Oral Oncology Treatment Regimens and the Role of Medication Therapy Management on Patient Adherence and Compliance
ORAL CANCER CARE THERAPIES: THE OPPORTUNITY AND THE CHALLENGE

Chemotherapy used to treat various cancers is increasingly available in oral form, resulting in greater patient convenience. Patients can self-administer these drugs in the comfort of their own homes instead of visiting their physician’s office for infusion therapy. The ability to self administrate chemotherapy has even more benefit as the course of some therapies has moved from intense short therapies to ones that cover several months to years.

As cancer becomes more chronic in nature, this convenience cannot be underestimated for patients living and working while undergoing treatment.

A common assumption around cancer treatment is that a patient, given the choice of self-administered chemotherapy doses, will be 100 percent compliant. Evidence suggests otherwise and points to patients administering these drugs inconsistently and irregularly. Compliance rates in some studies are as low as 20 percent.

Reasons for Non-compliance

Patients become non-compliant with their oral cancer care regimen for a variety of reasons including:

- Feeling better so they stop taking the drug;
- Feeling worse so they stop taking the drug;
- Dosing regimen is complicated and confusing;
- Inability to afford expensive medications;
- Inability to find designated pharmacy provider due to access restrictions imposed by payer and/or pharmaceutical manufacturer.

Regardless of the reasons, the impact of non-compliance has considerable health and cost implications.

SIDE EFFECTS AND ADVERSE EVENTS

Side effects are an expected element of all oncology therapies. If they escalate beyond what is tolerable or safe for the patient or if they become adverse drug events, therapy may be suspended until the side effects can be controlled. These “therapy holidays” can increase costs significantly as a result of wasted medications, the lost treatment benefits on the cancer itself, the resulting disease progression, and the service utilization that occurs as patient health status deteriorates.

Chemotherapy presented in oral form has similar toxicity profiles to infusion forms, and quite often results in serious side effects which can quickly progress to adverse drug events, resulting in additional medical intervention. Because the patient is not physically in the physician office when their medication is taken (administered), there can be a gap in patient—physician contact with regard to medication issues. This gap can allow for side effects to escalate and a patient’s condition to deteriorate between visits, resulting in additional medical intervention. Additionally, non-compliance becomes a greater risk for patients who try to avoid side effects and adverse events by adjusting the dosing regimen on their own or stopping treatment completely, negatively impacting the success of their prescribed therapy.

In short, medication compliance is impacted by a number of complex factors and non-compliance with oral oncology dosing regimens can result in reduced quality of care, increased costs for patients and payers and unnecessary suffering for the patient.

As the availability of oral oncology agents increases and more patients have the opportunity to participate in therapies that include oral agents, it will be increasingly important to address issues that impact therapy compliance.

ROLE OF MEDICATION THERAPY MANAGEMENT

Medication Therapy Management programs are designed to help patients (1) remain more closely aligned with the prescribed drug regimen, and (2) better manage the expected side effects of the chemotherapy, allowing patients to stay more compliant with the prescribed regimen and reduce costs associated with side effects.

In addition to optimizing the oncology drug’s impact and patient quality of care, there is also a direct cost impact. The result can be lower overall drug costs due to reduced therapy holiday and re-started regimens, reductions in avoidable medical costs such as emergency room visits and hospitalizations due to side effect progression to adverse drug event status.
This paper reviews existing literature for causes and effects of non-compliance with oral oncology agents and explores dimensions of Medication Therapy Management (MTM) programs that are effective in meeting the purpose described above. Many MTM programs are relatively new, but key features signaling successful programs are described, as are lessons from non-oncology programs.

In discussing compliance with oral oncology regimens, understanding the terminology is an important first step. According to the International Society for Pharmacoeconomics and Outcomes Research, medication compliance (adherence is offered as a synonym) is “the extent to which a patient acts in accordance with the prescribed interval and dose of and dosing regimen. The unit of measure for compliance is administered doses per defined period of time, reported as a proportion (%) of prescribed doses (D) taken at the prescribed time interval (T) as measured by the period of time, i.e., % of TD, measured by percentage.”

Medication persistence is the accumulation of time from initiation to discontinuation of therapy, and is measured by time metric (weeks/months).

