original report

# Clinician Report of Oral Oncolytic Symptoms and Adherence Obtained via a Patient-Reported Outcome Measure (PROM)

Victoria R. Nachar, PharmD<sup>1,2</sup>; Karen Farris, PhD<sup>2,3</sup>; Katie Beekman, MD<sup>4</sup>; Jennifer Griggs, MD, MPH<sup>1,3</sup>; Shannon Hough, PharmD<sup>1,3</sup>; and Emily Mackler, PharmD<sup>3</sup>

bstrac

**PURPOSE** Patient-reported outcome measures (PROMs) for symptom monitoring during cancer therapy have been shown to have a positive impact on outcomes. These findings have primarily been shown for patients receiving intravenous chemotherapy. In addition, there is known discordance between physician reporting of symptoms and patient self-report. This initiative sought to describe patient-reported symptom burden and medication adherence and to indicate the degree of PROM results being discussed with the provider as indicated by documentation in the medical record for patients taking oral oncolytic therapy.

**METHODS** The Michigan Oncology Quality Consortium (MOQC) PROM, which included symptom ratings, medication adherence, and patient confidence in self-management, was completed during outpatient visits and compared with corresponding data documented in the electronic medical record (EMR).

**RESULTS** There were 82 completed PROMs. Approximately half included at least one symptom rated as severe (46%). Sixty-five percent of reported severe symptoms were documented in the EMR. Patient-reported moderate-to-severe pain was most likely to be documented in the EMR (100%), whereas patient-reported moderate-to-severe depression and anxiety were least likely to be documented (21%). Of the total symptoms documented, grading of symptom severity matched that of the patients' own report for 11% of severe symptoms. Adherence to oral oncolytics was excellent for 63% of patients, and patient adherence was documented in 7% of provider notes.

**CONCLUSION** Patients frequently reported moderate-to-severe symptoms, and approximately 40% of patients reported nonadherence. Clinician report (documented in the EMR) of the patient symptom burden, symptom severity, and adherence to oral oncolytic therapy was not consistent with the patients' self-report. Use of a PROM for patients taking oral oncolytics has the opportunity to improve symptom management and medication adherence.

Clin Cancer Inform. © 2019 by American Society of Clinical Oncology

# INTRODUCTION

Increase in use of oral oncolytics for the treatment of cancer allows patients a more convenient and less invasive treatment option compared with intravenous therapy administered in a clinic setting. In addition to improved ease of administration and patient preference, oral oncolytics may be better tolerated, allowing patients to stay on treatment much longer. <sup>1</sup>

It is known that patients taking oral oncolytic medications experience a high symptom burden, most commonly fatigue and pain.<sup>2</sup> Physician reporting of patient symptoms is neither sensitive nor specific in detecting common adverse effects resulting from chemotherapy when compared with patient self-reporting.<sup>3-6</sup> In addition, agreement between multiple clinicians when reporting adverse symptom events is moderate at best.<sup>7</sup> Evidence suggests that patients

are better at reporting their own symptoms than physicians are at recording them.<sup>8</sup> Patient reports of their symptom burden are more highly correlated with measures of underlying health, and symptom reporting by patients to prescribers increases communication, intensifies symptom management, and improves symptom control.<sup>9-12</sup> Patient-reported outcomes (PROs) for symptom monitoring during cancer treatment have been found to have a positive impact on outcomes, including overall survival.<sup>13</sup>

Adherence to oral oncolytics, in addition to management of symptoms, is necessary to achieve the desired clinical response. Patients who experience adverse effects are more likely to be nonadherent to their cancer treatment. <sup>14</sup> In fact, a large portion of patients will discontinue their oral oncolytic within the first month of therapy because of unreported adverse effects. <sup>15</sup> Patient-reported adherence has been shown

Author affiliations and support information (if applicable) appear at the end of this article.

