The Melanoma Letter

A Publication of The Skin Cancer Foundation www.skincancer.org

Perry Robins, MD, President Vol. 26, No. 3, 2008 Mary Stine, Executive Director

Surviving Advanced Melanoma: A Dermatologist's Personal Perspective

Vivian W. Bucay, MD
Clinical Assistant Professor
Department of Physician Assistant Studies
University of Texas Health Science Center
San Antonio, TX

As a dermatologist in clinical practice since 1991, I have had many opportunities to make a positive impact on patients' lives by being the first to diagnose and treat skin cancers, above all nonmelanoma skin cancers. Fortunately, almost every patient has had a good outcome, primarily because of early diagnosis and intervention. Like most dermatologists, I understand that if I encounter high-risk melanoma or advanced disease, clinical management will most often become the responsibility of surgical and medical oncologists, while I will navigate shallower waters, such as screening family members and reviewing pertinent but often confusing literature to assist the patient and family in making important decisions regarding treatment.

I have gained quite a new perspective on melanoma, however, since becoming an advanced melanoma patient myself in 2006. I have previously chronicled my personal battle with the disease twice before, first in *San Antonio Medicine*, a publication of the Bexar County Medical Society, in an issue dedicated to the physician as patient,[1] and second, in the 2008 *Skin Cancer Foundation Journal*, a publication targeted to the lay public.[2]

My purpose in this issue of *The Melanoma Letter* is twofold: to present treatment options for Stage III and Stage IV melanoma in the manner in which they became relevant for me, and to emphasize that good outcomes are not only possible, but becoming more attainable every day despite seemingly unfavorable odds.

Diagnosis

On May 5, 2006, I asked my physician assistant (PA) to look inside my umbilicus to see whether or not she noticed anything unusual; I had noticed a white "residue" that appeared on dark clothing. There was no itching, bleeding, or tenderness, just a whitish discharge that had appeared intermittently for the previous few weeks. I had no recollection of any existing abnormality in the region, keeping in mind that I had seen my umbilicus at its peak convexity during each

continued on page 2

From the Editors

In this edition of *The Melanoma Letter*, we diverge from our usual attempt to provide objective coverage of clinical advances and important research. Instead, we have invited Dr. Vivian Bucay to provide a detailed and very personal account of her battle with melanoma over the past two years. Her insights as an expert coupled with her experiences as a patient give her report a powerful immediacy as she touches on the wide range of diagnostic tests and treatments, both traditional and experimental, currently available for metastatic melanoma.

While we often lament in these pages the lack of highly effective treatments for advanced melanoma, Dr. Bucay's story personalizes the hopes of patients and their physicians in their search for effective therapies. While to date the majority of patients may find improved disease-free survival at best, some persistent, fortunate souls will indeed experience remission and even dare we say "cure."

In sharing her story, Dr. Bucay reminds us that at the level of the individual patient, the statistics we often cite on prognosis and therapeutic response can be quite misleading. This point was well articulated by evolutionary biologist and science historian Stephen J. Gould, who was diagnosed with peritoneal mesothelioma, a deadly form of cancer that destroys the abdominal lining. When he learned that mesothelioma patients had a median lifespan of only eight months, he wrote a wonderful piece for *Discover* magazine, "The Median Isn't the Message," in which he noted that while half of all mesothelioma patients die before 8 months, some live much longer. After two difficult years of experimental treatment, he experienced a full remission.

Dr. Bucay's story echoes Gould's message that even in the face of dire statistics, patients often find reason to hope. It also reminds us that therapeutic interventions are continuously evolving. For example, the long-held belief that elective lymph node dissection improves survival eventually proved false, but knowledge gained from the research led surgeons to abandon ELND in favor of SLNB, which we now know provides valuable prognostic information. And while interferon has not proven to extend overall survival, investigating the effects of interferon has opened up new avenues of research aimed at harnessing the power of the body's immune system. Even our 'failed' therapies have benefited some patients; on the basis of those few successes the promise of better therapies grows.

