Factors that affect cancer patient compliance to oral anti-neoplastic therapy*

Fatores que influenciam a adesão de pacientes com câncer à terapia antineoplásica oral

Factores que influyen en la adhesión de pacientes con cáncer a la terapia antineoplásica oral

Patrícia Andréa Crippa Marques[1], Angela Maria Geraldo Pierin[2]

ABSTRACT

Objectives: To identify factors that can affect compliance to treatment with neoplastic oral drugs in a group of cancer patients. **Methods:** Interviews were performed on 61 patients diagnosed with cancer and under anti-neoplastic oral therapy in a private hospital. The interviews were carried out using instruments to assess compliance. **Results:** Most patients (95%) reported the oral treatment was not difficult. The Morisky and Green Test were positive in 28% of the patients. Factors that may affect following the treatment were significantly ($p<0.05$) associated with the time variable; patients who presented more difficulty had more treatment time. **Conclusions:** Patients presented positive attitudes toward the use of this anti-neoplastic oral treatment therapy, however 28% were considered non-compliant in the Morisky and Green Test.

Keywords: Neoplasms/drug therapy; Antineoplastic agents/therapeutic use; Patient compliance; Patient acceptance of health care

RESUMO

Objetivos: Identificar fatores associados à adesão ao tratamento com drogas de ação antineoplásica por via oral em pacientes com câncer. **Métodos:** Foram entrevistados 61 pacientes com câncer sob terapia antineoplásica via oral em hospital particular, com a aplicação de instrumentos para avaliar a adesão. **Resultados:** A maioria dos pacientes (95%) referiu que o tratamento oral não é difícil. O Teste Morisky e Green foi positivo em 28% dos pacientes. Os fatores que podem influenciar a realização do tratamento se associaram de forma significativa ($p<0,05$) com a variável tempo, os pacientes que apresentaram mais dificuldade, tinham mais tempo de tratamento. **Conclusões:** Os pacientes apresentaram atitudes positivas frente ao tratamento com medicamentos antineoplásicos orais, porém foram considerados não aderentes em 28% no Teste Morisky e Green.

Descritores: Neoplasias/quimioterapia, Antineoplásicos/uso terapêutico, Cooperação do paciente, Aceitação pelo paciente de cuidados de saúde

RESUMEN

Objetivos: Identificar los factores asociados a la adhesión al tratamiento con drogas de acción antineoplásica por vía oral en pacientes con cáncer. **Métodos:** Fueron entrevistados 61 pacientes con cáncer sometidos a terapia antineoplásica por vía oral en un hospital particular, con la aplicación de instrumentos para evaluar la adhesión. **Resultados:** La mayoría de los pacientes (95%) refirió que el tratamiento oral no es difícil. El test Morisky y Green fue positivo en el 28% de los pacientes. Los factores que pueden influir en la realización del tratamiento se asociaron de forma significativa ($p<0,05$) con la variable tiempo, los pacientes que presentaron más dificultad, tenían más tiempo de tratamiento. **Conclusiones:** Los pacientes presentaron actitudes positivas frente al tratamiento con medicamentos antineoplásicos orales, no obstante fueron considerados no adherentes en el 28% en el Test Morisky y Green.

Descriptores: Neoplasias/quimioterapia, Antineoplásicos/uso terapéutico, Cooperación del paciente, Aceptación por el paciente de cuidados de salud

---

* *Study performed at the Oncologic Center of the Hospital Israelita Albert Einstein – HIAE – São Paulo, (SP), Brazil.*

[1] *Master in Science, Nurse at the Oncologic Center of the Hospital Israelita Albert Einstein – HIAE – São Paulo, (SP), Brazil.*

[2] *Full Professor at the Escola de Enfermagem da Universidade de São Paulo – USP – São Paulo, (SP), Brazil.*

Corresponding Author: **Patrícia Andréa Crippa Marques**
R. Prof.º Monjardino, 130 - Apto. 32B - São Paulo - SP
CEP. 05625-160 E-mail: crippa.marques@ig.com.br

Received article **11/12/2006** and accepted **31/08/2007**

INTRODUCTION

One of the greatest challenges of the multiprofessional team assisting oncologic patients is to obtain treatment compliance to oral antineoplastics. Treatment compliance may be characterized as the extent to which the individuals' behavior agrees with the medical or health advice in terms of taking their medication, changing their life style, and attending medical appointments[1]. Compliance may be affected by several factors, which are associated with patients, treatment, health services, beliefs, and life habits[2]. Being aware of these factors is an important tool for health professionals who accompany the chronic patient evolution, especially cancer patients.

