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Dr. Stephen DeFelice Starts Clinical Study Combining Carnitine and Doxorubicin in Treatment of Advanced Ovarian Cancer

For the first time since I became a Townsend Letter columnist five years ago, the “inspiration” for one of my columns literally walked up to me. Saturday, May 2, I was sitting on a bench in front of a takeout place on Manhattan's Upper East Side, enjoying a morning coffee, when a tallish, lean man walked spryly into view.

Residents of this affluent neighborhood don casual clothes on weekends. The man approaching me, whose bearing betokened late middle age, wore a navy blue blazer, natty chinos – and a bowtie.

I know only one man who routinely appears publicly in formal garb, with a bowtie as his signature item. But that man doesn't live in NYC. He lives in central New Jersey, has his office there, and “retreats” weekends as often as he can to a cabin in the Catskills.

“Dr. DeFelice!” I called, “What brings you to my neck of the woods?”

“Ciao, Marco,” came the return greeting, “I'm going to Central Park to recruit patients for a clinical trial.”

“On carnitine in ovarian cancer?” I guessed.

“Yes, my top priority, my friend. The medical promise is too great for me to sit on the sidelines and let others do it.”

Background on Dr. DeFelice's Efforts to Promote Clinical Research

Stephen L. DeFelice, MD, has spearheaded nutraceutical research worldwide since the mid-1960s, after clinical studies he and colleagues conducted on carnitine, a naturally occurring substance required by the heart for energy, demonstrated that carnitine reduces the toxic effect of the anticancer drug Adriamycin on the heart.

The Oxford English Dictionary credits Dr. DeFelice with coining the term nutraceutical. He dates his coinage to 1989, during an after-dinner stroll in the Piazza Navona, Rome. He wanted a word or umbrella phrase for foods, compounds in food, dietary supplements, herbal remedies, functional foods, and the like that are beneficial (or promising) in treating or preventing disease. By giving this nebulous field a sound-byte identity, he believed that Congress might pass legislation to speed up clinical study of these substances.

I've published three interviews with Dr. DeFelice in Townsend Letter (July 2007, October 2007, January 2008). A paramount concern he expressed in these columns is that the public and media do not appreciate the need for more clinical research. (He characterizes this failing as a cultural blindness.) Clinical research, he has maintained through his career, is the crucial step in the process of medical discovery.

Dr. DeFelice's first book, Drug Discovery: The Pending Crisis (1972), emphasized the indispensable link between therapeutic breakthroughs and clinical trials – a message easy to grasp, he presumed. But on a tour to promote the book, the media's reception of the message surprised him. They concentrated on the potential risks involved in research with human subjects rather than on the possible benefits.

Receiving him “with suspicion, almost hostility,” he recalled, the media perceived him as a throwback to the doctors who tortured people in experiments during the Nazi and Stalinist eras (Townsend Letter, January 2008).

Undaunted, in 1976 Dr. DeFelice established the nonprofit Foundation for Innovation in Medicine (FIM), which he still chairs. Its primary mission: to convince the media and the public of the centrality of clinical research in medical discoveries. Again, he bumped up against the stone wall that confronted him during his book tour four years earlier.

Around 1990, another idea on how to draw attention to the importance of clinical trials occurred to Dr. DeFelice. He conceived the Nutraceutical Research and Education Act (NREA), aimed at accelerating Food and Drug Administration (FDA) approval of nutraceuticals while lowering the cost of the approval process.
Between 1993 and 2000, FIM sponsored nutraceutical conferences yearly, most of them at the Waldorf Astoria in NYC, several in Washington, DC. FIM invested heavily in a publicity campaign to attract the media to these conferences. With few exceptions, no mass media members attended.

In 2000, Congressman Frank Pallone (D-NJ) introduced the NREA in the House of Representatives. Absent the media exposure requisite for passage, Pallone’s bill has yet to gain serious consideration.