Allan C. Halpern, MD, Editor-in-Chief
Ashfaq A. Marghoob, MD, Associate Editor

Surviving Melanoma, *cont. from page 1*

of my three pregnancies. Nonetheless, as I mentally reviewed the differential diagnosis—psoriasis, eczema, seborrheic dermatitis —melanoma was not on the list while I was undergoing a routine shave biopsy; my PA chose to do the biopsy for safety's sake despite noting nothing unusual herself.

So we were both surprised when we received the diagnosis by phone on May 10 from the dermatopathologist to whom I routinely send my patients' biopsies: amelanotic malignant melanoma, possibly metastatic. I suspected (or hoped) that it was a false positive produced by using a shave specimen rather than a full excisional biopsy. However, there was no error in the diagnosis, as immunohistochemistry proved positive for S-100, HMB-45, and MART-1.

I immediately contacted Alex Miller, MD, the surgical oncologist I have relied on over the years, and he was able to see me that same afternoon. Within the next two days, I had undergone a complete metastatic workup that included CT scans, PET-CT scans, endoscopy, colonoscopy, capsule endoscopy to visualize the small bowel, and MRI, all negative for metastatic disease. On May 16, I underwent wide excision of the umbilical region along with a sentinel node biopsy in the right groin. Histopathologic examination of the umbilicus confirmed a diagnosis of amelanotic melanoma, 3.3mm in thickness, with ulceration. A waiting period of about four days ensued during which we awaited the results of the sentinel node biopsy. With no clinically palpable lymph nodes and a series of negative studies, I was considering my treatment options as a Stage IIB patient, namely a year-long course of interferon alfa-2b, currently the only FDA-approved option for the adjuvant treatment of melanoma for Stage II and IIIB melanoma. Adjuvant therapy with interferon alfa-2b was approved in 1995 based on the results of the Eastern Cooperative Oncology Group (ECOG) 1684 study.[3] Interferon has been proven to increase disease-free survival, but whether or not an increase in overall survival is attained remains a matter of debate.

A few days after surgery, the possibility of interferon treatment became a certainty when I was notified that the sentinel node was positive for micrometastases. According to the 2002 AJCC staging criteria, these findings placed me in Stage IIIB, with an average overall 5-year survival of 50 percent [See **Table 1**], according to statistics compiled by the American Cancer Society from a study of 40,000 patients diagnosed between 1988 and 2001.

I consulted with medical oncologist Ronald Drengler, MD, known in our medical community in San Antonio, TX, for his aggressive medical management of high-risk patients.

Stage	Histological Features/TNM Classification	Overall Survival 1-year	5-year	10-year
0	Intraepithelial/in situ melanoma (TisN0M0)		100%	100%
IA	< 1 mm without ulceration and Clark Level II/III (T1aN0M0)		95%	88%
IB	< 1 mm with ulceration or level IV/V (T1bN0M0)		91%	83%
	1.01-2 mm without ulceration (T2aN0M0)		89%	79%
IIA	1.01-2 mm with ulceration (T2bN0M0)		77%	64%
	2.01-4 mm without ulceration (T3aN0M0)		79%	64%
IIB	2.01-4 mm with ulceration (T3bN0M0)		63%	51%
	> 4 mm without ulceration (T4aN0M0)		67%	54%
IIC	> 4 mm with ulceration (T4bN0M0)		45%	32%
IIIA	Single regional nodal micrometastasis, nonulcerated primary (T1-4aN1aM0)		69%	63%
	2-3 microscopic regional nodes, nonulcerated primary (T1-4aN2aM0)		63%	57%
IIIB	Single regional nodal micrometastasis, ulcerated primary (T1-4bN1aM0)		53%	38%
	2-3 microscopic regional nodes, ulcerated primary (T1-4bN2aM0)		50%	36%
	Single regional nodal macrometastasis, nonulcerated primary (T1-4aN1bM0)		59%	48%
	2-3 macroscopic regional nodes, nonulcerated primary (T1-4aN2bM0)		46%	39%
	In-transit met(s)/satellite lesion(s) *without* metastatic lymph nodes (T1-4a/bN2cM0)		30-50%	
IIIC	Single microscopic regional node, ulcerated primary (T1-4bN1bM0)		29%	24%
	2-3 macroscopic regional nodes, ulcerated primary (T1-4bN2bM0)		24%	15%
	4 or more metastatic nodes, matted nodes/gross extracapsular extension, or in-transit met(s)/ satellite(s) *and* metastatic nodes (anyTN3M0)		27%	18%
IV	Distant skin, subcutaneous, or nodal mets with normal LDH (anyTanyNM1a)	59%	19%	16%
	Lung mets with normal LDH (anyTanyNM1b)	57%	7%	3%
	All other visceral mets with normal LDH or any distant mets with increased LDH (anyTanyNM1c)	41%	9%	6%