Chronic diseases have a key role in the morbimortality profile, and the need of prolonged or life-long treatments becomes a challenge[3]. In developed countries, compliance to prolonged treatments is roughly 50%. This rate is even lower in developing countries, due to a lack of financial resources[4]. Cancer is a public health issue in Brazil. It is the second cause of death, preceded only by cardiovascular conditions. In 2003, 133000 deaths due to malignant neoplasias were reported and more than half of them in the Southeast region[5].

The pharmaceutical industry has been developing drugs to fight cancer with less toxic effects, which patients can stand and handle well. They are orally administered antineoplastic drugs. Of the antineoplastic drugs available in the international market, 5% are oral. However, among the drugs studied 25% are oral[6]. The pros and cons of the new oral drugs are discussed by several authors. The main advantages are: patient convenience, no need of venous access, and less time outside the household and work. Furthermore, some medications are associated with fewer side effects, causing quite an impact on patients' quality of life. The disadvantages include variation in medicine absorption, patient compliance, handling side effects and medication costs[7]. Liu and colleagues have studied the preference of 103 patients regarding chemotherapy and identified that 90% preferred the treatment with oral drugs. The reasons for the preferences included convenience (57%), current interests or venous access difficulties (55%) and greater control over the chemotherapy administration[8]. Taking these considerations into account, the present study aimed to identify factors associated with treatment compliance to oral antineoplastic drugs in a group of cancer patients.

METHODS

This is an exploratory study that was carried out at a private health institution, in the city of São Paulo, after approval from the Ethics Committee. The sample was composed of 61 outpatients, randomly chosen. They fulfilled the following criteria: age equal or over 18 years, cancer diagnosis, under oral antineoplastic therapy and willing to participate in the study by signing the full consent form. Two instruments for data collection were used and filled out by means of interviews with the outpatients. The Morisky and Green Test, originally written in the English language[9] was translated and validated for the Portuguese language[10]. It evaluates attitudes regarding treatment. It is made up of four questions, described in Table 3, with Yes-No answers. Yes stands for 0 and No stands for 1. The patient compliance to treatment is considered for a score of four points. With three or fewer points, the patient is non-compliant. The other instrument used is made up of questions related to factors or attitudes that may affect patient treatment compliance. The answers are given in a Likert-like scale with five levels: totally agree, partly agree, indecisive, partly disagree or totally disagree, with values of 5, 4, 3, 2 and 1 respectively. Hence, the minimum score was 17 and the maximum was 85. The patients whose overall answers did not exceed 34 were regarded as having little or no difficulty in treatment. Those with values over or equal to 35 showed difficulty. These instrument questions, described in Table 4, were elaborated considering these people's professional practice and also the treatment compliance thematic regarding chronic diseases. The instrument was subjected to a body of judges so as to evaluate internal consistency, pertinence, clearness and equal value, that is, all the questions with similar values.

Data were also collected to characterize the sociodemographic variables, related to medical diagnosis and oral antineoplastic treatment.

The association between the qualitative variables studied was evaluated with the chi-square test or likelihood-ratio test or Fisher's exact test. The quantitative variables, shown as median and standard deviation, were compared with the student's t-test and the variables that did not show normal distribution were evaluated with the Wilcoxon signed-rank test. The $p<0.05$ values were considered statistically significant.

RESULTS

Most studied patients (Table 1) were females, white, married, with higher education and performing administrative or commercial activities, followed by self-employed individuals. The predominant age group was the fifth decade and family income was more than five minimum wages.

Gastrointestinal tract cancer was the most frequent, followed by breast cancer. Concerning their finding out

about the disease, around a third of the patients reported that "they felt bad" and had routine medical exams performed. Capecitabine was the most used oral medication with antineoplastic effect, and the mean time of treatment was eight months. Regarding associated treatments, most of them were subjected to endovenous systemic chemotherapy, surgical procedure and radiotherapy, and also alternative therapies such as massage and religious rituals (Table 2).

