

A monthly online news publication about the latest progress in treating cancer

by Ralph W. Moss, PhD

WELCOME

Welcome to the fourth issue of ADVANCES in Cancer Treatment. In this issue, I report on a new treatment modality called Radiovirotherapy. Aside from a lone press release, this is the first article on this new modality. A phase I clinical trial has just been concluded at Mayo Clinic: we can expect to hear a lot more about this new treatment in the near future.

I also continue my survey of West Coast CAM clinics with a report on my 2011 tour of CAM cancer clinics of Oregon and Washington.

I had a very busy month of June, with visits to clinics and laboratories in Moscow and St. Petersburg, Russia. Following this, I attended the annual meeting of the American Society of Clinical Oncology (ASCO) in Chicago. My recent co-authored ASCO submission (on the drug ipilimumab) was published in the special annual meeting issue of ASCO's Journal of Clinical Oncology:

http://www.asco.org/ASCOv2/Meetings/Abstracts?&vmview=abst_detail_view&confID=114&abstractID=99940

A few days later, I returned to Europe for the Second International Congress on Integrative Oncology of the German Society of Oncology in Munich. I kicked off the Congress with a speech on progress in the War on Cancer as it relates to the treatment of stage IV disease. A version of this speech is included in this issue.

RADIOVIROTHERAPY: A NEW FORM OF CANCER TREATMENT

Preparing a Measles Vaccine in Ethiopia

Mayo Clinic scientists have devised an ingenious new way of attacking cancer cells. They first administer a modified form of the common measles virus to invade and destroy

cancer cells. This virus is a version of the familiar Edmonston measles vaccine (abbreviated MV-Edm). Over the past 50 years, over 500 million doses have been given worldwide, with apparent safety. The measles virus hones in on the cancer.

Why measles? Starting in 1971, reports began to appear in medical journals such as *Lancet* of the spontaneous regression of various malignancies, including leukemia, Hodgkin's disease and Burkitt's lymphoma, after patients came down with ordinary (wild-type) measles (Bluming 1971, Pasquinucci 1971, Taqi, 1981). So measles is a prime candidate for the viral therapy of cancer.

At the Mayo Clinic, this standard vaccine has been genetically modified to incorporate a molecule that is part of a normal cell's way of transporting iodine across its surface. This molecule is called the "sodium iodide symporter" (abbreviated NIS). (A symporter is a protein embedded in a cell's membrane that helps to move several different molecules or ions into the cell.) When the measles virus is combined with the symporter it produces a new entity, dubbed MV-NIS.

The Rochester, Minnesota scientists deliberately infected cancer patients with MV-NIS. Once an excess of symporters was implanted in the membrane of the cancer cells, they then administered a radioactive form of iodine (either iodine-123 or iodine-131). The iodine was drawn to cells that had an abundance of receptor molecules. Thus, the cancer cells were hit twice in rapid succession with two separate cancer-killing substances, measles virus and radioactive iodine. In 2004, this combined treatment was given a new name, "radiovirotherapy."

The idea of combining viruses and isotopes goes back much further, however. Radioactive isotopes were incorporated into viruses by A.F. Graham and Laurella McClellan of the University of Toronto in 1949. They incorporated radioactive phosphorus into the influenza virus "to gain information about the mechanism of virus synthesis in the host cell..." At the time they reported "strong supporting evidence" that the isotope was actually incorporated into the virus structure (Graham 1949).

Nothing came of this therapeutically. But eight years ago David Dingli, MD, PhD, and colleagues at the Mayo Clinic reported on the use of their genetically modified measles virus in the treatment of a kind of cancer called multiple myeloma. Some grafts of myeloma cells, they reported, "regressed completely after a single intravenous dose of MV-NIS" (Dingli 2004).

In 2007, the same group used another virus, vesicular stomatitis virus (VSV), which was also genetically engineered to include NIS. This was followed by the administration of radioactive iodine-131. Again, in the laboratory, scientists observed tumor regression, without the toxicity normally associated with VSV (Goel 2007).

Next the group turned its attention to prostate cancer (PC) cells. This was a logical choice since PC cells typically overexpress the measles virus receptor, CD46. Mayo doctors again reported that MV-NIS "resulted in significant tumor regression" as well as highly

significant prolongation of survival in animals. Again, administration of iodine-131 “further enhanced the antitumor effect of MV-NIS virotherapy” in the laboratory (Msaouel 2009a).