Accepted on February 4, 2019 and published at ascopubs.org/journal/

cci on May 17, 2019: DOI https://doi.org/10. 1200/CCI.18.00128

**ASCO** 

**ICO**° Clinical Cancer Informatics

to be equal to or greater than objective adherence measures. <sup>16</sup> Importantly, nonadherence to cancer therapy is associated with poor health outcomes and decreased overall survival. <sup>17,18</sup> Use of PRO measures (PROMs) for patients taking oral oncolytics—assessing both symptom burden and medication adherence—is imperative for improving the quality of care, given that the responsibility for managing symptoms and adherence to the treatment plan lies heavily on the patient. In addition, there is a growing body of evidence that the quality and completeness of the information found within the electronic medical record (EMR) is lacking. <sup>19</sup> A PROM for oral oncolytic therapy as an alternative data source could fill these gaps in the EMR with high-quality and complete data.

The Michigan Oncology Quality Consortium (MOQC) is a quality improvement collaborative supported by Blue Cross Blue Shield of Michigan that aims to improve the quality of oncology care in Michigan. MOQC developed a PROM to monitor patients' symptom burden and medication adherence during treatment with oral oncolytic therapy.<sup>20</sup> Although the majority of PRO data exist for intravenous chemotherapy administered in the context of a clinical trial, MOQC has previously demonstrated the use of a PROM for oncology patients receiving oral oncolytic therapy. 14 The aim of this analysis was to describe symptom burden, confidence to selfmanage, and adherence reported by patients seen in a large nonacademic oncology practice and to compare patient-reported symptoms and adherence with symptoms and adherence documented by the oncologist in the EMR.

## **METHODS**

# Study Design

This observational study occurred at a National Cancer Institute-designated community clinical oncology practice with 10 medical oncologists from July 2016 to June 2017. Patients were eligible to be included in the study if they were age 18 years or older, English speaking, taking an oral oncolytic prescribed by the practice, and able to self-report their own symptoms and adherence. The practice started administering the PROMs to patients taking the following five medications: abiraterone, capecitabine, enzalutamide, erlotinib, and temozolomide. These medications were selected because of their high volume of use within the practice. Midway through the program, the practice began administering the PROMs to patients receiving any oral oncolytic medication. Patient and provider participation was voluntary. The qualityimprovement study project was designated as not regulated by the University of Michigan's Institutional Review Board.

# **Data Collection**

A PROM<sup>14,20</sup> was used to examine symptom burden, confidence to self-manage adverse effects, and adherence

to oral oncolytics. The PROM was reviewed by MOQC's Patient and Caregiver Council and was also tested by several clinicians before being rolled out in this practice. The PROM is two pages long and takes approximately 3 minutes to complete.

The PROM was completed by the patient in the office while waiting to see the physician. The intent was for the completed document to be given to the provider for review before the patient appointment. However, it was found that providers were not routinely seeing the PROM before the patient visit. Charts were abstracted to compare the oncologist documentation for that visit in the patient EMR with findings from the completed and corresponding PROM. Within the oncologists' documentation, data were abstracted from both the free-text and standard review of systems (ROSs). Pain was always found and scored numerically within the ROS. The majority of the other symptoms were found within free text. In addition to recording whether the symptoms or adherence were documented in the medical record, we also recorded whether symptom severity was mentioned, and if so, if it matched the patient's report. For classification of symptom burden, we considered scores of 1 to 3 mild, 4 to 6 moderate, and 7 to 10 severe. 14 Wording differences for symptoms in the EMR were recorded and collapsed into final classification as mild, moderate, or severe upon final analysis if they were not explicitly stated as such in the oncologists' documentation. Scores for confidence in managing adverse effects were 0 to 3 for low, 4 to 6 for moderate, and 7 to 10 for high. Participants who self-reported excellent adherence were considered adherent and those self-reporting less than excellent were considered nonadherent because ratings below excellent are associated with adherence of less than 80%.14

## **Data Analysis**

Demographic and clinical variables were quantified and analyzed by using descriptive statistics. The data set was analyzed by using Microsoft Excel 2010 software (Redmond, WA).

