

An Assessment of the Utilization of Complementary and Alternative Medication in Women With Gynecologic or Breast Malignancies

Marisa A. Navo, Julie Phan, Christy Vaughan, J. Lynn Palmer, Laura Michaud, Kellie L. Jones, Diane C. Bodurka, Karen Basen-Engquist, Gabriel N. Hortobagyi, John J. Kavanagh, and Judith A. Smith

From the College of Pharmacy, University of Houston; Division of Pharmacy, Division of Cancer Medicine, Division of Surgery, and the Division of Cancer Prevention, The University of Texas M.D. Anderson Cancer Center, Houston, TX.

Submitted April 23, 2003; accepted December 4, 2003.

Authors' disclosures of potential conflicts of interest are found at the end of this article.

Address reprint requests to Judith A. Smith, Pharm D, BCOP, Department of Gynecologic Medical Oncology, Division of Cancer Medicine, University of Texas M.D. Anderson Cancer Center, 1515 Holcombe Blvd, Unit 401, Houston, TX 77030-4009; e-mail: jasmith@mdanderson.org.

© 2004 by American Society of Clinical Oncology

0732-183X/04/2204-671/\$20.00

DOI: 10.1200/JCO.2004.04.162

A B S T R A C T

Purpose

To describe and assess the current utilization of complementary and alternative medicines (CAMs) in women with a diagnosis of either gynecologic or breast cancer and evaluate their reasons for use.

Patients and Methods

This study included 250 female patients from the Multidisciplinary Breast Center and 250 patients from the Gynecologic Oncology Center of The University of Texas M.D. Anderson Cancer Center (Houston, TX). Patients were selected by having an odd-numbered medical record number, and they were contacted before their clinic visit. The goals of the study were explained, and verbal consent was obtained. Patients who agreed to participate were asked to bring a written list and the medication bottles of all over-the-counter prescriptions and CAMs with them to clinic. In clinic, the investigator obtained a written informed consent and administered the survey. All patients and surveys were assessable.

Results

The most frequently used herbal products and megavitamins/minerals were identified from the patient medication histories. Overall, we found the proportion of patients using CAM to be 48% (95% CI, 44% to 53%; 241 of 500 patients). CAM use was related to patients' educational status: 62% had postgraduate degrees, 50% had college degrees, 56% had some college, and 33% had a high school education or less. Also, among patients using CAMs, only 53.5% had spoken to a healthcare provider regarding CAM therapy.

Conclusion

The use of CAM is common among women with cancer. Studies need to be conducted to establish if there are any potential drug interactions and/or therapeutic benefit of CAM products. Moreover, there is a need to educate patients and healthcare providers on appropriate and safe use of CAM products.

J Clin Oncol 22:671-677. © 2004 by American Society of Clinical Oncology

INTRODUCTION

The use of complementary and alternative medicine (CAM) such as herbal, vitamin, and nutritional supplements has increased over the past decade. An estimated 20% to 60% of patients in the United States use some form of CAM in various practice settings, with an estimated 16% to 20% using CAM along with prescription (RX) medication [1-3]. This is a major concern because the literature suggests that patients do not routinely report the use of CAM when pro-

viding a medication history [4,5]. Often this is an error of omission because the healthcare professional fails to ask specifically about these products, and patients do not classify these products as medications [6,7].

In the past, the use of CAM seemed somewhat innocuous. However, as with other medications, CAMs have pharmacologic activity that will cause biologic responses, adverse effects, and will contribute to drug-drug interactions [8,9]. Recent case reports regarding the drug interactions with St John's Wort have increased awareness of

the need to evaluate the pharmacologic activity of each CAM [1,10]. Recently reported examples of adverse effects include renal failure and urothelial carcinoma with the Chinese herb *Aristolochia fangchi*, and severe liver dysfunction with kava [11-14]. In addition, there is currently no uniform standard on the herb content among different manufacturers; therefore increasing the difficulty of predicting the potential drug interactions, adverse effects, and efficacy of various CAMs.

There is increased concern about use of CAM by oncology patients because potential adverse drug interactions could cause patients to experience increased toxicity or decrease the efficacy of the conventional systemic therapy used to treat cancer. In our particular patient population, we were concerned about CAM therapies that have estrogenic or hormonal properties, such as derivatives of soy isoflavones or Chinese Licorice. The use of antioxidants is also concerning because of the free-radical sequestering ability of these agents, thus leading to potential drug interactions with chemotherapy agents that interrupt DNA replication through the formation of free-radicals, such as the platinum or nitrogen mustards agents.