A number of studies have documented how difficult it is to accurately measure patient compliance with home-administered oral oncology agents. Difficulties include the inherent measurement inaccuracies of self-reporting, the lack of applicability of external measurements, such as pill counts, as well as the Hawthorne effect, wherein the study subject acts differently because of the measurement itself. In other words, documenting that they took a pill helps patients remember to take the pill, thereby skewing the results.

Furthermore, a survey of the literature shows that patients become non-compliant with oral oncology regimens for a wide range of reasons: drug cost, dosing complexity and limited patient education. In addition, Jansen, et al found that patient age, health literacy and education level were significant factors in patient non-compliance as well.

CAUSES OF MEDICATION NON-COMPLIANCE

Despite the fact that a cancer patient’s survival and well-being may depend on accurate administration of oral medications, over-use, under-use and misuse of prescription drugs remains highly problematic; as many as 80% of patients do not take oral oncology agents according to their doctor’s instructions.

For cancer patients, like patients with other diseases, many factors contribute to the non-compliant use of oral oncology agents. Several studies have attempted to identify the causes for patients not complying with the dosing regimens their physicians provide:

• Complexity of dosing regimen;
• Patient age has limited impact, with adolescents being especially susceptible to compliance problems;
• Patient expectations of the effectiveness of the regimen;
• The severity of the illness and the expected change;

The rate of growth of oral oncology agents is estimated anywhere between 20% to 30% year over year with over a third of the 650 oncology agents in the drug pipeline coming in an oral form. Given this rate of increase, it is reasonable to expect oral oncology drugs will comprise between $5B to $7B in annual drug spend by 2010.
• Patient and family medication education was cited by one study as the “most important factor in successful outcomes of patients receiving oral chemotherapy”.

• Reduced clinical supervision

A recent article suggests that economic considerations, including but not limited to medication cost, may play an important role in medication compliance decision-making by individuals. In brief, “Economic models (utility maximization, time preferences, health capital, bilateral bargaining, stated preference, and prospect theory) may contribute to the understanding of medication-taking behavior.”

The best answer seems to be that medication compliance, perhaps especially in an oral oncology setting, is a highly complex puzzle with many dimensions for any individual. There being no simple causality, there are no easy answers for this potentially dangerous situation.

**EFFECTS OF MEDICATION NON-COMPLIANCE**

The reason that medication compliance rates are so concerning is that patients who are non-compliant with their prescribed medication dosing regimens can have a wide range of adverse responses. Since non-compliance includes both over- and under-administration of drugs and improper timing, the range of response is equally great.

Patients who are non-compliant with their oral oncology regimens may fall into one or more of the following scenarios:

<table>
<thead>
<tr>
<th>Cause</th>
<th>Situation</th>
<th>Effect</th>
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<tr>
<td>Confusing dosing instructions</td>
<td>Dosing instructions often confusing, number and frequency of administration change within a dosing schedule, causing patients to over-administer or mis-administer drugs.</td>
<td>Toxicity of drugs increases with dosing increases, causing patients to have adverse reactions, increasing ER visits and hospitalizations. Patients under-administering drugs or missing timings can result in significant reduction in the effectiveness of the chemotherapy regimen, allowing disease progression and requiring additional therapy administration.</td>
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<td>Reduced clinical supervision</td>
<td>Patients visit their oncologist less frequently than when receiving infusion therapy; side effects are not observed and interventions are not made until side effect severity escalates.</td>
<td>Side effects escalate to adverse drug events; ER and hospitalizations increase and patient condition deteriorates. Patients may require therapy holiday to recuperate before resuming treatment.</td>
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<td>Insufficient patient and family health education</td>
<td>Patient and family caregivers may not recognize signs of patient status deterioration and forgo treatment pending scheduled oncologist visit.</td>
<td>Rapid deterioration of patient status may occur, resulting in ER visit/hospitalization, as well as requiring a therapy holiday to allow the patient to recover before resuming treatment.</td>
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<td>Patient expectation of impact on illness</td>
<td>Patient expects oral oncology agent to impact perception of disease and its progression, and misunderstands onset of side effects, resulting in breaks in therapy administration.</td>
<td>Patient may inadvertently cause therapy holidays and allow disease to progress without treatment.</td>
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Fig. 2