In the following year, MV-NIS was used against pancreatic cancer in the lab. “Mice treated with intratumoral MV-NIS exhibited significant tumor growth delay...and prolonged survival...compared with untreated mice,” they wrote (Penheiter 2010).

In April 2012 a related group at Mayo showed that the technique also worked in an animal model of brain cancer (the aggressive type called glioblastoma multiforme): “Administration resulted in significant increase of MV-NIS antitumor activity as compared with virus alone” (Opyrchal 2012). The authors concluded: “MV-NIS-based radiovirotherapy has significant antitumor activity against glioblastoma multiforme and represents a promising candidate for clinical translation.” (ibid.)

The new treatment has also been extended to the study of squamous cell cancers of the head and neck (SCCHN). Mayo scientists used MV-NIS to infect squamous cells in the lab. They modified the treatment by including a small amount of an old chemotherapeutic drug, cyclophosphamide (Cytosan): “The antitumor effect could be boosted significantly either with concomitant cyclophosphamide therapy or with appropriately timed administration of radioiodine (¹³¹I).” The authors concluded: “MV-NIS could be a promising new anticancer agent that may substantially enhance the outcomes of standard therapy after intratumoral administration in patients with locally advanced SCCHN” (Li 2012, emphasis added).

As a result of all this laboratory research, physicians at Mayo, in collaboration with the National Cancer Institute (NCI), launched a human clinical trial in 2007. The target was multiple myeloma. This trial was scheduled to conclude in June 2012. Patients in the trial received MV-NIS, and then both before and after the new drug received radioactive iodine-123. In addition, some also received cyclophosphamide. This phase I study is, at best, only the first step in a prolonged testing process. It is designed to address issues of dose, safety and tolerability. However, a secondary goal will be to look at whether there are any complete or partial responses, or even stabilization, following treatment. If the treatment is at all successful it will probably be followed by larger phase II and III trials in myeloma or possibly other cancers. It is important to emphasize, Dr. Dingli told me, that the bulk of the research has been done in test-tube and animal models, and the results of the phase I human trial have not yet been published.

Radiovirotherapy is an exciting new concept. Cancer-targeted viruses not only kill cancer cells outright but can stimulate the immune system in a beneficial way. In the case of the measles virus (as in some other viruses), its effect is mainly due to an abundance of CD46 (a marker that normally activates a component of the immune system called complement) on the surface of cancer cells (Studebaker 2010). A variety of different viruses and of different isotopes are available for experimentation in Radiovirotherapy. There are bound to be many interesting new combinations in the years ahead.

(Full reference citations are given below.)

CAM CLINICS OF OREGON AND WASHINGTON

The Pacific Northwest is a center of naturopathy

In September 2011, I took a 1,000-mile trip to visit CAM cancer clinics in the Pacific Northwest. The trip began in San Francisco, with stops in many cities along the way. In Oregon I visited Ashland, Eugene, and Portland; in Washington I visited Renton and Seattle, Washington. Now I will discuss Oregon and Washington clinics.

JONATHAN TREASURE

I began my Oregon journey with a visit to the home office of the British-American herbalist, Jonathan Treasure. At the time of my visit, Jonathan was working at the Mederi clinic of Donald R. Yance, C.N., M.H., A.H.G., who unfortunately was out of town and could not meet with me. However, I did tour his clinic in the company of Mr. Treasure. A few months later, Treasure informed me that he had branched out on his own and was no longer associated with the Mederi clinic.

Treasure was educated in the rigorous herbal traditions of the UK and has a Masters degree in Medical Sciences from Cambridge University. He graduated in herbal medicine from the now-defunct UK School of Phytotherapy. In 1994, after he had moved to the Pacific Northwest, he became a professional member of the American Herbalist Guild (AHG) and editor of their Journal; he currently serves on the Scientific and Medical Advisory Board of the Life Extension Foundation (where I first met him), and is also on the Advisory Board of Dr Peter D'Adamo's Center of Excellence for Generative Medicine at the University of Bridgeport. He is also a member of The Society of Integrative Oncology.