The purpose of this study is to describe the current use of CAMs in women with a diagnosis of either gynecologic or breast cancer and to evaluate their reasons for use. Because of the infinite number of possible combinations of CAM with traditional chemotherapy, this study focused specifically on herbs, homeopathy, phytochemicals, minerals, and megavitamins. Data has shown that various CAM therapies, including mind and body interventions, was higher in women, persons with a higher level of education, and those between 35 and 54 years of age [15]. The data also shows that CAM use among varying ethnicities is similar [15]. In order to assess CAM use in our patient population, a survey instrument was developed based on previous literature in order to gather demographic data such as age, ethnicity, and level of education, as well as medication history and general opinion on CAM therapy.

PATIENTS AND METHODS

Patients with appointments in The University of Texas M.D. Anderson Cancer Center Multidisciplinary Breast Center (MBC) or Gynecologic Oncology Center (GOC) were screened to participate in this study. All patients with medical records ending in an odd number were asked to participate. The patient was contacted by telephone before her appointment to obtain verbal consent to participate in the study. Patients were asked to bring a written list of all the CAM, over-the-counter (OTC), and RX medications that they were currently using, along with all medication containers, to the clinic.

Eligible patients had to be female, over the age of 18 with a current or past diagnosis of a gynecologic or breast cancer, speak and understand the English language, and understand and sign the institutional informed consent. Patients with uncontrolled psychiatric illness or altered mental status interfering with their ability

to answer survey questions were excluded. After written informed consent was obtained, the investigator conducted a one-on-one survey with each participant and verified the information on the medication list with the medication/product labels and instructions. CAM use was defined as the use of any formulation of herbs, homeopathy, phytochemicals, mineral supplements, or megavitamins to promote well-being or treat health conditions. A detailed medication history, including the dose, duration, and frequency of use of each medication was obtained. All medications were then classified by the investigator into one of four categories: 1) RX, 2) OTC, 3) herbal/alternative medication products, and 4) megavitamins and/or minerals. The term mega-vitamin and/or mineral was defined as ≥ 10 times the recommended daily allowance [16-18]. Combination multivitamin with herbals were classified as an herbal product. If only one component of a combination product was dosed in excess of 10 times the recommended daily allowance then only that component was listed as a mega-vitamin/mineral.

The survey instrument consisted of 20 questions. All patients completed five general demographic questions including age, birth and current hometown, education and ethnic background as well as two additional questions to describe disease status and treatment. A complete medication history was also obtained that included medication name, dosage, directions, indications for use, and the approximate duration of use. Also, eight questions were asked on medication usage that focused on compliance and CAM therapy safety and efficacy. Only patients actively taking CAM products were asked to complete the remaining four questions. These included questions to identify the sources of information, such as family, friends, internet, and media, that were used as guides by patients to select individual CAM therapies; which, if any, healthcare professionals were consulted about CAM use; patient impression of the healthcare professional's response to their inquiry about CAM therapy; and the primary indications of past or present CAM use. The estimated time for completion was approximately 15 minutes. Initially, a pilot study was completed with 10 to 15 patients to assess the functionality of the patient medication assessment survey to identify and clarify any problem questions. Proper adjustments were made to the survey instrument based on the pilot study.

The study planned to accrue 500 women with gynecologic cancer or breast cancer (250 from each center) who may or may not use complementary and alternative medicine, to allow for an estimation of the proportion of patients who currently use CAMs to be within a maximum 95% CI of $\pm 5\%$. Prospectively, two study groups were defined for this study: CAM users or nonusers. A descriptive analysis of all data was accomplished. χ^2 tests evaluated differences between patients in the MBC and GOC and between other categorical variables. In addition, a stepwise multivariate logistic regression was employed to determine if the participant demographic variables, such as age, ethnicity, education, disease type, and treatment history, could predict CAM use. Initially, variables that were significant at the 0.20 level were considered, and in the final model, only those variables significant at the 0.05 level were included. The independent variables of age, clinic, disease status, ethnicity, and education were entered into the model. CAM use was coded as "zero" if there was no CAM use and "one" if CAM was used. Variables other than age were analyzed as categorical variables. The Logistic procedure in SAS software (Version 6, SAS Institute, Cary, NC, 1990) automatically created a dummy variable for each distinct value of the original variable.