According to Morisky and Green Test., 28% of patients were observed as non-compliant, given that they answered yes at least once. There was a statistically significant association ($p<0.05$) among the test and treatment time and the type of medication. Patientes with positive values for Morisky and Green Test. were being treated for a longer period. Patients who used Mercaptopurine, Dexamethasone, Thalidomide and hormone therapy drugs obtained positive values for Morisky and Green Test; therefore, non-compliant to treatment. Those using Imatinib and Temozolamide were totally compliant to treatment (Table 3).

Analyzing the data in Table 4, the patients indicated few drawbacks that may affect treatment compliance to oral antineoplastics. Such fact can be observed when they totally or partly disagreed with the following questions: oral treatment is neither difficult nor complicated and they knew how to take the medication (95%); they do not have difficulty in remembering the day to resume treatment (89%); the medication is not difficult to swallow (88%); they do not need help to take medicine, and they know whether the medication should be taken before, during or after meals (87%); they do not forget to take the medication (84%). Most of them alleged not to forget to attend consultations

Table 1 – Sociodemographic variables of patients under oral antineoplastic treatment

Variables	N	%
Gender		
Female	39	64.0
Male	22	36.1
Ethnic group		
White	58	95.2
Black	1	1.6
Yellow	2	3.2
Marital status		
Married	45	73.8
Single	8	13.1
Widow	4	6.6
Separated	4	6.6
Educational background		
Higher Education	49	80.4
High School	8	13.1
Ninth Grade	4	6.6
Occupation		
Administrative, commercial activities	18	29.5
Self-employed	16	26.2
Homemaker	10	16.4
Teaching Activity	8	13.1
Visual Communication Activities	5	8.1
Others*	4	6.5
Income (minimum wages)		
1 to 5	9	15.8
5 to 10	21	36.8
15 to 20	9	15.8
> 20	18	31.6
Age (mean±SD, months)	54.8 ±15.6	

* others: chemist (2), sociologist (1), student (1)

Table 2 – Patients with cancer under oral antineoplastic treatment, according to medical diagnosis, treatment performed, disease onset, treatment and chemotherapy period

Variables	N	%
Medical diagnosis		
Gastrointestinal Cancer	21	34.5
Breast Cancer	17	27.9
Glioma/Astrocytoma	8	13.1
Leukemia	7	11.5
Gynecological Cancer	3	4.9
Prostate Cancer	2	3.3
Genitourinary Cancer	1	1.6
Lung Cancer	1	1.6
Ocular Melanoma	1	1.6
Discovery of disease		
"Felt bad"	20	32.8
Routine medical exam	19	31.1
Alterations, signals, specific symptoms	12	19.7
Self-exam	10	16.4
Oral Antineoplastic Medication		
Capecitabine	23	37.7
Hormone therapy drugs*	15	24.5
Temozolamide	7	11.5
Erlotinibe	7	11.5
Imatinib mesylate	7	11.5
Mercaptopurine	2	3.3
Associated treatments		
Endovenous Systemic Chemotherapy	44	72.1
Surgery	43	70.5
Radiotherapy	36	59.0
Hormone therapy	3	4.9
Immunotherapy	1	1.6
Alternative Therapies	26	42.6
Massage	9	34.6
Religious Rituals	7	26.9
Yoga, meditation	5	19.2
Home-made medicine, teas	4	15.3
Homeopathy	4	15.3
Acupuncture	3	11.5
Flower remedies	3	11.5
Anthroposophic Medicine	3	11.5
Disease onset (mean±SD, months)	37.1 ± 62.2	
Treatment time (mean±SD, months)	14.4 ± 25.1	
Oral chemotherapy time (mean±SD, months)	8.6 ± 14.8	

*Hormone therapy drugs: Anastrozol, Exemestane, Bicalutamide, Tamoxifene

Table 3 –Morisky-Green Test and association with oral antineoplastic used and treatment time

Morisky-Green Test	**Yes**		**No**		
	N	**%**	**N**	**%**	**p**
Have you ever forgotten to take your medication?	4	6.6	57	93.4	
Are you sometimes careless regarding the time to take your medication?	9	14.8	52	85.2	
When you feel good, do you quit taking medication?	1	1.6	60	98.4	
When the medication makes you feel sick, do you abandon it?	6	9.8	55	90.2	
Morisky-Green test	**Positive**		**Negative**		
	17	27.9	44	72.1	
Oral antineoplastic medication					0.022
Imatinib	-	-	6	100.0	
Temozolamide	-	-	7	100.0	
Hormone therapy drugs	4	26.6	11	73.3	
Mercapturine	2	100.0	-	-	
Capecitabine	8	38.1	13	61.9	
Erlotinib	2	33.3	4	66.6	
Others (Dexamethasone and Thalidomide)	1	25.0	3	75.0	
Treatment time (mean±SD, months)	27.3±40.5		9.5±13.9		0.008