Treasure has dual expertise in traditional herbal therapeutics combined with a fluency in biomedical science. This is exemplified by his contribution to the collaborative textbook *Herb, Nutrient and Drug Interactions: Clinical Implications and Therapeutic Strategies* (Mosby Medical, 2008) for which he authored the herbal content. For two decades his clinical practice has centered on botanical medicine and nutritional therapeutics for people with cancer. A long-time proponent of using internet technology to advance herbalism, Treasure's clinical practice employs virtual tools to consult on-line with patients and healthcare professionals across the United States and abroad.

TINA KACZOR, ND

Following my visit to Jonathan Treasure, I went to visit Christina (Tina) Kaczor, ND, at her naturopathic clinic in Eugene, OR. Tina is a Fellow of the American Board of Naturopathic Physicians and bears the initials FABNO after her name. This certifies that the naturopathic doctor in question has passed a very difficult examination on the principles of integrative oncology. It is the equivalent of being a board-certified oncologist in the naturopathic sphere.

Kaczor has an outstanding educational background. She graduated magna cum laude with dual undergraduate degrees from SUNY-Buffalo in biochemistry and English, an unusual accomplishment. While still an undergraduate she did the work that resulted in a peer-reviewed publication in the field of molecular biology (Kaczor 1994). She is a 2000 graduate of the National College of Naturopathic Medicine (NCNM) in Portland and then completed a two-year clinical residency in integrative oncology at the Cancer Treatment Center of America in Tulsa, OK. Because of this, she is well aware of the world of conventional cancer care. This enables her to safely integrate complementary treatments into a patient's protocol.

Dr. Kaczor is senior medical editor of the peer-reviewed journal *Natural Medicine Journal*, which is the official publication of the American Association of Naturopathic Physician. This is an open access journal. She has served on the board of the Oncology Association of Naturopathic Physicians (OncANP) from 2005-2011. She has served as the group's president and treasurer. She was a prominent organizer and participant in the wonderful conference OncANP held in Carefree, AZ in late February 2012. She is currently secretary of the American Board of Naturopathic Oncology Board of Medical Examiners, which is the governing body for board certification in naturopathic oncology. She is also a member of the more allopathic Society for Integrative Oncology (SIO).

Now, I am sure it would be possible for an ambitious person to have all of these titles and accomplishments and still be an inferior doctor. But in Tina Kaczor's case, the accomplishments are a 'side effect' of the high regard with which she is held by patients and colleagues alike. She is universally regarded as cheerful, intelligent and progressive. If you are a cancer patient in Oregon this should be a top destination for the naturopathic half of integrative oncology.

TORI HUDSON, ND

I followed this with a visit to the Portland, OR clinic of Tori Hudson, ND called *A Woman's Time*. Through her *Townsend Letter* column, other writing and lectures, for almost three decades she has been a well known figure in the field of complementary medicine as it relates to women's health. She is program director at the Institute for Women's Health and Integrative Medicine and an adjunct professor at three naturopathic medical schools, including Bastyr University, in Seattle. For many years she has been associated with her Portland alma mater (1984), the National College of Naturopathic Medicine. She has been both Medical Director and Interim Academic Dean there. In 1990, she won the American Association of Naturopathic Physicians' President's Award for research in the field of women's health care and in 1999 was Naturopathic Physician

of the Year. She was the first Woman in the United States to become a full professor of Naturopathic Medicine and has been a guest lecturer at many (allopathic) medical schools and hospitals. She also conducts symposia and training sessions for health care professionals (at which I have spoken). She has also appeared on “Good Morning America”, PBS’s “Healthy Living Series”, and Lifetime’s “New Attitudes.”

My only caveat is that Dr. Hudson is a specialist in gynecology more than cancer. Some of her areas of expertise are the use of botanical treatments for menopause as well as natural treatment protocols for cervical dysplasia (a kind of pre-cancer). Cancer patients should therefore keep this in mind in choosing their physician as sometimes one may need a doctor with specialized knowledge in one’s particular area of concern. But within her area of specialization there is probably no one more knowledgeable in the US.

NCNM and KEN WEIZER, ND

On the following day I visited the National College for Natural Medicine (formerly National College of Naturopathic Medicine), the nation’s first modern naturopathic medical school. While there, I met with top administrators and also with Ken Weizer, ND, an old friend who is associated with the school and also practices naturopathy in the Portland area. The clinic is a great resource for patients in the Portland area. Thanks to recent donations, it is modern and thriving. (Some of the other NCNM buildings, by contrast, seem rudimentary.) The staff of attending physicians includes naturopathic, Chinese medicine, chiropractic and medical doctors. Some of them have over 35 years of health care experience. The clinic is open six days a week and offers the chance of either seeing one of the providers on their teaching rotation or making an appointment with a private physician. The clinic excels at treating such relatively minor conditions as anxiety, depression, sleep issues, fatigue, etc. It is not necessarily where I would go with any complicated cancer issue. But what a great resource to have in one’s own locale!