Rationale for Dr. DeFelice’s Trial of Carnitine-Doxorubicin

A website created for Dr. DeFelice’s carnitine-doxorubicin study, www.carnitine-ovariancancerpromise.com, contains detailed information for patients and physicians interested in participation.

My interviews with Dr. DeFelice refer to clinical studies he conducted on carnitine in the 1960s. As I’ve said above, these studies demonstrated that carnitine dramatically protects the heart against Adriamycin. (Adriamycin is one of the anthracyclines, drugs with similar anticancer activity and cardiac toxicity. Doxorubicin and daunomycin belong to the same class.)

Dr. DeFelice’s website for the clinical trial of carnitine in ovarian cancer adds that his studies in the 1960s also showed that carnitine is effective against shock caused by various toxins – for instance, E. coli bacteria and viper venom – and that, through parenteral (intravenous) administration, carnitine prevents and treats myocardial ischemia, cardiac arrhythmias, and congestive heart failure.

All these findings, says the website, have been confirmed and published in both preclinical and clinical studies.

Here is additional background information about Dr. DeFelice and carnitine from FIM’s website (www.fimdefelice.org) and the new website. It strengthens his rationale for testing the carnitine-doxorubicin combination. None of these significant background bits appear in my interviews with him.

In 1965, while Dr. DeFelice was training to become a clinical pharmacologist at St. Vincent’s Hospital, NYC, a colleague told him about European trials reporting that carnitine helped in the management of hyperthyroidism (overactive thyroid gland). Dr. DeFelice also had training as an endocrinologist and had treated many patients with thyroid disease, so he tried carnitine in a small group of patients to learn why it helped in hyperthyroidism.

He discovered that carnitine does not block production of thyroid hormone in the thyroid itself, but thyroid hormone activity in the cells of the body – and only if the hormone levels are high. It has no effect on normal thyroid levels.
During the Vietnam War, Dr. DeFelice pursued his investigation into the multiple benefits of carnitine at the Walter Reed Army Institute of Research (WRAIR), where he had been stationed as chief of clinical pharmacology.

His "coinvestigator" in researching carnitine at WRAIR, Maj. James Vick, was a cardiovascular pharmacologist specializing in research on shock, particularly shock due to toxins. Dr. DeFelice had grown keenly interested in carnitine's potential to reverse shock generally.

At the time, the government was intent on investigating various toxins - for reasons involving both national defense and medicine. Dr. DeFelice and Maj. Vick initiated a series of acute and chronic animal studies, ranging from isolated dog hearts to intact monkeys, to determine the effect of carnitine on Adriamycin.

It was well known that Adriamycin is very effective in killing cancer cells. But its cardiac toxicity can lead to heart failure, limiting its dose significantly. Dr. DeFelice and Maj. Vick wondered: could carnitine reduce Adriamycin's toxicity? That would allow for higher doses, increasing Adriamycin's tumor kill capacity and quite possibly saving or prolonging many lives.

In every laboratory model, carnitine dramatically reduced Adriamycin's cardiac toxicity! But a key unknown remained. Did carnitine reduce Adriamycin's capacity to kill cancer cells as well? A colleague, eminent cancer researcher Dr. Sam Barranco, agreed to find out.

Dr. Barranco tested the carnitine-Adriamycin combination in exponentially growing monolayered cultures of Chinese hamster ovary cells, and obtained a surprising answer: Carnitine synergistically increases Adriamycin's kill capacity tenfold!

To see if carnitine might have the same effects on other anthracyclines, Dr. DeFelice and Maj. Vick tested carnitine on Daunomycin. Again, carnitine reduced the toxicity. Note that other investigators have confirmed these findings for Adriamycin and Daunomycin.