Table 1. AJCC 2002 Revised Melanoma Staging
Breslow thickness is defined as the thickness of the lesion using an ocular micrometer to measure the total vertical height of the melanoma from the granular layer to the area of deepest penetration. The Clark's level refers to levels of invasion according to depth of penetration of the dermis. Adapted with permission from Balch et al. Final Version of the American Joint Committee on Cancer Staging System for Cutaneous Melanoma. ***J Clin Oncol*** 2001; 19:3635-3648. Lippincott Williams & Wilkins.

Although the benefits of complete (therapeutic) lymph node dissection (CLND) in the absence of clinically palpable lymph nodes remains an area of continuous debate and controversy, I opted for this procedure, based on published reports.[4] On May 30, I underwent radical dissection of the right groin. Histopathologic examination of an additional 28 nodes revealed micrometastatic disease in two of them.

Randomized controlled trials are ongoing to determine the effect of observation alone vs. immediate complete lymph node dissection in patients with positive sentinel lymph nodes. The data collected hopefully will shed further light on the role of initial aggressive surgical management.[5]

Stage III Treatment Options

Multiple treatment options were presented to me, including observation alone, adjuvant therapy with high-dose interferon-alfa-2b, a (nonclinical) trial of biochemotherapy, or enrolling in a clinical trial. Dr. Drengler encouraged me to seek opinions at multiple institutions before committing to a treatment. During the recovery period from the CLND, I went to see Patrick Hwu, MD, at the M.D. Anderson Cancer Institute in Houston, TX, as well as John Kirkwood, MD, at the University of Pittsburgh Hillman Cancer Center in Pittsburgh, PA. Both recommended that I undergo the FDA-approved high-dose intravenous (i.v.) interferon alfa-2b therapy for one month followed by subcutaneous injections for 11 months. Furthermore, Dr. Hwu mentioned Jeffrey Weber MD, PhD, then at the USC Norris Cancer Center in Los Angeles, CA (before being recruited to the H. Lee Moffitt Cancer Center in Tampa, FL), who was expected to begin a clinical trial evaluating the use of an anti-cytotoxic T-lymphocyte antigen 4 (anti-CTLA-4) antibody (ipilimumab) as adjuvant therapy in high-risk melanoma.

A negative regulator of T-cell response, CTLA-4 can inhibit the body's antitumor response. An antibody to CTLA-4 could enhance the immune response against tumors by blocking the effect of this negative regulatory cytokine. The initial studies using an anti-CTLA-4 antibody were conducted in 14 patients with Stage IV melanoma at the National Cancer Institute (NCI) under lead researcher Steven Rosenberg, MD, PhD, and encouraging results were published in 2003.[6]

Drs. Miller and Drengler also advised me to touch base with Dr. Weber about the anti-CTLA-4 therapy. I made the decision to begin treatment with high-dose interferon while awaiting notification about if and when the trial with Dr. Weber would begin. It was not a difficult decision. My HLA type excluded me from every other clinical trial available in the U.S. at that time, and, other than interferon, there was really nothing else. A wait and see approach was completely out of the question.

From Stage IIIB to Stage IV

I completed one month of high-dose i.v. interferon and two months of subcutaneous interferon, when I received the news that I had been accepted for enrollment in the clinical trial with Dr. Weber. He had already seen objective tumor responses in patients with Stage IV disease.[7]

My repeat CT scans and MRI performed in October 2006 as a prerequisite for inclusion in the trial remained negative for metastatic disease. From October 2006 through January 2007, I then commuted every two weeks between San Antonio and Los Angeles for either treatment or laboratory work. The infusion of anti-CTLA-4 was uneventful and well tolerated, especially compared to the serious flu-like side effects I'd experienced with interferon. As part of the study requirements, I underwent repeat CT scans on January 18, 2007, and received the news, again by telephone, that there were multiple pulmonary nodules bilaterally not seen on previous studies.