Ken Weizer is an interesting doctor and represents a real option for cancer patients in the Portland area. He is a naturopathic graduate of NCNM. But his background is in movies. He was a film director and editor for 15 years. He worked on highly rated children’s programs.

In 1989, however, his whole life and career were turned upside down by a cancer diagnosis. Through the judicious combination of conventional and complementary treatments, he was able to reclaim his health. This led him to focus on helping others similarly affected by launching a study of naturopathic medicine. He graduated from NCNM in 1999.

Because of this personal history, Weizer has a strong dedication to people who have serious and life-challenging illnesses such as cancer. He believes that hope and knowledge are fundamental to the recovery process. He is well known in the Portland area for his workshops on naturopathic medicine, and his talks to local cancer support groups. Weizer is an adjunct faculty member of the NCNM and has taught at Marylhurst

University, a private Catholic university in Portland, where he has given classes on oncology, healing, stress reduction, and communication.

MILES HASSELL AND PROVIDENCE ST. VINCENT MEDICAL CENTER

On the following day I visited Dr. Weizer again, but this time in the context of his work at the Providence St. Vincent Medical Center in Portland. The hospital is part of Providence Health & Services in Oregon, a huge not-for-profit network of hospitals, health plans, physicians, clinics and affiliated health services. It is symbolic of the degree to which CAM has become integrated into regular medicine in Oregon that this major 451-bed health care center (the state's first permanent hospital) has a thriving CAM center in its midst.

Miles Hassell, MD, is a very warm and friendly presence at the Center. He is medical director of Providence Integrative Medicine Program at Providence Cancer Center, and a clinical instructor for the training of internal medicine residents. He received his medical degree from the University of Western Australia and completed his residency in internal medicine at Providence St. Vincent Medical Center in Portland. He is board-certified in internal medicine but works closely with the oncologists on staff there.

“Conventional medicine should be a vital part of every person's plan for good health,” he says. “By adding evidence-based but unconventional therapies to that approach, Providence maximizes a patient's ability to recover, to live well and to flourish.”

He is the principal investigator in a trial using nutritional interventions to reduce side effects of conventional cancer therapies. His internal medicine practice, which is called the Comprehensive Risk Reduction Clinic, emphasizes evidence-based nutritional lifestyle management in the context of a traditional medical model. He and his wife, Mea Hassell, have written a book called “Good Food, Great Medicine,” based around a diet-and-exercise program (now in its second edition). They give the evidence for the benefit of a whole food, Mediterranean diet. Hassell specializes in what he calls “patient-directed, noninvasive, non-pharmacological approaches to medicine.” This emphasizes natural approaches such as exercise, diet and natural medicines. What an amazing resource this is for people in the Portland area, especially those who are also pursuing conventional cancer care at Providence.

CANCER TREATMENT AND WELLNESS CENTER

Finally, as the month drew to a close, I visited the Seattle Cancer Treatment and Wellness Center, which is actually located in Renton, Washington. (Some readers may wonder why I did not also visit the Tahoma Clinic, located just blocks away. The reason is that my inquiries to Jonathan Wright, MD, were referred to his cancer specialist, Davis Lamson, ND. But my emails to Lamson went unanswered, hence the omission.)

The Seattle Cancer Treatment and Wellness Center (CTWC) is a branch of the Cancer Treatment Centers of America (CTCA), the chain of hospitals that I have discussed in

other newsletters and reports. The Seattle center differs from the other CTCAs in a number of regards. First, unlike all the other CTCA facilities, this is not an inpatient hospital but entirely an outpatient clinic. This is because of its unique history. CTWC was founded by a naturopathic physician and a medical oncologist. It was later purchased by CTCA and made part of its chain. However, the Seattle facility retains a semi-independent status. One can see this in the fact that one can book appointments directly with the center, without having to go through the central CTCA patient intake. More significantly, CTWC administers some treatments that are not available at other CTCAs (outside the possibility of receiving them through clinical trials). Most conspicuous among these are intravenous vitamin C treatment (which is used, I was told, to reduce the chances of cancer recurrence) and metronomic chemotherapy.