Table 4 – Level of agreement with attitudes and factors that may affect on treatment compliance to oral antineoplastic

Factors and attitudes	**I completely agree (5)**		**I partially agree(4)**		**I AM indecisive (3)**		**I partially disagree (2)**		**I completely disagree (1)**	
	N	%	**N**	%	**N**	%	**N**	%	**N**	%
1. Medication causes undesirable adverse effects	20	32.8	16	26.2	4	6.6	7	11.5	14	23.0
2. I forget to take medication	3	4.9	7	11.5			3	4.9	48	78.7
3. I need help to take medication	2	3.3	5	8.2	1	1.6	5	8.2	48	78.7
4. I have to take a lot of medication	17	27.9	11	18.0	1	1.6	7	11.5	25	41.0
5. I do not know how to take medication	1	1.6	2	3.3					58	95.1
6. Oral treatment is complicated, difficult.	1	1.6			2	3.3	6	9.8	52	85.2
7. I have difficulty to remember the day to resume medication	4	6.6	2	3.3	1	1.6	4	6.6	50	82.0
8. I have difficulty to buy medication	8	13.1	10	16.4			4	6.6	39	63.9
9. I do not know whether I have to take medication before, during or after the meals	3	4.9	5	8.2			6	9.8	47	77.0
10. The medication is hard to swallow			7	11.5			3	4.9	51	83.6
11. I forget to attend consultations.			1	1.6			1	1.6	59	96.7
12. Oral medication treatments causes fewer job absences	24	39.3	11	18.0	6	9.8	5	8.2	15	24.6
13. The health team has helped with oral medication treatment	30	49.2	10	16.4	6	9.8	1	1.6	14	23.0
14. I have specific hours to take medication	48	78.7	10	16.4	2	3.3			1	1.6
15. I check name and dosage before taking the medication	53	86.9	3	4.9			3	4.9	2	3.3
16. I store the medication in an appropriate place	56	91.8	4	6.6	1	1.6				
17. I take the medication even when I feel sick	47	77.0	8	13.1	2	3.3	2	3.3	2	3.3

Table 5 – Variables with significant statistical association with factors that may affect treatment compliance

Variables / Factors, attitudes	Forgets to take medication				p value
	Yes		No		
Massage	**N**	**%**	**N**	**%**	0,032
Yes	4	44.4	5	55.5	
No	6	11.5	46	88.4	
Has difficulty to remember the day to resume oral treatment					
Radiotherapy					0.03
No	5	20.0	20	80.0	
Yes	1	2.7	35	97.2	
Has difficulty to buy oral medication					
Radiotherapy					0.03
Yes	7	19.4	29	80.5	
No	11	44.0	14	56.0	
The health team has helped with oral medication treatment					
Medication					0.04
Imatinib	1	16.6	5	83.3	
Temozolamide	-	-	7	100.0	
Hormone therapy drugs*	7	46.6	8	53.3	
Mercaptopurine	-	0.0	2	100.0	
Capecitabine	4	19.1	17	80.9	
Erlotinib	3	50.0	3	50.0	
Others (Thalidomide/Dexamethasone)	-	-	4	100.0	
	Treatment difficulty <35		**Treatment difficulty ≥35**		
Oral treatment time (mean±SD, months)	5.9±7.5		18.3±27.2		0.03

(80%). They did not abandon medication, not even when they did not feel well (90%), which are compatible answers with Morisky and Green Test.

The factors or attitudes that may affect the treatment and, eventually, compliance had a significant association ($p<0.05$), with the following variables: alternative treatment as massage, radiotherapy, treatment time and type of antineoplastic medication. Considering patients who did not get massages (n=51), most of them (88.4%) did not forget to take the medication. Among the patients who had radiotherapy (n=36), nearly all of them (97.2%), did not have difficulty in remembering the day when they had resumed treatment with oral medication. They did not mention difficulty in buying medication either (80%). All the patients using Temozolamide and Mercaptopurine reported the lack of health team support regarding treatment. Concerning other drugs, patients referred to health professionals' lack of support. Treatment time with oral antineoplastics also had a significant association with the obtained score in the instrument that evaluated the hindrance factors during treatment. Patients who showed higher scores (≥35), thus, with more difficulty in relation to oral antineoplastic treatment, were being treated for longer (Table 5).