This was a rude surprise, because I was completely asymptomatic, working normal hours, planning my youngest daughter's bat mitzvah, etc. Drs. Drengler and Weber insisted on a lung biopsy, which I underwent on February 5, two days after the bat mitzvah. Two pulmonary nodules were biopsied by thoracoscopy; one was positive for melanoma, and one was suggestive of melanoma. Dr. Drengler arranged to have a portion of a specimen sent to the Molecular Profiling Institute (445 N. Fifth Street, Third Floor, Phoenix, AZ, 85004; phone 602-358-8900) for extensive immunohistochemistry and DNA microarray studies. These were performed to elucidate possible targets for therapy should additional therapy fail. Technically, I had failed two biologic therapies, a requirement for this specialized testing to be performed.

Treatment Options for Stage IV Disease

With confirmed Stage IV disease, I was dropped from the anti-CTLA-4 trial and moved quickly to explore alternative treatment options. My husband, cardiologist Moises Bucay, MD, not only supported my desire to seek an appointment with Steven Rosenberg, MD, PhD, at the National Cancer Institute (NCI), but along with Dr. Drengler, coordinated the logistics to make it happen quickly.

We scheduled a February 27 appointment at NCI for me to be evaluated by Dr. Rosenberg and his team for inclusion in a clinical trial for Stage IV melanoma patients. (See bethesdatrials.cancer.gov/clinical-research, which shows some of the ongoing clinical trials currently available.) I had been given the option of high-dose interleukin-2 (IL-2) infusions, an immunotherapy whose use was also pioneered by Dr. Rosenberg.[8] It was first approved for use in Stage IV renal cell carcinoma patients and then in 1994 for Stage IV melanoma patients. However, I wanted to explore other options, given the relatively low success rate (around 6 percent) of IL-2 in achieving a complete response in Stage IV patients. After another extensive evaluation at NCI, Dr. Rosenberg's team agreed to accept me in a clinical trial using a non-myeloablative lymphocyte-depleting regimen of chemotherapy followed by infusion of anti-tumor autologous lymphocytes (or some variation thereof), provided that I first undergo treatment with IL-2 and fail it. In the clinical trial, chemotherapeutic agents would be given to suppress the bone marrow without completely ablating it. This contrasts with traditional methods incorporating total-body irradiation to ablate all bone marrow in preparation for a marrow transplant. However, through good fortune, I never had to proceed to this therapy.

As agreed, I undertook the IL-2 therapy first, opting to receive it in San Antonio rather than at NIH because it is my home and because the nurses at the Methodist Hospital in San Antonio are experienced in managing IL-2 patients.

Interleukin-2 can be quite toxic and is usually administered over a 5 to 6 day period in the setting of a medical intensive care unit. It is given in one-week cycles; two cycles spaced one week apart constitute a course of treatment. One month after the first course is completed, radiologic imaging studies are performed to assess the response of the tumor. Based on the outcome, the decision can be made whether or not to continue with another course of IL-2. I received my first course of IL-2 in March and was fortunate to see a 60 percent reduction in tumor volume by April. This was considered a partial response rate, and is seen in about 14 percent of patients who receive IL-2. In June, I tolerated another course of IL-2 and played the waiting game until August 1, 2007, when I would again undergo CT scans. There was not a day when I did not pray for membership in the "6 percent club," the group of complete responders. To date, a complete response has been equated with a durable remission. The CT scan was available for interpretation almost immediately after it was performed. I was led to the radiology reading room, where the radiologist read the study and showed me that the pulmonary nodules had completely disappeared–consistent with a *complete response*.

I have had repeat scans in October 2007, January 2008, April 2008 and August 2008; all have been negative for disease. Never one to look at statistics, I nonetheless was curious about what defines a durable remission, so I have allowed myself to look at survival rates for Stage IV melanoma patients treated with IL-2. For those achieving a partial response, median survival is 5 months; for those with a complete response, median survival is 10 years and counting. I hope to keep on counting.