## **RESULTS**

#### **Patient Characteristics**

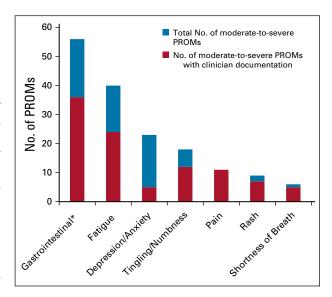
Eighty-two PROMs were completed by 57 patients who had a median age of 67 years (range, 25 to 94 years), and 56% were female. Most patients had solid tumors (n = 56; 98%). The most prevalent types of tumors among patients were colorectal (n = 19; 33%), glioblastoma (n = 10; 17%), breast (n = 9; 16%), non–small-cell lung (n = 4; 7%), small-cell lung (n = 2; 3%), and pancreatic, non-Hodgkin lymphoma, liver and intrahepatic bile duct, and gastric or stomach (n = 1 each; 2% each). Nine patients (16%) selected other cancer diagnosis. Capecitabine (n = 30; 53%), temozolomide (n = 15; 26%), erlotinib (n = 8; 14%), palbociclib (n = 3; 5%), and ibrutinib (n = 1; 2%) accounted for the medications that patients received.

# Symptom Burden

Of the PROMs (n = 82), 38 (46%) included at least one symptom rated as severe and 15 (18%) had four or more rated as severe (Table 1). Fifty-eight PROMs (71%) had at least one symptom rated as moderate-to-severe, and 27 (33%) had four or more symptoms rated as moderate or severe. Fatigue (reported as tiredness or drowsiness) was the individual symptom causing the highest overall burden (mild to severe) reported by 63 PROMs (83%) followed by anxiety reported by 36 PROMs (50%). There were 101 most bothersome symptoms reported on 61 PROMs (74%). Of them, GI symptoms were most common (n = 28; 27%), followed by skin complications (n = 18; 18%), and fatigue (n = 16; 16%).

# **Comparison of Oncologist Documentation**

Of the total PROM symptoms rated as severe (n = 68), 44 (65%) were identified in the EMR. Similarly, of the total PROM symptoms rated as moderate (n = 95), 57 (60%) were identified in the EMR. Documentation in the EMR of patient-reported moderate-to-severe symptoms ranged from 21% to 100% per symptom (Fig 1). Pain, reported on 11 PROMs, was the symptom most commonly documented in the EMR (n = 11; 100%), followed by shortness of breath (six PROMs and five corresponding EMR notes; 83%), rash (nine PROMs and seven corresponding EMR notes; 78%), tingling or numbness (18 PROMs and 12 corresponding EMR notes; 67%), GI symptoms (56 PROMs and 37 corresponding EMR notes; 66%), and fatigue (63 PROMs and 33 corresponding EMR notes; 60%). Although experienced frequently by patients (n = 23; 31% of PROMs rated as moderate-to-severe), depression and anxiety were the least commonly documented symptoms in the EMR (n = 5; 21%). Patients reported 195 total symptoms as mild, and 106 (54%) were identified in the EMR. Of the symptoms documented in the EMR, physician grading of



**FIG 1.** Clinician documented symptoms for patient-reported outcome measures (PROMs) rated as moderate to severe. (\*) Includes nausea, lack of appetite, constipation, diarrhea, and mouth sores.

symptom severity matched that of patients' own reports for 11% of severe symptoms, 19% of moderate symptoms, and 25% of mild symptoms.

## **Patient Confidence**

Confidence in self-managing symptoms was high for 43 patients (75%), moderate for eight patients (13%), and low for six patients (12%). Confidence in knowing when to seek medical attention for symptoms was high for 52 patients (92%).