The Cochran-Armitage Trend Test was used to statistically test the trend in education for both the MBC and GOC patients. We estimated the maximum likelihood estimate of each parameter in the final model, as well as the significance of each parameter, evaluated by the Wald χ^2 statistic. Odds ratio estimates and 95% CIs were calculated for different levels of significant variables as compared to each variable's corresponding reference level.

RESULTS

A total of 500 patients were accrued and completed the study. Of the 635 patients originally called before clinic visit, 539 (85%) agreed to participate in the study, while 96 (15%) declined because of time constraints in their schedule. Of the 539 patients who agreed to participate, two patients declined at their visit and 37 patients were either missed by the investigator or did not show up for their appointment. The baseline demographics of all patients surveyed are shown in Table 1. A total of 48% of patients had a medication history involving the use of CAM. Fifty-two percent (129 of 250) of patients in the MBC and 45% (112 of 250) in the GOC reported CAM use. ($\chi^2 = 2.32$; $P = .13$). The most commonly used herbal preparation reported was the combination product glucosamine sulfate and chondroitin; among the megavitamins and/or minerals, the most commonly used was vitamin E. (Table 2 represents data from all patients.) When medication histories were divided into categories defining the use of RX, OTC products, herbal/alternative medication products, and mega-vitamins and/or minerals, the largest portion of patients were taking RX medications alone (32%) or RX medications in combination with OTC products (16%). There were no patients

using CAM alone. More often patients were using a combination of RX and OTC medications in combination with either herbs (11%), megavitamins/minerals (13%), or both categories (14%).

CAM Use by Disease Status

There were no statistically significant differences in the proportions of CAM users among breast cancer patients based on disease status ($\chi^2 = 3.51$; $P = .17$); however, these differences were statistically significant in the GOC ($\chi^2 = 7.99$; $P = .02$). In all patients, there was a statistically significant difference of CAM use associated with disease status. Thirty-eight percent of newly diagnosed patients, 49% of patients with recurrence or relapse, and 55% of patients who were in remission reported using CAM ($\chi^2 = 9.34$; $P = .009$; Table 1 represents data from all patients).

CAM Use by Ethnicity

We used four categories of ethnicity in statistical analyses: white, black, Hispanic, and "other." There were no significant differences found between CAM use among these four ethnic groups in either clinic or the combined population. Fifty-one percent of white patients and 48% of "other" patients reported using CAM, but differences were not statistically significant ($\chi^2 = 6.26$; $P = .10$; Table 1 represents data from all patients).

CAM Use by Level of Education

For statistical comparisons we used four education categories: high school or less, some college, college graduate, and postgraduate education. In both clinics there were significant differences in CAM use by these categories of edu-

Table 1. Demographic Characteristics of CAM Users Versus Nonusers

Characteristic	No. of Patients	%	CAM User		Nonuser	
			No. of Patients	%	No. of Patients	%
Clinic						
Breast	250		129	51.6	121	48.4
Gynecologic	250		112	44.8	138	55.2
Education level in both clinics						
High school or less	153	30.6	51	33	102	66.7
Some college	142	28.4	80	56.3	62	43.7
College graduate	140	28	70	50	70	50
Postgraduate education	65	13	40	61.5	25	38.5
Race/ethnicity in both clinics						
Black	46	9.2	17	37	29	63
White	391	78.2	199	50.9	192	49.1
Hispanic	40	8	14	35	26	65
Other*	23	4.6	11	47.8	12	52.2
Patient status in both clinics						
Newly diagnosed	144	28.8	55	38.2	89	61.8
Recurrent/relapsed disease	138	27.6	67	48.6	71	51.4
Remission	218	43.6	119	54.6	99	45.4

Abbreviation: CAM, complementary and alternative medication.

*Asian, American Indian, Indian, Middle Eastern, biracial/multiracial.