Discussion

I maintain that even though the appearance of the nodules in my lungs reclassified me as Stage IV, it reflected an improved immune system that could now target the tumor burden which had been invisible in prior studies. Whether this belief is the result of denial or the consequence of extensive reading on immunotherapy, I have never regarded the appearance of the pulmonary nodules as disease progression.

continued on page 5

Women and Melanoma: Cause for Alarm

It is well known that incidence rates of the two most common nonmelanoma skin cancers, basal and squamous cell carcinoma, have recently increased significantly among young women. Now the same appears true for melanoma, the deadliest form of skin cancer. A report from the National Cancer Institute appearing in the *Journal of Investigative Dermatology* (*JID*) reveals startling melanoma trends among young Caucasian women.

Melanoma incidence had been skyrocketing among older adults for decades, but it wasn't until the 2001 publication of a study from the Surveillance, Epidemiology, and End Results (SEER) program, covering the period from 1973 to 1997, that a melanoma increase was seen among Caucasian women born after 1960. Now, seven more years of SEER data—through 2004—have produced even more definitive findings.

In the period from 1973 to 2004, melanoma incidence among men aged 15 to 39 increased from 4.7 cases to 7.7 cases per 100,000. In that same age group, the figures more than doubled among women, leaping from 5.5 cases per 100,000 in 1973 to *13.9* in 2004. After soaring in the 1970s, the rate of increase in women had actually declined from 1978 to 1987, but it began increasing again after 1992.

Many experts believe that the reported increases in melanoma incidence are partly a blessing because they mean we have become better at detecting melanoma, especially at early stages. And the great majority of cases *are* found early, when they are most curable. However, alarmingly, more *advanced* cases are being found in women as well. From the 1990s on, cases in Caucasian women increased both for thin (<1mm) melanomas and thicker (>1mm), more worrisome melanomas, as well as highly dangerous melanomas that had spread.

These changes, the authors point out, parallel reported increases in exposure to ultraviolet radiation (UVR), "the primary environmental cause of melanoma" according to the landmark study by Armstrong and Kricker in 2001. The authors also noted that in sun surveys taken from 1998 to 2004, the prevalence of sunburn and the average number of days spent at the beach increased (most notably among adolescents 16-18 years old), representing the patterns of sun exposure considered to be most likely to cause melanoma. Similarly, tanning bed usage, recently found to be a probable cause of melanoma by the International Agency for Research on Cancer, has been rapidly increasing among U.S. adults, and is most prevalent among young women.

"While more research is needed to confirm the link between melanoma and UVR exposure, this study shows that melanoma is becoming an ever greater danger for young women, and strongly suggests concrete, effective ways to minimize the danger—namely, protect yourself against the sun, and stay out of tanning booths," concluded Perry Robins, MD, President of The Skin Cancer Foundation.

The Foundation advises *everyone* to make these sun safety habits part of their daily health care:

- Seek the shade, especially between 10 AM and 4 PM.
- Do not burn.
- Avoid tanning and UV tanning booths.
- Cover up with clothing, including a broad-brimmed hat and UV-blocking sunglasses.
- Use a sunscreen with an SPF of 15 or higher every day.
- Apply 1 ounce (2 tablespoons) of sunscreen to your entire body 30 minutes before going outside. Reapply every two hours or after swimming or excessive sweating.
- Keep newborns out of the sun. Sunscreens should be used on babies over the age of six months.
- Examine your skin head-to-toe every month.
- See your doctor every year for a professional skin exam.

Surviving Melanoma, *cont. from page 4*

I will try to explain. One of the side effects I had experienced from the anti-CTLA-4 infusion was an intermittent, generalized, erythematous, pruritic, urticarial eruption, which Dr. Weber called the "good rash," appearing in patients who had experienced a positive response to treatment. Immune-related adverse events also associated with a positive response to anti-CTLA-4 therapy include autoimmune colitis, hepatitis, nephritis, and hypophysitis, findings reported by Dr. Weber.[9] Although I did not experience any of these autoimmune breakthrough phenomena, a differential white blood cell count performed every two weeks was consistently remarkable for a highly elevated proportion of eosinophils (comprising almost 50 percent of all white blood cells in the differential count, according to automated equipment that was highly sensitive to but not specific for eosinophils). In reality, these proved to be activated T-lymphocytes and not eosinophils at all; what was reported as eosinophilia was really the immune system's good response to the IL-2 – greatly increased production of activated T-lymphocytes. I concluded that this finding and the rash signified a vastly improved immune system. Unfortunately, adherence to the study criteria still dictated that I be excluded from the clinical trial.