# **Adherence**

Adherence to oral oncolytic therapy was answered for 78 PROMs. Self-reported adherence to oral oncolytics was excellent for 49 patients (63%), very good for 20 patients

**TABLE 1.** Individual Symptom Reporting of PROs

Symptom	Total PROs With Response	Severe		Moderate		Mild	
		No.	%	No.	%	No.	%
Fatigue	76	13	17	27	35	23	30
Constipation	74	11	15	5	7	13	18
Tingling or numbness	71	8	11	10	15	16	22
Anxiety	72	6	8	7	10	23	32
Lack of appetite	73	6	8	9	12	19	26
Nausea	74	5	7	2	3	10	13
Rash	69	4	6	5	7	8	12
Diarrhea	72	4	6	12	17	10	14
Pain	76	4	5	7	9	25	33
Depression	73	3	4	7	10	17	23
Shortness of breath	75	3	4	3	4	22	29
Mouth sores	70	1	1	1	1	9	13

Abbreviation: PRO, patient-reported outcome.

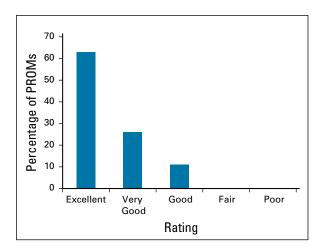
JCO Clinical Cancer Informatics 3

(26%), and good for nine patients (11%) (Fig 2). No patients self-rated their adherence as fair to poor. Of the reasons selected for nonadherence (n = 30), a concern about possible adverse effects was most common (n = 7): 23%), followed by long-term effects from medication (n = 5; 17%), experiencing adverse effects (n = 4; 13%), simply missing or forgetting (n = 4; 13%), missing because of a busy schedule (n = 3; 10%), problems with forgetting things in daily life (n = 2, 7%), concerns about taking any medication in general (n = 2; 7%), not being able to afford the medication (n = 1: 3%). lack of medication in the pharmacy (n = 1: 3%). and belief that the medication was not needed anymore (n = 1; 3%). No patients indicated that they had difficulty managing the medication they were receiving or that they believed their oral oncolytic was not working any longer as reasons for nonadherence. Of 81 records examined, patient adherence was documented in six (7%) provider notes.

#### **DISCUSSION**

We have shown that patients taking oral oncolytics have a high symptom burden, with many of these symptoms frequently reported as moderate-to-severe. Furthermore, we identified discordance between patient-reported symptom severity and oncologist documentation in the medical record. Moderate-to-severe symptoms reported by patients were documented in the medical record approximately 60% of the time. Finally, we found that 37% of patients reported less-than-excellent adherence to their oral oncolytic medication.

One possible explanation for our findings is that symptoms are discussed and managed but not documented in the medical record because of the burdens associated with documentation.<sup>21-24</sup> Lack of communication or miscommunication between oncologists and their patients during appointments may occur if agenda setting does not take place or because many other issues, such as prognosis, goals of care, financial concerns, dealing with



**FIG 2.** Self-reported adherence to oral oncolytics taken across the sample of patients. PROM, patient-reported outcome measure.

uncertainty, and numerous symptoms, are addressed. Another explanation is that patients' reporting of their symptoms is influenced by the method of collection—self-report via a questionnaire versus open-ended questions (eg "How are you feeling?") from their oncologist. Finally and importantly, implementing PROs in clinical oncology practice has multiple challenges. Much of the experience to date is in the setting of clinical research. A framework for successful implementation should be comprehensive in addressing the clinical setting (eg where in treatment and/or monitoring it will be used and with whom communication will occur), the PROM tool itself (eg valid, reliable, simple), the feedback and documentation system, and support of implementation.<sup>25</sup>

Of the symptoms reported by the patients, depression and anxiety were infrequently documented in the medical record. Almost half of patient assessments indicated moderate-to-severe depression or anxiety, with only 20% of depression and anxiety reported by patients documented in the EMR. A recent report recapitulates our results, finding that patients who reported depression and anxiety were least likely to have the symptom acknowledged and be offered assessments and interventions. 26 These symptoms are not only independent risk factors for nonadherence, but both have been associated with higher rates of cancer mortality.<sup>27,28</sup> The discrepancy between patient report versus that documented by the provider for depression and anxiety identifies an important area in which additional research would be helpful for determining whether the cause is a result of patient discomfort in discussing depression and anxiety with their provider and/or provider avoidance of discussing depression and anxiety.