Table 2. Top CAM Products

	No. of Patients	%
Herbals		
Glucosamine chondroitin; sulfate	33	6.6
Garlic (<i>Allium sativum</i>)	25	5.0
CQ10	24	4.8
Green tea (<i>Camellia sinensis</i>)	19	3.8
Flaxseed	16	3.2
Echinacea (<i>Echinacea purpurea</i> , <i>angustifolia</i> , and <i>pallida</i>)	16	3.2
Cod liver oil/fish oil/3,6,9 omega (EPA/DHA/omega-3-fatty acids)	14	2.8
Acidophilus	12	2.4
Lecithin	11	2.2
Grape seed extract	10	2.0
Bee pollen	10	2.0
Angelica root/dong quai (<i>Angelica archangelica</i> , <i>Angelica sinensis</i>)	10	2.0
Slippery elm (<i>Ulmus fulva</i>); Rose hips; ginkgo (<i>Ginkgo biloba</i>)	9	1.8
Kelp/bladderwrack (<i>Fucus vesiculosus</i>); Greenbarley; Barley leaf; Barley grass powder (<i>Hordeum vulgare</i>)	8	1.6
Turkish rhubarb root (<i>Rheum emodi</i> , <i>Rheum officinale</i> , <i>Rheum acuminatum</i> , <i>Rheum speciforme</i> , <i>Rheum webbianum</i> , <i>Rheum moorcroftianum</i> , <i>Rheum australe</i> , <i>Rheum palmatum</i>); Psyllium husks/seed (<i>Plantago ispagula</i> , <i>Plantago ovata</i>); pau d'arco bark extract; burdock root (<i>Arctium lappa</i>); aloe vera	7	1.4
Spirulina (<i>Spirulina maxima</i> , <i>Spirulina platensis</i>); sheep sorrel (<i>Rumex acetosella</i>); Royal jelly; papaya; MSM; L-lysine; ginger rhizome; Ginger tea (yogi tea); Zingiber officinale Roscoe; Cranberry powder/caps (<i>Vaccinium macrocarpon</i> / <i>Oxycoccus quadripetalus</i>); Astragalus.	6	1.2
Yarrow flowers (<i>achillea millefolium</i>), senna/sennosides A & B from senna leaf (<i>Cassia acutiplia</i> , <i>Cassia angustifolia</i> , <i>Cassia senna</i>); red raspberry leaves (<i>Rubus idaeus</i>); Noni juice/olankino noni (<i>Morinda sp.</i>); MGN-3 (modified rice bran); L-glutamine; chlorella/chlorella A/chlorella green algae powder; betaine	5	1.0
Mega-vitamins and/or minerals [6,13]		
Vitamin E	145	29.0
Vitamin C	60	12.0
Vitamin B (Complex,B3,B6,B12,B-50,B-100,B-150)	51	10.2
Vitamin A	15	3.0
Quercitin	8	1.6
Multivitamin/minerals (High Potency Multivitamin, GNC Multivitamin, Healthy Directions Performance Vitamins, Liquid Health Ultra Antioxidant)	7	1.4
Alpha lipoic acid	5	1.0
Zinc	2	0.4
Boron, GNC Inhultra Caps, magnesium oxide, malic acid, vitamin D, VitaStress	1	0.2

NOTE. The term mega-vitamin and/or mineral was defined as greater than or equal to 50 times the recommended daily allowance [16-18]. Products within each row were analyzed separately.

Abbreviations: CAM, complementary and alternative medication; EPA, eicosapentaenoic acid; DHA, docosahexanoic acid; MSM, methyl-sulfanyl-methane; GNC, General Nutrition Center.

education. In the MBC, among patients with some college education, 64% reported CAM use. The remaining portions were: 62% of postgraduates, 49% of college graduates, and 34% of high school graduates or less ($\chi^2 = 14.00$; $P = .003$). Patients in the GOC had a similar trend, although in this group of patients the ordering was more consistent with a trend of increasing CAM use at each higher education level. In the GOC, the proportions of patients who reported CAM use were: 61% of postgraduates, 51% of college graduates, 47% of those with some college education, and 33% of high school graduates or less ($\chi^2 = 10.10$; $P = .02$). For the MBC, although the proportions of CAM use did not strictly increase with increased education, the trend test was significant ($Z = 2.49$; $P = .01$). Patients in the GOC had a more significant trend for increased CAM use with increased education ($Z = 3.16$; $P = .002$). When information from the two clinics was combined,

associations found using the χ^2 table ($\chi^2 = 22.12$) and the trend test ($Z = 4.12$) were highly significant in both cases ($P < .0001$; Table 1 represents data from all patients).