Metronomic chemotherapy is the use of lower doses of chemotherapy than normal but on a more frequent (hyperfractionated) schedule. Its efficacy was first proposed by the great cancer scientist, Judah Folkman, in the 1990s as part of an anti-angiogenic strategy. Dr. Nick Chen, the leading medical oncologist, at CTWC, makes a persuasive case that by giving drugs metronomically (in conjunction with naturopathic post-care) he can get exceptional results in a number of different cancers. In 2008, he presented a poster at a cancer conference in Hawaii that showed remarkable results in non-small cell lung cancer. This work definitely needs to be reproduced, but it is promising. Nick Chen impressed me greatly with his intelligence and experience. Several of our clients have gone to him since then and some have had really exceptional results. This was a fitting end to a very memorable clinic tour.

Nick Chen is the rare medical oncologist who recognizes the importance of nutritional, mental and emotional health in cancer. He works closely with the two naturopaths at CTWC, Marc Gignac, ND, FABNO and Paul Reilly, ND, LAc, FABNO. Nick is not only board certified in oncology but has a PhD in immunology from the University of Iowa. He completed hematology fellowships at University Libre de Bruxelles in Belgium and Shanghai Medical University in China.

Dr. Chen completed his internal medicine residency at the University of Nebraska Medical Center, and a fellowship in medical oncology at Moffitt Cancer Treatment Center and Research Institute in Tampa, Florida, one of the top cancer centers in the nation. He joined CTCW in 2002. His focus is on innovative treatments for difficult-to-treat cancers, such as lung cancer, metastatic melanoma, brain cancer, and relapsed lymphoma.

I also visited my good friend Leanna Standish, ND, PhD, at Bastyr University in Seattle. I hope to discuss this outstanding school and its programs in a future issue of ADVANCES.

Bottom Line: In Oregon and Washington, when it comes to integrative oncology, "I have seen the future, and it works." Naturopathy functions there as a fully accepted and integrated part of medical care (including cancer care) in these states. As a resident of a part of the country where naturopathy is not even licensed, I cast envious eyes on the

Pacific Northwest, whose residents have far greater options when it comes to the varieties of treatment they can access. I think those who fear the sky will fall if they license naturopathy should study how well it works in states such as Oregon and Washington, where naturopathy has been accepted since the 1920s.

ARE WE MAKING PROGRESS IN THE 'WAR ON CANCER'?

President Nixon Signed
The National Cancer Act
On Dec. 23, 1971

This is a version of the speech that I gave in Munich on June 16, 2012, at the 2nd Annual International Conference on Integrative Oncology of the German Society of Oncology (DGO).

First, I want to acknowledge that some progress has been made in the War on Cancer. For instance, cancer death rates in the US have been falling, albeit slowly. Initially, they rose a bit. But then after 1979 in women and after 1993 in men they began to fall. For example, between 2001 and 2007 the general cancer death rate fell by 1.9 percent. That is very good news. Some of this improvement has been due to the effort to discourage cigarette smoking. That effort has paid off in declining rates of deaths from lung (and some other forms of) cancer.

Other achievements are the full extension of the Pap smear for cervical cancer to a larger portion of the female population, the creation of increasingly sensitive molecular markers for cancer, and a general improvement in less disfiguring cancer surgery. Another important development has been the use of adjuvant chemotherapy in women, especially those with high-risk breast cancer. This has saved many lives. We might also mention the general improvement in medical and nursing care since the early 1970s, some of which was funded by War on Cancer money. So, despite what I say below, the news is not all bad.

In Time for the Bicentennial?

When President Nixon signed the National Cancer Act on December 23, 1971, he dubbed it “a national crusade to be accomplished by 1976 in commemoration of the 200th anniversary of our country.” In other words, the President, Congress, the general public and even some in the scientific community believed that this “crusade” would be accomplished by July 4, 1976, which was less than five years away. What did “accomplish” mean in this context? There was little doubt that the public expected a cure, either for cancer as a whole, or for some major forms of cancer. That certainly did not mean just curing early-stage disease. It meant finding a way to do away with advanced,

invasive, metastatic, stage IV disease and restore the patient to health. It also meant feeling secure that the disease would not recur.

