Patient education and regular communication between patients and their oncology care team are key to the success of oral treatments for multiple myeloma to promote medication adherence, proper symptom management, financial assistance, and medication acquisition.

References

tions can disrupt a person’s normal sleep habits and daily routine. The high cost of cancer medications is another concern for most patients, as are the safe handling and storage of the pills.

FREQUENTLY ASKED QUESTIONS

The following are suggestions for 3 of the most frequently asked questions about oral cancer treatments:

Q. What are some ways to help me take my medication exactly as it is prescribed?

Members of your healthcare team can help you develop simple strategies for getting used to taking a new medication. The “silly pat,” patting your head or using another body gesture when taking your medication, has been shown to help people develop a new routine.

Chart your achievement on a calendar each time you take your medication as prescribed, and reward yourself with something nice at the end of a successful week. When you take your medication, send yourself a positive message by raising your water glass and toasting “to life.”

Q. What financial resources can help with the cost of my cancer medication?

There are several financial resources for patients taking oral medications for multiple myeloma. The Leukemia & Lymphoma Society, Patient Access Network foundation, and Good Days have grants and copay assistance programs for qualifying patients. In addition, some drug companies have patient assistance programs for qualifying patients. Cancer centers often have staff dedicated to helping patients find national and local financial resources. Make sure to ask if assistance is available.

Q. What should I do if I experience side effects, such as diarrhea, nausea, or a rash?

Preparing for side effects can help you keep your life as normal as possible. If your medicine causes diarrhea, be prepared with extra clothing or wear protective briefs. Work with your healthcare provider to find the right solutions for nausea. Use sunscreen when outdoors, and notify your cancer care provider of any itching or a rash. Cancer therapy does not need to equal suffering.

Following the 5 medication rights is vital. As discussed in the feature article, taking less or more of a medication can have serious consequences for patients with cancer. Fortunately, barriers to adherence can be overcome when patients, caregivers, and the healthcare team work together toward that common goal.

There remains no consensus of agreement regarding a cure for multiple myeloma, but the past several years have seen tremendous progress in terms of patient support, treatment, and drug innovation for this devastating cancer. Now more than ever, patients with multiple myeloma have unprecedented numbers of treatment options to choose from for their deadly plasma-cell neoplastic diseases.

EFFECTIVE ORAL THERAPIES

In a remarkable change from previous years, effective all-oral combination therapies will soon become a reality for patients with multiple myeloma. In 2015, Farydak (panobinsonostat) was added as a new-in-class oral pan-HDAC inhibitor to the already approved immunomodulatory agents—Thalomid (thalidomide), Revlimid (lenalidomide), and Pomalyst (pomalidomide).

In addition, the significant possibility of the accelerated approval of ixazomib by the FDA and the various phase 1 and phase 2 clinical trials that are...
currently in progress for oprozomib make this exciting development a very close and likely reality.

As stated in the main article, an all-oral future treatment plan opens the door for more treatment options, more convenience, and an overall better quality of life for patients and their care team.

WITH MORE TREATMENT OPTIONS, CONVENIENCE, AND CONTROL, PATIENTS MUST ACCEPT THE ADDED BURDEN OF RESPONSIBILITY TO BECOME EDUCATED.

ADDED RESPONSIBILITY FOR PATIENTS

With more treatment options, convenience, and control, patients must accept the added burden of responsibility to become educated. Likewise, their oncology care team, including pharmaceutical companies, must create the means by which patients can become educated.

Frequent, open communication between patients and their oncology care team is critical in addressing the drug adherence issues that are described in the main article. With less frequent visits secondary to the home delivery and administration of oral drugs, communication needs to be more intentional.

PATIENT–DOCTOR TRUST

Also critical is a patient–doctor bidirectional trust. Patients need to trust that their doctors have their best interest at heart, and doctors need to trust that patients will be fully responsible in their care; this, however, can lead to a “catch-22.” Without education and communication, trust is built on thin soil; without adequate trust, the willingness to teach, learn, and communicate is minimized.

Regardless, patients with multiple myeloma need to fully understand that multiple myeloma is a vicious cancer that they cannot trust, even when they are feeling well. As a result, patients need to take their prescribed medication during induction and maintenance therapy, when they are feeling well as much as when they are not feeling well.

A 360 VIEW OF THE PATIENT

It is important that the extended healthcare team have a 360 view of their patient’s financial, emotional, physical, and psychological situation to provide dynamic and personalized care. Surveys and one-on-one discussions at the doctor’s office are useful in getting that started.

However, these encounters are only points in time, and they can result in a “halo effect” of side effect, symptom, and overall situation reporting. Can the power of emerging technologies, such as wearable devices, mobile technology, and big data, be used to pull data from patients to get an ongoing view of their condition and, based on that accumulated data, allow the oncology care team to provide pertinent information for the patient?

IT IS IMPORTANT THAT THE EXTENDED HEALTHCARE TEAM HAVE A 360 VIEW OF THEIR PATIENT’S FINANCIAL, EMOTIONAL, PHYSICAL, AND PSYCHOLOGICAL SITUATION.

In the end, education will only address the patient’s lack of adherence to their oral cancer therapies. The 5 Ps—patients, providers, pharma, payers, and policymakers—need to work globally and collaboratively to address the causes of high drug prices, to innovate and reduce treatment-altering side effects, and, in general, to address the availability of and access to drugs for those who need them most.

References