CAM Use by Age

The mean and median age of CAM users was slightly higher for users versus nonusers; 57.7 and 56.5 versus 55.0 and 54.0, respectively. The standard deviations of the two groups were approximately equal at 11.8 and 12.9. A *t* test comparing these differences was statistically significant with a significance level of 0.018. The range of ages of the two groups was 26 to 87 for CAM users and 22 to 91 for CAM nonusers.

Medication Safety

In the GOC, 151 patients (60%) felt that CAM therapies were both safe and effective. However, in the MBC, 121 patients (48%) felt that CAM therapies were safe and only

112 (45%) felt that they were effective. Lastly, only 142 patients (28%) out of the total number of patients surveyed considered CAM supplements as a type of medication.

Participants Taking CAM

The sources of information about CAM therapies were classified into five categories: health professional, alternative care specialist, internet/media, formal education, and friends and family. Some patients had used multiple resources. Over half (52.2%; 126 of 241) of CAM users had learned about CAM from the internet or media. The next most common resource was friends and family (37%), followed by a healthcare professional (21.6%). Fewer patients than expected, only 11.2% (27 of 241), had sought out information from an alternative care specialist.

Unlike previous reports, the majority (53.5%, 129 of 241) of CAM users in our study reported that they had discussed using CAM therapies with a healthcare professional, most commonly their oncologist (56%). Seventy-four percent of patients in the MBC and 63% of patients in the GOC felt positive about discussing CAM therapies with a healthcare professional. A higher proportion of patients in the GOC were unsure (28%) compared to patients in the MBC (10%), and more patients in the MBC answered that they felt negative about discussing CAM therapies (16%) than patients in the GOC (9%).

Of those who did not speak with a healthcare professional, the most common reason was that they were not asked and that it just never came up during their appointment. The distribution of the reasons provided by participants for taking CAM were significantly different in the two clinics ($\chi^2 = 31.1$; $P < .0001$). Briefly, one major difference appeared to be that many more CAM users in the MBC stated their reason was to “reduce adverse drug reactions” and/or to “improve quality of life” as compared to GOC (30% v 10%). However, more CAM users in the GOC when compared to the MBC reported “treatment of cancer” (15% v 4%) as their reason for taking CAM. Yet despite these differences, the number one reason for use among both the GOC and MBC was stated to be to “improve overall health” (61% and 55%, respectively).

Multivariate Analyses of CAM Use and Demographic Variables

The three variables that remained significant in the multivariate logistic regression model were education ($P < .0001$), age ($P = .0079$), and status ($P = .0080$). We found that older patients were more likely to use CAM. For the categorical variables, these significance levels refer to the null hypothesis that all the coefficients in the set were equal to zero. In addition, in Table 3 (represents data from all patients), we present estimated odds ratios for each comparison of the distinct value of the categorical variables of education and status to their reference value as shown in the table. The significance levels in the last column refer to the null hypothesis that the individual coefficients are equal to zero.

DISCUSSION

This study contains the largest patient cohort surveyed to date, and it includes a comprehensive, one-on-one interview that also has not been used in previous reports. Each patient surveyed was contacted before their clinic visit in order to prepare the patient to provide a complete medication history and thorough overview of all medications including RX, OTCs, and CAM use. Then the one-on-one interview was an opportunity to confirm and clarify all medication use. Specific emphasis was on use of herbs, homeopathy, phytochemicals, minerals, and megavitamins. This information was used to define what should be the focus of future drug interactions studies to determine the influence of using CAM on therapeutic outcomes in the gynecologic and breast oncology patient populations. The study was conducted in a comprehensive cancer center with a large referral base from a variety of community settings, so the information learned in this study can be extrapolated to the community cancer setting as well.

Because it has been reported that CAM use is frequent among cancer patients [19] and women [2], this study was initiated to evaluate the use of CAM therapy in patients being seen in the MBC and GOC. As anticipated, a large proportion of our patients (48%) were current users of

Table 3. Patient Demographic Characteristics Associated With CAM Use

	Estimated Odds Ratio	95% Wald Confidence Limits	Pr > χ^2
Education (compared to postgraduate)			
High school or less	0.274	0.148 to 0.509	< 0.0001
Some college	0.745	0.404 to 1.374	0.1759
College graduate	0.645	0.349 to 1.192	0.6709
Status (compared to remission)			
Newly diagnosed	0.494	0.317 to 0.771	0.0074
Recur/relapse	0.755	0.486 to 1.174	0.7327
Age	1.021	1.003 to 1.037	0.0079

Abbreviation: CAM, complementary and alternative medication.