In 1971, as today, there were some fairly effective cures of early-stage disease. These were surgery and radiation therapy (and later, in some cases, chemotherapy). If your surgeon completely removed the tumor —"got it all" in common parlance—you then had a very good chance of living out your natural life span without a recurrence of the disease. Then and now, it was metastatic disease that needed conquering. While the percentage of people reaching stage IV has declined somewhat, the conquest of metastatic disease still represents the greatest challenge, and the area in which, as I shall show, the least progress has been made.

Let us then look briefly at the current situation in a number of statistically important cancers. Bear in mind, that I am only talking about advanced disease, which is disease that has generally failed to respond to conventional treatments.

Colorectal Cancer

Colorectal cancer affects over 143,000 Americans per year. In stage IV disease, a number of drug regimens have been introduced over the past 40 years. FOLFOX and FOLFIRI are the most widely used combinations. But as Leonard Saltz, MD, of Memorial Sloan-Kettering Cancer Center, has said, the drug 5-FU (discovered in the late 1950s) still remains the key to colorectal cancer treatment (Curreri 1958). Nor, we might add, is it conspicuously effective in the stage IV setting.

“It is a source of frustration and humility for investigators,” Saltz wrote in the DeVita textbook, “that over 50 years later [5-FU] remains at the very core of most chemotherapeutic approaches to colorectal cancer” (Saltz 2011).

To give some idea of the current state of the art in colorectal cancer, let’s look at the recent so-called CORRECT trial, whose results were announced at the 2012 meeting of the American Society of Clinical Oncology (ASCO). This was a randomized controlled trial of a new drug, regorafenib, vs. placebo for stage IV colorectal cancer that had failed to respond to other treatments. The median overall survival with this drug was 6.4 mos for regorafenib vs. 5.0 mos for placebo. The median progression-free survival was 1.9 mos for regorafenib and 1.7 mos for placebo. The overall response rate was just 1.6% for regorafenib and 0.4% for placebo (Grothey 2012).

Despite these unimpressive numbers, Bayer is banking on this drug “to be one of the future standouts in its portfolio of cancer medicines... eyeing the program to yield blockbuster returns on the company's R&D investment.” In fact, business writers say that Bayer expects the drug will eventually top more than \$1 billion in yearly revenue (Fiercebiotech 2012).

Brain Cancer

Next, let us look at a particularly difficult form of brain cancer, glioblastoma multiforme. According to the DeVita textbook: “In a landmark international trial, patients were randomized to radiotherapy with or without concurrent and adjuvant temozolomide. Median and 2-year survival were increased by 2.5 months and 16.1%, respectively...A randomized phase 2 trial of temozolomide versus procarbazine in 225 patients with GBM at first relapse demonstrated that treatment with temozolomide improved median progression-free survival (12.4 weeks vs. 8.3 weeks). Radiographic responses were disappointing (5.4% vs. 5.3% (DeVita, et al. Cancer, 9e, 2011, ch. 121). This speaks for itself.

Comparison of recent clinical trial results to European results (EORTC) presented at ASCO 2012 showed median survival was 15.8 months vs. 14.6 months...” Results show that only < 50% of GBM patients complete standard of care in the real-world setting and prognosis remains dismal for patients who do not receive CRT.” This is an important point to which I shall return below.

Breast Cancer

In recent decades there has been a great deal of research into breast cancer and its treatment. However, so far there has been little progress in treating stage IV BC with chemotherapy and targeted agents. For example, in patients with stage IV breast cancer previously treated with an anthracycline and a taxane addition of the targeted agent Avastin (bevacuzumab) to Xeloda (capecitabine) increased response rates from 9.1 to 19.8%. But this did not result in longer progression-free survival (4.86 months vs. 4.17 months). Overall survival was 15.1 months with Avastin vs. 14.5 months without (a non-significant difference). This is the basic reason that the FDA removed its approval for Avastin in advanced breast cancer (Miller 2005).

Lung Cancer

In non-small cell lung cancer (NSCLC) the picture unfortunately isn't much brighter. According to the DeVita textbook, “Patients with stage IV NSCLC typically die from their disease, with an overall median survival time of 10 to 12 months. The fraction of patients who are alive 1 year after diagnosis has increased slightly over the past decade” (Schrump 2011). A 2003 meta-analysis confirmed an increase in median survival of 1.5 months (from 4.5 to 6 months) (Pfister 2004).