Published reports now show that response to anti-CTLA-4 therapy can involve some unique characteristics which may account for the extended response time ("lag time") seen in patients. In fact, melanoma investigators presented data in 2008 at the American Society of Clinical Oncology (ASCO) 44th Annual Meeting that support revised criteria to preclude patients with disease progression from being prematurely dropped from clinical trials involving agents that may result in a delayed immune response. In other words, patients would be allowed more time to mount an immune response.[10, 11]

Summary

Currently, other than routine imaging studies, physical examination, and some laboratory blood work such as following LDH levels, maintenance therapy for Stage IV melanoma patients does not exist. The standard treatment with IL-2 consists of four cycles or two courses. There is nothing to suggest that additional courses of IL-2 will confer an additional survival advantage. In fact, I had undergone a third course of IL-2 in September, 2007, during which I experienced severe side effects including capillary leak syndrome with prolonged edema, as well as an intensely pruritic episode of exfoliative erythroderma, and severe agitation, none of which I had experienced during the previous cycles.

It has become increasingly clear that in addition to aggressive surgical management, targeted immunotherapy will play an ever more important role in the management of high-risk and metastatic melanoma. Taking into account the new and compelling data that support the use of immunotherapy in treating advanced disease, it is now our responsibility to counsel patients regarding these new and promising treatment options. Although the adjuvant use of interferon alfa-2b for Stage II/III disease may not have lived up to expectations regarding increased survival, it has no doubt opened the gate to research for more effective treatments for advanced disease. I routinely encourage patients to participate in clinical trials when appropriate. A recent article published in the July 2008 issue of *Practical Dermatology* offers guidelines for management of intermediate risk melanoma;[12] it has been useful to me because the published data is presented clearly in a way that is readily applicable to daily clinical practice.

When I was first diagnosed with melanoma, I received numerous copies of Lance Armstrong's book *Forget the Bike*, his account of his experience and "defeat" of metastatic testicular cancer. I never managed to finish the book, perhaps because what I needed to know is stated early on: "People die…Why we should go on, you might ask? Why don't we all just stop and lie down where we are? But there is another truth, too. People live. It's an equal and opposing truth."[13] As physicians, we have the unique responsibility to help others gather all the facts they need to develop a personal strategy to achieve the best possible outcome in the fight against melanoma.

The Melanoma Letter is a publication of The Skin Cancer Foundation, 149 Madison Avenue, Suite 901, New York, NY 10016. (212)725-5176; www.skincancer.org. Opinions expressed do not necessarily reflect those of the Foundation or its Medical Council. Mark Teich, *Editor* (mteich@skincancer.org); Michelle Marcano, *Production Coordinator.*