DISCUSSION

The main finding in the present study suggested that treatment compliance to oral antineoplastic drugs in cancer patients under ambulatory treatment was not total when analyzed by the Morisky-Green Test. In this evaluation instrument, the medication hours and patients' health status were pointed out as barriers for taking medications, since all patients were seen to be careless regarding schedules. Depending on the case, some patients would quit using medication. Likewise, the analysis through the specific instrument of factors and attitudes when it comes to drug treatment also indicated negative aspects such as forgetting to take medication, which compromises treatment compliance.

Analyzing the compliance behavior is required in order to plan effective treatment and guarantee that the recommendations are followed. No formulas are able to measure compliance behavior, but a combination of varied strategies may aid the nursing practice, regarding chronic diseases. A method chosen to evaluate the behavior in the studied patients was with positive values for Morisky-Green test. It was initially used with hypertensive patients, but it can also be used with oncologic patients. The authors recommend the test in other contexts and other health problems[9]. Patients with cancer show characteristics similar to hypertensive patients regarding disease chronicity, naturally prolonged, long asymptomatic course, clinical manifestations with remission and exacerbation periods, and evolution to varied incapacity levels or death.

Indeed, the test also showed association with interfering variables in the treatment compliance such as the type of antineoplastic drug. Except for patients using Imatinibe and Temozolamide, all the others who were

taking other drugs obtained positive values for Morisky and Green Test.

The association with the disease onset and consequent treatment also indicates this test's predictive value. It identifies that the longer the treatment, the higher are the odds that the patient quit following it correctly or even abandon it, which is the highest level of lack of treatment compliance.

The patients' biosocial characteristics should also be considered due to the fact that they are likely to affect on treatment compliance. However, the present study did not identify this fact, which can be explained by the educational background and satisfactory socioeconomic condition, probably as a mirror of where the study was carried out: a private hospital in a noble area in São Paulo. Another point that deserves attention refers to oral drugs with antineoplastic action. Alone, Capecitabine was the most used medication. It is indicated for breast and gastrointestinal cancer, the most frequent in this study. This drug has often been used and studies have found benefits in the oral intake by oncologic patients[11-12].

The association of more than a therapeutics modality and the use of alternative therapies may serve as support for the cancer patient treatments and maximize the antineoplastic effect[13-14]. The use of alternative methods has increased both the oncologic interest and applicability. The search of alternative therapies such as massage and acupuncture may provide better comfort to patients[15].

In relation to factors and attitudes that may hinder treatment compliance, most patients showed to be able to lead treatment. The undesirable adverse effects inherent to treatment were the most crucial facts. A study on patients with hematologic diseases analyzed no-compliance related to drug adverse effects and found that there was not association of compliance to presence or frequency of adverse effects, but with the difficulty in handling these effects when they became severe[16].

Patients who acknowledged having more difficulties in the oral antineoplastic treatment were being treated for longer. This is relevant since the longer the treatment, the higher are the odds that the individual forgets and has complications. This finding is similar to another study that sought to estimate compliance and the no-compliance in women using Tamoxifene as a breast cancer adjuvant therapy. The study found that the use rates gradually fell during the four following years from 77% to 50%[17]. Nevertheless, in this item, what draw the most attention was the relationship between the types of antineoplastic drugs used and the mentioning of lack of support from the health team. Maybe the professionals working with this clientele have the perception that as the drugs were administered orally, with less complexity, they did not dispense as much attention as the patients expected. In this context, the nurse has a fundamental role and should act effectively to promote treatment compliance. Some resources may aid the patients, namely proper guidance about treatment, expected and undesirable drug effects and medication intake allied to patients' routine activities. The evaluation ought to be constant in the ambulatory returns. The search of the missing patients ought to be adopted as a practice[18].

The use of oral antineoplastic drugs has indicated a new paradigm of cancer patient treatments. Nowadays, an effective therapeutic arsenal is available and it allows the treatment to be performed in the household or at the workplace. However, the health care professionals should be ready for that, identifying undesirable drug effects, patient treatment compliance, antineoplastic drugs interaction with other medications and foods, pharmacokinetic properties and treatment costs[19].