CAM. However, only approximately half of these patients have discussed CAM use with a healthcare professional. Although we found a high prevalence of use, the CAM use in the MBC at our institution was slightly less than what was previously reported. In a study by Richardson et al [20] conducted in 1997, 453 male and female patients from eight different cancer outpatient clinics, including the MBC, completed a questionnaire regarding use of a variety of CAM approaches; 62.6% of these cancer patients reported use of herb and vitamin products. The difference could have occurred because we focused only on women or because our survey instrument was a one-on-one interview rather than a self-administered questionnaire. Other survey articles have used a broader definition of CAM that encompasses other therapies such as mind and body interventions; however, we compared our results to the herb and vitamin use in these studies. A different interpretation of these results is that the use of CAM might be declining in our referral population. However, the prevalence of CAM use by gynecologic oncology patients at our institution was similar to the prevalence reported in other studies ranging from 49.6% to 56.3% [4,21].

In this study as in many others, patients who used CAM were typically taking other RX or OTC medications. These data, along with the increasing number of reports of interactions and adverse effects, reveal the importance of exploring the pharmacology of CAM to elucidate potential drug interactions and therapeutic outcomes. Of the patients defined as CAM users, most gathered information about CAM on their own by using resources such as the internet or the media. CAM users also seemed to look to their social support like friends and family for their opinion. Not surprisingly, healthcare professionals were third in line when listed as a likely resource for patients. This information demonstrates that patients are making an effort to take an active role in their own healthcare. Also, less than a third of all patients considered CAM a type of medication, which may contribute to the low incidence of reporting of CAM use to healthcare professionals when giving a medication history. The majority of patients who spoke to any healthcare professional felt positive about their conversation. Of those who had not discussed CAM with a professional, the most common reason was that it was never brought up during their visit. This emphasizes the importance of multiple health care professionals repeatedly asking patients about their knowledge and use of CAM in an open dialogue during a clinic visit. It is important for all health-care professionals to be receptive, to learn from the patient about CAM therapy options, and to provide the patient with any medical literature that may support or refute the therapeutic use or safety of a particular CAM. Since there is considerable variation in the dose and components of the CAM products, the patient

should also be asked to bring the container to their next visit in order to obtain accurate dosing information for their medical record.

A higher proportion of patients in the MBC stated their reasons for CAM use to be to improve quality of life and to decrease the adverse effects of other medications that they may be using. Also, 15% of patients in the GOC stated that their reason for use was to treat their cancer. We found a wide variety of CAM in various formulations and doses being used for multiple indications. Identifying the most frequently used CAM was just one approach to prioritize the agents to evaluate first in the laboratory for drug interactions.

There were a few limitations of this study. Common to many surveys, there is potential for investigator and patient bias. Some patients may have been hesitant to disclose use of CAM. Also, because of language barriers, the survey could only be done with English-speaking patients, which excluded some ethnic influences. However, among the patients surveyed, there was not a statistically significant relationship between ethnicity and CAM use. There may have also been emotional distractions, such as anxiety, associated with a visit to see the physician regarding their cancer that could have influenced patient responses to the survey questions. Because patients needed to be called ahead of time in order to receive consent and to specify the requirements of the study, there were some geographical limitations for accrual to this study. Lastly, education in the area of the definition of CAM was a limitation for some patients. Although the definition of CAM was explained to all participants, only verbal confirmation of comprehension of definition was obtained. However, there was a breach between comprehension and application of the definition when patients were asked to provide a medication history to the investigator. This was evident when patients would self-report no CAM use but when their medication histories were reviewed, in fact they were using agents that by definition were types of CAM.