References

1. Bucay VW. Ironic diagnosis changes life forever. ***San Antonio Medicine*** 2006; 59(10):32-33.
2. Bucay VW. A dermatologist's battle with melanoma. ***The Skin Cancer Foundation Journal*** 2008; XXVI:52-56.
3. Kirkwood JM, Strawderman MH, Ernstoff MS, et al: Interferon alfa-2b adjuvant therapy of high-risk resected cutaneous melanoma: The Eastern Cooperative Oncology Group Trial EST 1684. ***J Clin Oncol*** 1996; 14:7-17.
4. Morton DL, Thompson JF, Cochran AJ, et al. Sentinel node biopsy or nodal observation in melanoma. ***N Engl J Med*** 2006; 355(13): 1307-17.
5. Complete lymph node dissection or observation in treating patients with localized melanoma and sentinel node metastasis in patients who have undergone sentinel lymphadenectomy. Available from ClinicalTrials.gov Identifier: NCT00389571.
6. Phan GQ, Yang JC, Sherry RM, et al. Cancer autoimmunity induced by cytotoxic T lymphocyte-associated antigen 4 blockade in patients with stage IV melanoma. ***Proc Natl Acad Sci*** 2003; 100:8372-7.
7. Walsh N. Antibody may act to halt melanoma. ***Skin & Allergy News*** 2006; 37(12):1.
8. Rosenberg SA, Mule JJ, Spiess J, et al. Regression of established pulmonary metastases and subcutaneous tumor mediated by the systemic administration of high-dose recombinant interleukin-2. ***J Exp Med*** 1985; 161:1169-88.
9. Weber J. Review: Anti-CTLA-4 antibody ipilimumab. Case studies of clinical response and immune-related adverse events. ***Oncologist*** 2007; 12(7):864-72.
10. Hody FS. The Global Ipilimumab Melanoma Study Group. Novel efficacy criteria for antitumor activity to immunotherapy using the example of ipilimumab, an anti-CTLA-4 monoclonal antibody. ***J Clin Oncol*** 2008; 26:134s.
11. Hamid O, Urba WJ, Yellin M, et al. Kinetics of response to ipilimumab (MDX-010) in patients with stage III/IV melanoma. ***J Clin Oncol*** 2007; 25:478s.
12. Yancovitz M, Polsky D. Answering the tough questions in melanoma care: a comprehensive guide to management of high risk intermediate melanoma. ***Practical Dermatology*** 2008; 5(7):30-5.
13. Armstrong L, Jenkins S. ***It's Not About the Bike: My Journey Back to Life.*** Berkley Books, New York, 2000; 3-4.

About the Editors

Allan C. Halpern, MD, is Chief, Dermatology Service, Memorial Sloan-Kettering Cancer Center, New York City. **Ashfaq A. Marghoob, MD**, is Clinical Associate Professor, Department of Dermatology, Memorial Sloan-Kettering Cancer Center. **Alfred W. Kopf, MD**, is Professor Emeritus of Dermatology, New York University School of Medicine; he is Chairman of the Melanoma Committee of The Skin Cancer Foundation.

12th World Congress on Cancers of the Skin

Tel Aviv, Israel, May 3-6, 2009

COMMITTEES:

Congress President
Joseph Alcalay, *Israel*

Honorary President
Perry Robins, *USA*

Congress Secretaries
Alex Ginzburg, *Israel*
Shmuel Yorav, *Israel*
Isaac Zilinsky, *Israel*

Congress Treasurer
Boaz Amichai, *Israel*

Scientific Committee
Reuven Bergman, *Israel*
Antonio de Silva Picoto, *Portugal*
Leonard H. Goldberg, *USA*
Allan C. Halpern, *USA*
Emmilia Hodak, *Israel*
Roland Kaufmann, *Germany*
Michal Lotem, *Israel*
Scott W. Menzies, *Australia*
Hubert Pehamberger, *Austria*
Jason Rivers, *Canada*
Julian Sanchez Conejo-Mir, *Spain*
Jacob Schechter, *Israel*

SPONSORED BY:

The Skin Cancer Foundation
www.skincancer.org

Israel Society of Dermatology and Venerology

CO-SPONSORED BY:

Israel Cancer Association

ONCOLOGY

ABSTRACT SUBMISSION DEADLINE DATE: JANUARY 5, 2009

JOIN US TO FACE THE GLOBAL CHALLENGE

As the number of skin cancer sufferers reaches epidemic levels, the 12th World Congress on Cancers of the Skin (WCCS) will provide hundreds of attendees with future and global strategies to combat the most common cancer worldwide.

MAIN CONGRESS TOPICS:

- Epidemiology of skin cancer
- Primary and secondary prevention of skin cancer
- Actinic Keratoses
- Sunscreens and skin cancer
- Biology and treatment of non-melanoma skin cancer
- Skin cancer in organ-transplant patients
- Viruses and skin cancer
- Melanoma
- Cutaneous lymphomas
- Mohs micrographic surgery
- Spindle cell tumors of the skin

CONGRESS ORGANIZERS:

KENES International
CARES FOR YOUR ORGANIZATION
GLOBAL CONGRESS ORGANIZERS AND ASSOCIATION MANAGEMENT SERVICES

12th World Congress on Cancers of the Skin
c/o Kenes International - 1-3 rue de Chantepoulet, P.O. Box 1726, CH-1211 Geneva 1, Switzerland

For more information, please visit:
www.kenes.com/wccs