CONCLUSION

In the present study, although patients referred to positive attitudes regarding treatment with oral antineoplastics, almost a third presented positive values for the Morisky-Green Test, which means no treatment compliance. Non-compliance is a problem with many determinants and there should be cooperation to solve it. Analyzing compliance behavior is required to plan effective treatment and trust in the health professional, with emphasis on the nurse. It may impact on the patient-family attitudes and affect reactions with the new experiences. Oral antineoplastic drug therapy is an advance in cancer treatment, especially due to the fact that it is less invasive, which favors treatment compliance.

REFERENCES

1. Horwitz RI, Horwitz SM. Adherence to treatment and health outcomes. Arch Intern Med. 1993; 153(16):1863-8. Review.
2. Pierin AMG. Adesão ao tratamento. In: Nobre F, Pierin AMG, Mion Júnior D. Adesão ao tratamento: o grande desafio da hipertensão. São Paulo: Lemos; 2001. p.23-33.
3. Mendonça GAS. Tendências da investigação epidemiológica em doenças crônicas. Cad Saúde Publica = Rep Public Health. 2001;17(3):697-703.
4. Poor adherence to long-term treatment of chronic diseases is a worldwide problem. 2003. Rev Panam Salud Publica. 2003; 14(3):218-21.
5. Brasil. Ministério da Saúde. DATASUS. Taxa de mortalidade específica por neoplasias malignas, segundo região [Internet]. Brasília (DF): Ministério da Saúde; 2002 [citado 2006 nov. 22]. Disponível em: http://www.datasus.gov.br
6. Hartigan K. Patient education: the cornerstone of successful

oral chemotherapy treatment. Clin J Oncol Nurs. 2003; 7(6 Suppl):21-4.

7. Hoff PM, Pazdur R. Oral chemotherapy. In: Abeloff MD, Armitage JO, Lichter AS, Niederhuber JE, editors. Clinical oncology. New York: Churchill Livingstone; 1998. p.1-14.
8. Liu G, Franssen E, Fitch MI, Warner E. Patient preferences for oral versus intravenous palliative chemotherapy. J Clin Oncol. 1997; 15(1):110-5.
9. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. Med Care. 1986; 24(1):67-74.
10. Strelec MAAM, Pierin AMG, Mion Júnior D. A influência do conhecimento sobre a doença e a atitude frente à tomada dos remédios no controle da hipertensão arterial. Arq Bras Cardiol. 2003; 81(4):343-54.
11 Fan L, Liu WC, Zhang YJ, Ren J, Pan BR, Liu DH, et al. Oral Xeloda plus bi-platinu two-way combined chemotherapy in treatment of advanced gastrointestinal malignancies. World J Gastroenterol. 2005; 11(28):4300-4.
12. Walko CM, Lindley C. Capecitabine: a review. Clin Ther. 2005; 27(1):23-44. Review.
13. Faria Sergio L, Oliveira Filho JA, Garcia AR, Amalfi C, Spirandeli JMB, Campos EC. Quimioterapia concomitante à radioterapia no tratamento adjuvante do câncer da mama localizado. Rev Bras Cancerol. 2001; 47(2):153-8.
14 Elias MC, Alves E. Medicina não-convencional: prevalência em pacientes oncológicos. Rev Bras Cancerol. 2002; 48(4): 523-32.
15 Cantinelli FS, Camacho RS, Smaletz O, Gonsales BK, Braguittoni E, Rennó Júnior J. A oncopsiquiatria no câncer de mama: considerações a respeito de questões do feminino. Rev Psiquiatr Clin (São Paulo). 2006; 33(3): 124-33.
16 Richardson JL, Marks G, Levine A. The influence of symptoms of disease and side effects of treatment on compliance with cancer therapy. J Clin Oncol. 1988; 6(11):1746-52.
17 Partridge AH, Avorn J, Wang PS, Winer EP. Adherence to therapy with oral antineoplastic agents. J Natl Cancer Inst. 2002; 94(9):652-61. Review.
18. Viele CS. Managing oral chemotherapy: the healthcare practitioner's role. Am J Health Syst Pharm. 2007; 64(9 Suppl 5):S25-32.
19. Aisner J. Overview of the changing paradigm in cancer treatment: oral chemotherapy**.** Am J Health Syst Pharm. 2007; 64(9 Suppl 5):S4-7.