It is common knowledge that many patients are using CAM. Both patients and healthcare professionals need to be educated on the appropriate use of CAM during conventional treatment. However, before we can define the role of CAMs in conventional treatment of cancer, we need to learn more about the complex pharmacology of CAMs in appropriate preclinical studies and to design and initiate prospective clinical studies to establish the role of CAM therapy in modern medicine. Based on our findings in this study, further *in vitro* studies are being initiated to specifically evaluate alteration of cytochrome P450 metabolism and plasma protein binding displacement interactions when CAM therapies are coadministered with commonly used antineoplastic agents used in the treatment of gynecologic

logic and breast malignancies. In addition, the potential cytotoxic activity of each CAM agent will be evaluated alone and in combination with commonly used antineoplastic agents, in human ovarian or breast cancer cell lines. The determination of interactions between CAM and other traditional chemotherapy agents will provide information for clinicians to guide their cancer patients

in use of these CAM products in order to avoid unnecessary toxicities and optimize therapeutic outcomes.

REFERENCES

1. Yoon SJ, Horne CH: Herbal products and conventional medicines used by community-residing older women. *J Adv Nurs* 33:51-59, 2001
2. Eisenberg DM, Davis RB, Ettner SL, et al: Trends in alternative medicine use in the US, 1990-1997. *JAMA* 280:1569-1575, 1998
3. Kaufman DW, Kelly JP, Rosenberg L, et al: Recent patterns of medication use in the ambulatory adult population of the United States: The Sloane survey. *JAMA* 287:337-344, 2002
4. Von Gruenigen VE, White LJ, Kirven MS, et al: A comparison of complementary and alternative medicine by gynecology and gynecologic oncology patients. *Int J Gynecol Cancer* 11:205-209, 2001
5. Harnack LJ, Rydell SA, Stang J: Prevalence of use of herbal products by adults in the Minneapolis/St Paul Minn, metropolitan area. *Mayo Clin Proc* 76:688-694, 2001
6. Margolis ML: A survey of the use of herbal agents among Philadelphia veterans affairs medical center pulmonary outpatients. *Chest* 119:1981-1982, 2001
7. Barone GW, Gurley BJ, Ketel BL, et al: Herbal supplements: A potential for drug interactions in transplant recipients. *Transplantation* 71:239-241, 2001
8. Leady MA, Wolsefer JS, Sweet BV: Survey of alternative supplement use within a hospitalized population. *Hosp Pharm* 37:1295-1300, 2002
9. Ernst E: Herb-drug interactions: Potentially important but woefully under-researched. *Eur J Clin Pharmacol* 56:523-524, 2000
10. Barone GW, Gurley BJ, Ketel BL, et al: Drug interaction between St. John's wort and cyclosporine. *Ann Pharmacother* 34:1013-1016, 2000
11. Nortier JL, Martinez M-CM, Schmeiser HH, et al: Urothelial carcinoma associated with the use of a Chinese herb (*Aristolochia fangchi*). *N Engl J Med* 342:1686-1692, 2000
12. Lord GM, Cook T, Arlt VM, et al: Urothelial malignant disease and Chinese herbal nephropathy. *Lancet* 358:1515-1516, 2001
13. Grossman L: The curious case of kava: Why did it take the FDA so long to finally sound the alarm? *Time* 58: April 8, 2002
14. Chitturi S, Farrell GC: Herbal hepatotoxicity: An expanding but poorly defined problem. *J Gastroenterol and Hepatol* 15:1093-1099, 2000
15. Ni H, Simile C, Harday AM: Utilization of complementary and alternative medicine by United States Adults. *Med Care* 40:353-358, 2002
16. Recommended Dietary Allowances, 10th Edition National Academy of Sciences, National Academy Press, Washington, DC, 1989
17. Wooliscroft JO: Megavitamin: Fact and fancy. *Disease-A-Month* 29:1-56, 1983
18. Nutrition Committee, Canadian Paediatric Society: Megavitamin and megamineral therapy in childhood. *CMAJ* 143:1009-1013, 1999
19. DiGianni LM, Garber JE, Winer EP: Complementary and alternative medicine use among women with breast cancer. *J Clin Oncol* 20:34s-38s, 2002 (suppl 18)
20. Richardson MA, Sanders T, Palmer JL, et al: Complementary/alternative medicine use in a comprehensive cancer center and the implications for oncology. *J Clin Oncol* 18:2505-2514, 2000
21. Swisher EM, Cohn DE, Goff BA, et al: Use of complementary and alternative medicine among women with gynecologic cancers. *Gynecol Oncol* 84:363-367, 2002

Authors' Disclosures of Potential Conflicts of Interest

The authors indicated no potential conflicts of interest.