The proportion of nonadherence was 37% in this study, which is in line with previous reports of this patient sample.<sup>29-33</sup> It is important to note that patients vary in what they consider excellent adherence. Although total pill consumption is important for assessing adherence, other factors that may be pertinent to a particular oral oncolytic, such as timing of administration with regard to time of day or surrounding meals would be important factors of adherence to assess in future endeavors. Only a small percentage of patients (7%) had adherence to their oral oncolytic therapy documented in their medical record. This may indicate either a lack of assessment, lack of documentation of assessment, or a lack of communication between the patient and provider regarding oral oncolytic adherence. Previous literature has shown that the use of PROMs for patients taking oral oncolvtics leads to greater adherence to the regimen.<sup>15</sup>

There are several limitations to this study. First, it was conducted at a single practice and results may not be generalizable to other oncology practices. In addition, given the lack of clear communication of the PROM to the provider, it is unclear how the patients completed the document and whether symptoms were truly current versus something the patient previously experienced. A provider-

patient discussion provides an opportunity for clarifying the symptoms reported by the patient, taking the symptoms into context, given prior visits and symptom-based therapies, and determining whether symptoms are current or no longer relevant, given the clinical scenario. Because the PROM was not consistently reviewed at the time of the visit, we were not able to determine how documentation would vary after communication with the patient about the document. There lies an inherent challenge to abstracting data from the oncologist's documentation and variability in provider documentation from one provider to another. Although 100% documentation for pain may indicate hypervigilance to this potential adverse effect, inclusion of pain in a standard ROS designed to uncover dysfunction or adverse effects may account for this. By including the ROS in the data abstract, information included in this section of the oncologist documentation may not represent what was truly discussed and documented in that clinic visit. Future endeavors should aim to assess whether the use of PROMs for patients taking oral oncolytic therapy improves patient provider communication and enhances clinical management in regard to symptoms and, ultimately, adherence to oral oncolytic therapy.

These limitations notwithstanding, PROMs have the opportunity to accurately capture symptom burden, severity, and adherence to cancer therapy for patients taking oral oncolytic therapy. PROMs may also provide oncologists with a mechanism for enhancing patient self-management education and identifying symptoms and adherence that require intervention at an earlier point. In an era of health care reform, new payment and delivery models to improve care and lower costs through episode-based payment models will link outcomes associated with patient symptom burden and adherence to their treatment (hospital admissions, emergency room visits, resources used) to provider reimbursement. Thus, the consistent use of a PRO tool to assess and address patient outcomes may be beneficial, specifically in the realm of oral oncolytic therapy.

In conclusion, inconsistencies were seen between patient self-report of symptoms and adherence on a PROM and clinician reporting via documentation in the EMR. More symptoms and higher symptom severity were reported via patient self-report. Documentation contained within the EMR relating to patient symptom burden and adherence to their oral oncolytic lacks relevant information. This may indicate either communication errors or a lack of assessment and provides a poor representation of the patient's symptom burden and adherence to their regimen. This analysis is important, because patients who are receiving oral oncolytics now have more responsibility in identifying and self-managing their symptoms. Use of a PROM for patients receiving oral oncolytics has the opportunity to improve symptom management and adherence to their regimen.

#### **AFFILIATIONS**

<sup>1</sup>University of Michigan, Ann Arbor, MI

<sup>2</sup>University of Michigan College of Pharmacy, Ann Arbor, MI

<sup>3</sup>Michigan Oncology Quality Consortium, Ann Arbor, MI

<sup>4</sup>IHA Hematology Oncology Consultants, Ypsilanti, MI

#### **CORRESPONDING AUTHOR**

Emily Mackler, PharmD, Michigan Oncology Quality Consortium, North Campus Research Complex, 2800 Plymouth Rd, Building 14, G210, Ann Arbor, MI 48109; e-mail: estunteb@umich.edu.