Success at Last! Dr. DeFelice Obtains a Clinical Trial of Carnitine in Cancer

It has taken Dr. DeFelice more than 40 years to obtain a clinical trial of the carnitine-Adriamycin combination in ovarian cancer. In my interviews with him, he repeatedly returns to how long it took, how difficult it proved to be. I quote from my October 2007 column:

I approached oncologists specializing in ovarian cancer, where the late stages are almost invariably fatal. I proposed that they try the Adriamycin – carnitine combination to see whether it could kill more ovarian cancer cells. I stressed to them that both products are on the market and readily available. None agreed. None would give an explanation for their rejection. When I proposed to these oncologists that they ask the patient about using the combination, none would do it.

Meanwhile, the thought of how many patients might survive cancer if a clinical trial of the carnitine-Adriamycin combination was conducted and the combination proved effective stayed in Dr. DeFelice's mind – reinforced by the cancer deaths of family members, friends, and others close to him.

Nearly two years ago, Dr. DeFelice arranged for Vanderbilt University (Tennessee) to study the effects of carnitine and doxorubicin on human ovarian cancer culture cells in the laboratory. The investigators found that carnitine not only increased doxorubicin's anticancer activity, but – a big surprise – carnitine by itself killed more than 50% of the ovarian cancer cells.

Discovering that carnitine kills ovarian cancer cells turned out to be the decisive step in Dr. DeFelice's quest. The final step was a recent chance meeting with Dr. Ernest Federici, a cardiologist, and program director of the Seton Hall Internal Medicine Registry (New Jersey).

Dr. Federici put Dr. DeFelice in touch with members of the fellowship program on hematology and oncology jointly operated by three area hospitals: St. Joseph's, St. Michael's, and Trinitas; and from meetings with the fellowship members, Dr. DeFelice's long-sought clinical trial of carnitine-doxorubicin in ovarian cancer soon transited from wish to reality.

Recruitment of patients is now ongoing. Dr. Michael Maroules, chairman of the hematology/oncology department at St. Joseph's, is principal clinical investigator. Dr. DeFelice is screening all patients who volunteer for the trial. To qualify, patients must have stage III or IV ovarian cancer that is resistant or refractory to taxane-platinum therapy. Refractory is defined as having tumor growth recur within six months after cessation of taxane-platinum therapy or tumor growth occurring while under taxane-platinum therapy.
Measuring reduction of tumor size over a six-month period of carnitine-doxorubicin therapy is the primary objective of the study. If the response to the carnitine-doxorubicin combination is positive, the patient will continue on this therapy. The trial is being conducted on an outpatient basis.

Comment by an Ovarian Cancer Survivor

The photograph accompanying this column shows Dr. DeFelice and Lois Myers, an 11-year survivor of ovarian cancer, on May 2, the day of the Entertainment Industry Foundation-Revlon Walk/Run for Women’s Cancers in Central Park. Dr. DeFelice had gone to Central Park to spread word of his study.

In 2000, Ms. Myers, along with two other survivors of ovarian cancer, created the nonprofit Kaleidoscope of Hope Foundation (www.kohnj.org). The foundation serves as New Jersey’s primary advocate and fund-raising organization dedicated solely to boosting the survival rate from ovarian cancer, the fourth leading cause of cancer death among American women.

I asked Ms. Myers why she was following Dr. DeFelice’s study.

“I’m a long-term activist,” she said, “always doing my best to stay current with ovarian cancer research. I’m eager to learn about new clinical trials. Given the sobering statistics associated with ovarian cancer, I feel it incumbent upon me to enlighten other survivors about potentially promising trial opportunities. This is my way of constantly sharing a message of hope with them.”

Marcus A. Cohen’s “baptism” in the whirlpools of medical politics dates to 1984, when he served as government and media liaison for patients under alternative cancer therapy. Subsequently, he has advocated broadening plausible treatment options for patients unresponsive to conventional care. A Townsend Letter columnist since 2004, he has reported and commented on a wide range of health-care topics; he is also the author of a paperback, Lyme Disease Update, published by the Lyme Disease Association in 2004.