*What is clear is that the effects of non-compliance with prescribed dosing regimens are as widespread as the causes.*
EFFECTIVE METHODS FOR INCREASING MEDICATION COMPLIANCE

Given the broad-based causes and impacts of non-compliance, Medication Therapy Management solutions align around a few key interventions:

- **Therapy support (Dosing reminders):** Clearly laying out the dosing schedule and having clearly labeled containers is the obvious first step to helping cancer patients get the right dosing of drugs. Providing regular telephonic or electronic coaching (reminders) about taking medications may be an effective tool for many populations as well.\(^\text{14, 15}\)

- **Education:** Patients and caregivers need to thoroughly understand the dosing schedule, the disease progression, what they should expect from the medications, and the anticipated side effects. As with many complex topics, providing multiple touch-points and multiple ways of reaching the audience (patients, the families and their caregivers) is essential to conveying complete understanding about the topic. Improved patient education and on-going support has been shown conclusively to improve patient outcomes and satisfaction.\(^\text{16, 17}\)

- **Side effect management:** In addition to understanding what the side effects are, patients need to know how to best manage the side effects to keep them from turning into adverse events.

With cancer drugs, some say that side effects are the way to know that the drug is working; however, when the side effects turn into adverse events, significant health risks can occur. Having a nurse available for inbound calls, as well as making regular and frequent outbound calls, helps ensure that patients receive timely interventions and advice for managing their side effects, allowing them to better stay compliant with the drug regimen.\(^\text{18}\)

Given the frequency of outbound contacts required to be truly effective, some programs involve oncologist nurses to provide a Medication Therapy Management program telephonically. This approach provides the advantage of allowing for frequent contact (weekly or more often), expertise with oncology treatment protocols, drugs and their side effects and an understanding of protocols to mitigate side effects.\(^\text{19}\)

An alternate methodology for delivering this service follows Medicare’s lead in proposing that pharmacists provide the education and counseling for patients to ensure compliance.\(^\text{20}\) Pharmacists are a critical resource in validating medication dosing appropriateness and have the ability to expand their consultative role in medication therapy. Given the frequency of side effects and issues of compliance, the traditional pharmacist approach would need to be modified to address the confounding factors of patients on oral oncology therapies.

CONCLUSION

Medication non-compliance is a major factor impacting the overall efficacy of oral oncology agents. For a variety of reasons, patients do not accurately follow their prescribed dosing regimens completely or accurately as often as 80% of the time. The effects can be devastating for both patient and payer. Non-compliance results in poorer outcomes for the patient, emergency room visits and hospitalizations as the patient’s status deteriorates and side effects turn to adverse events. In many cases, deteriorated patient status requires a therapy holiday to allow the patient to recover, delaying further curative treatment, and providing an opportunity for the disease to progress. For payers, all of these situations result in higher cost, from ER visits and hospitalizations to wasted therapy regimens when a therapy holiday occurs.

The good news is that there are solutions available to help patients better manage their medication compliance with oral oncology agents. Medication Therapy Management programs that focus on dosing clarity, patients and caregiver education, and side effect monitoring and advice can yield dramatic benefits for patients and for payers. These programs are best administered telephonically due to the repetitive nature of the program and ideally involve an oncology nurse and, as needed, a pharmacist to provide the detailed medical assessment of a patient’s status and to help that patient obtain appropriate service as their condition dictates.
**OncologyRx Care Advantage** is a national specialty pharmacy developed to bring oncology expertise to the delivery and management of oral chemotherapies. Through our CARxES (Chemotherapy Adherence & Prescription Education Support) program, we support practices with the increased responsibilities that come with the growing number of oral chemotherapies. We seek the patient financial assistance these drugs may require and utilize oncology certified nurses to make weekly follow-up calls to support adherence and help patients manage side effects. Patient information is shared with the prescribing physician to help ensure continuity of care between the pharmacy and the practice. Care Advantage patients also benefit from 24-hour access to oncology certified pharmacists. To learn how OncologyRx Care Advantage can support you and your patients on oral therapies, call 888-4RXMEDS (888-479-6337) or visit www.mycareadvantage.com.

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