## **PRIOR PRESENTATION**

Presented as a poster at the 14th Annual Hematology Oncology Pharmacist Association Meeting, Fort Worth, TX, April 4-6, 2018.

## **SUPPORT**

Supported by Blue Cross Blue Shield of Michigan (BCBSM) as part of the BCBSM Value Partnerships Program.

**AUTHOR CONTRIBUTIONS** 

Conception and design: Karen Farris, Katie Beekman, Shannon Hough, Emily Mackler

Administrative support: Karen Farris

Collection and assembly of data: Victoria R. Nachar, Shannon Hough, Emily Mackler

Data analysis and interpretation: All authors

Manuscript writing: All authors

Final approval of manuscript: All authors

Accountable for all aspects of the work: All authors

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/jco/site/ifc.

Karen Farris

Consulting or Advisory Role: Leavitt Partners, QuiO

Shannon Hough

Stock and Other Ownership Interests: Amgen (I)

No other potential conflicts of interest were reported.

#### **REFERENCES**

- 1. Carney DN: The pharmacology of intravenous and oral etoposide. Cancer 67:299-302, 1991
- 2. Mackler E, Petersen L, Severson J, et al: Implementing a method for evaluating patient-reported outcomes associated with oral oncolytic therapy. J Oncol Pract 13:e395-e400, 2017