Lest you think that the introduction of targeted agents has greatly changed things, here is a paper from the 2012 ASCO meeting. In an Italian phase III clinical trial called TAILOR, which compared second-line treatment with the standard drug Taxotere (docetaxel) vs. the targeted drug Tarceva (erlotinib) in the common or "wild" type of lung cancer, there was:

A total response rate of 14% with Taxotere vs. 2.2% with Tarceva

A 3.4 mos median progression-free survival with Taxotere vs. 2.4 mos with Tarceva

A complete response (CR) rate of 4.3% with Taxotere vs. 0.0% with Tarceva (Garassino 2012).

As a result, a Bronx oncologist Stephen E. Vogl, MD, asked whether a fair summation of this study might be that “docetaxel is not a very good drug and erlotinib is a terrible drug.” When the first author agreed, this was greeted with a “round of laughter and applause” by the ASCO audience (Weindling 2012). Oncologists very much want better drugs with which to treat their patients.

A similar presentation could be made of the other common cancers, including stage IV esophagus, liver, pancreas, bile duct, sarcoma, etc. There are only a few bright spots in an otherwise bleak picture. And this is more than 40 years since initiation of Pres. Nixon's “five year war.”

Cost of Treatment

Meanwhile, the cost of research and treatment for cancer has become astronomical. According to Newsweek, the US spent \$100 billion on cancer research from 1971 to 2008. The FYI 2011 budget request for the National Cancer Institute was \$5.2 billion. According to the Journal of the National Cancer Institute, medical expenditure on cancer reached \$125 billion per annum in 2010. This is expected to rise to \$158 to \$207 billion per annum by 2020.

The driving force in this market is the pharmaceutical industry, particularly Big Pharma. This is a long and complicated discussion, since Big Pharma obviously does much good in society by providing reliable and effective drugs for many conditions. But there are negative aspects of the growth of an oligopoly in medicines as well.

Cancer is said to be “one of the most important growth segments among the pharmaceutical markets...” At \$47.7 billion per year for drugs alone, “cancer is one of the largest, fastest growing markets in the pharmaceutical industry” (Business Insights 2009).

One disturbing trend is the increasing cost of new anticancer drugs provided by Big Pharma. Thus,

Avastin (bevacuzumab) for colon, etc. = \$88,000 per person

Provenge for prostate cancer: \$31,000 per injection = \$93,000 per person

Yervoy (ipilimumab) for melanoma = \$30,000 per infusion = \$120,000 for four months

Herceptin + Perjeta = \$187,000 per person for 18 months (Pollack 2012).

Meanwhile, many inexpensive drugs are in short supply, possibly because of a lack of profitability compared to the newer targeted agents. To quote one doctor, writing in

Forbes: “Generic drugs which are off patent that are costly to produce, but usually cheap to purchase, are generally the medications in short supply” (Glatter 2012).

Potential Contribution of CAM

There is no single solution to this complex problem. However, I would suggest that one underutilized resource is the broad world of treatments called Complementary and Alternative Medicine (CAM). This is a repository of new concepts and treatments. Some are undoubtedly ineffective. But, in our lifetime, we have seen two important treatments that were branded as quackery (immunotherapy and hyperthermia) transition into conventionally accepted treatment modalities. So a special program should be launched to dip into the treasury of CAM for fundamentally new treatment ideas.

I would also argue that the results with integrative oncology (IO), i.e., a combination of conventional oncology and CAM, might turn out to be better than when using conventional oncology alone. This at least is suggested by the careful study of Block et al. showing that stage IV breast cancer patients at a private CAM clinic in a Chicago suburb had 38 mos overall survival compared to 20 months at comparable non-CAM center. To quote the paper: “There currently is no drug that has demonstrated the potential to double the life expectancy of metastatic breast cancer patients, as evidenced in these findings” (Block 2009).

My conclusions are as follows:

Progress in the War on Cancer, when measured by improvement of survival in stage IV disease has generally been disappointing
The needs of Big Pharma basically drive major developments in oncology
Cancer treatment is and remains Big Business
Fundamentally new strategies are necessary to bring about major changes. CAM is a repository of such ideas. A considerable amount of attention should be paid to the serious exploration of such ideas, up to and including the performance of definitive randomized controlled trials of the best CAM concepts.

(Complete list of references below)

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