JCO Clinical Cancer Informatics 5

- 3. Fromme EK, Eilers KM, Mori M, et al: How accurate is clinician reporting of chemotherapy adverse effects? A comparison with patient-reported symptoms from the Quality-of-Life Questionnaire C30. J Clin Oncol 22:3485-3490, 2004
- Efficace F, Rosti G, Aaronson N, et al: Patient- versus physician-reporting of symptoms and health status in chronic myeloid leukemia. Haematologica 99:788-793. 2014
- 5. Basch E, Jia X, Heller G, et al: Adverse symptom event reporting by patients vs clinicians: Relationships with clinical outcomes. J Natl Cancer Inst 101:1624-1632, 2009
- Basch E, Iasonos A, McDonough T, et al: Patient versus clinician symptom reporting using the National Cancer Institute Common Terminology Criteria for Adverse Events: Results of a questionnaire-based study. Lancet Oncol 7:903-909, 2006
- 7. Atkinson TM, Li Y, Coffey CW, et al: Reliability of adverse symptom event reporting by clinicians. Qual Life Res 21:1159-1164, 2012
- 8. Basch E: The missing voice of patients in drug-safety reporting. N Engl J Med 362:865-869, 2010
- 9. Seow H, Sussman J, Martelli-Reid L, et al: Do high symptom scores trigger clinical actions? An audit after implementing electronic symptom screening. J Oncol Pract 8:e142-e148, 2012
- 10. Detmar SB, Muller MJ, Schornagel JH, et al: Health-related quality-of-life assessments and patient-physician communication: A randomized controlled trial. JAMA 288:3027-3034, 2002
- 11. Kotronoulas G, Kearney N, Maguire R, et al: What is the value of the routine use of patient-reported outcome measures toward improvement of patient outcomes, processes of care, and health service outcomes in cancer care? A systematic review of controlled trials. J Clin Oncol 32:1480-1501, 2014
- 12. Cleeland CS, Wang XS, Shi Q, et al: Automated symptom alerts reduce postoperative symptom severity after cancer surgery: A randomized controlled clinical trial. J Clin Oncol 29:994-1000, 2011
- 13. Basch E, Deal AM, Kris MG, et al: Symptom monitoring with patient-reported outcomes during routine cancer treatment: A randomized controlled trial. J Clin Oncol 34:557-565, 2016
- Salgado TM, Mackler E, Severson JA, et al: The relationship between patient activation, confidence to self-manage side effects, and adherence to oral oncolytics: A pilot study with Michigan oncology practices. Support Care Cancer 25:1797-1807, 2017
- 15. McNamara E, Redoutey L, Mackler E, et al: Improving oral oncolytic patient self-management. J Oncol Pract 12:e864-e869, 2016
- Atkinson TM, Rodríguez VM, Gordon M, et al: The association between patient-reported and objective oral anticancer medication adherence measures: A systematic review. Oncol Nurs Forum 43:576-582, 2016
- 17. Bestvina CM, Zullig LL, Rushing C, et al: Patient-oncologist cost communication, financial distress, and medication adherence. J Oncol Pract 10:162-167, 2014
- 18. Hershman DL, Shao T, Kushi LH, et al: Early discontinuation and non-adherence to adjuvant hormonal therapy are associated with increased mortality in women with breast cancer. Breast Cancer Res Treat 126:529-537, 2011
- Valikodath NG, Newman-Casey PA, Lee PP, et al: Agreement of ocular symptom reporting between patient-reported outcomes and medical records. JAMA Ophthalmol 135:225-231, 2017
- Michigan Oncology Quality Consortium: Patient Assessment Tool for Oral Chemotherapy. https://moqc.org/wp-content/uploads/2017/07/PROAssessment-1. pdf
- 21. Sinsky C, Colligan L, Li L, et al: Allocation of physician time in ambulatory practice: A time and motion study in 4 specialties. Ann Intern Med 165:753-760, 2016
- 22. Babbott S, Manwell LB, Brown R, et al: Electronic medical records and physician stress in primary care: Results from the MEMO Study. J Am Med Inform Assoc 21:e100-e106, 2014
- 23. Shanafelt TD, Dyrbye LN, Sinsky C, et al: Relationship between clerical burden and characteristics of the electronic environment with physician burnout and professional satisfaction. Mayo Clin Proc 91:836-848, 2016
- 24. Margalit RS, Roter D, Dunevant MA, et al: Electronic medical record use and physician-patient communication: An observational study of Israeli primary care encounters. Patient Educ Couns 61:134-141, 2006
- 25. Porter I, Gonçalves-Bradley D, Ricci-Cabello I, et al: Framework and guidance for implementing patient-reported outcomes in clinical practice: Evidence, challenges and opportunities. J Comp Eff Res 5:507-519, 2016
- 26. Hurwitz G, Ismail Z, Moody L, et al: A tale of 2,000 charts: Measuring provider response to patient-reported outcome measures. J Clin Oncol36, 2018(suppl; abstr 157)
- 27. Sherbourne CD, Wells KB, Meredith LS, et al: Comorbid anxiety disorder and the functioning and well-being of chronically ill patients of general medical providers. Arch Gen Psychiatry 53:889-895, 1996
- 28. Batty GD, Russ TC, Stamatakis E, et al: Psychological distress in relation to site specific cancer mortality: pooling of unpublished data from 16 prospective cohort studies. BMJ 356:j108, 2017
- 29. Mackler ER, Beekman KW, Bushey L, et al: Utilizing patient reported outcomes for patients receiving oral chemotherapy. J Clin Oncol35, 2017(suppl; abstr
- 30. Ruddy K, Mayer E, Partridge A: Patient adherence and persistence with oral anticancer treatment. CA Cancer J Clin 59:56-66, 2009
- 31. Huang WC, Chen CY, Lin SJ, et al: Medication adherence to oral anticancer drugs: Systematic review. Expert Rev Anticancer Ther 16:423-432, 2016
- 32. Greer JA, Amoyal N, Nisotel L, et al: A systematic review of adherence to oral antineoplastic therapies. Oncologist 21:354-376, 2016
- 33. McCue DA, Lohr LK, Pick AM: Improving adherence to oral cancer therapy in clinical practice. Pharmacotherapy 34:481-494, 2014

---