

LE Magazine August 2003

AS WE SEE IT

FDA's Lethal Impediment

The FDA stifles the discovery and availability of life-saving therapies by making the cost of getting them approved prohibitively expensive. The FDA is a major obstacle that prevents scientific findings from being translated into therapies to stave off age-related disease.

Compared to the advancement of other technologies over the past 40 years, medicine has progressed the slowest as far as finding solutions for lethal diseases. Those in the medical establishment may debate this assertion, but the undeniable fact is that for most types of cancer and neurological diseases, there have been few substantive improvements in survival, let alone a cure.



Most of you remember attending funerals in the 1960s to 1970s of those who perished from cancer. If you thought the way I do, you would have been certain that a cure for cancer would have been found by year 2000. In fact, the propaganda being released by the cancer establishment at that time was that doctors were on the verge of eradicating most cancers. (This misguided optimism was primarily based on the premise that chemotherapy was the solution.)

When it comes to therapies designed to slow or reverse aging, the FDA still does not officially recognize aging as a disease process. That means when a company tries to gain approval to market an anti-aging therapy, it first has to overcome the hurdle of educating the FDA that aging is indeed a lethal disease. The new therapy then has to show sufficient efficacy to warrant approval. To date, no one has succeeded in convincing the FDA to approve an anti-aging drug.

In today's world of ever-expanding technological achievement, the fact that medicine remains bogged down in a regulatory quagmire is a disgrace. More than 6,000 Americans die every single day, yet most of these deaths could be prevented if it were not for the strangulation of innovation caused by the FDA, State regulatory agencies, HMOs and apathetic physicians.

In each issue of Life Extension magazine, we seek to uncover therapies that have shown efficacy in well-controlled studies, but have not yet been translated into conventional medical practice. We know our efforts have lengthened the lives of tens of thousands of Life Extension members, yet what we offer is only the tip of the iceberg when one looks at the many life-extending drugs that are denied to human beings in need.

Does Geron have an effective cancer vaccine?

Geron Corporation was originally established to develop anti-aging drugs. Their research, however, led them to discover a potentially effective cancer treatment. On March 18, 2003, Geron released the results of a study that an experimental cancer vaccine might be effective against all types of cancer. This bold announcement was based on a study published in the journal *Cancer Gene Therapy* (March 2003).

Geron's vaccine works in a relatively simple manner. It programs powerful dendritic immune cells to attack cells that express high levels of an enzyme called telomerase. It just so happens that 85% of human tumor cells overly express telomerase¹ whereas normal healthy adult cells express very low and/or transient telomerase levels. Using telomerase as the target for dendritic cells, Geron's vaccine was shown to provoke a massive attack against prostate and kidney cancer cells as well as breast, melanoma and bladder cancer.



William Faloon

What the public thinks about the FDA-

Beginning May 8, 2003, Life Extension initiated an Internet poll on a website (www.deathclock.com) that has about 400,000 new visitors each month. The

Most cancer cells require high levels of telomerase to prevent them from undergoing a healthy cellular removal process called apoptosis (programmed cell death). The concept of attacking cells high in telomerase makes cancer cells particularly vulnerable, because if they try to hide from this vaccine by making less telomerase, then they will die via normal apoptosis.

There are 558,000 people in the United States who will die of cancer over the next 12 months. Most of them know they are likely to die. We believe these cancer-stricken individuals should have the right to access any potentially effective therapy under the guidelines of an objective yet humanistic formal scientific protocol. While there is no assurance that Geron's new vaccine will cure cancer, we vehemently oppose the power given to the FDA to withhold this and other potential cancer therapies.

The cancer establishment maintains that only carefully controlled studies can establish safety and efficacy. This sounds reasonable and Life Extension agrees with this concept. The reality, however, is that the FDA's current clinical trial requirement has produced flawed data that enabled bad drugs to be approved while potentially effective drugs are denied.^{2,3,4}

It takes so long for a new drug to make it through the FDA approval process, that if Geron's new drug is effective, most cancer patients reading this column today will perish long before the vaccine ever became available. A real world example of this occurred with an anti-cancer agent for childhood leukemia called Vumon®. This drug was first studied in 1972, but only attained FDA approval in 1992.

A Phase I study of Geron's telomerase vaccine is currently underway in patients with prostate cancer at Duke University in North Carolina. As described in previous issues of Life Extension magazine, there are two fundamental problems with Phase I studies. First of all, they usually mandate that cancer patients fail all "proven" therapies first. As has been repeatedly shown in published scientific studies, most so-called "proven" cancer therapies do not cure the disease. Since Phase I studies only test for safety, extremely small doses of the anti-cancer agent are used. This dooms virtually all the terminal cancer patients who participate in Phase I trials to certain death, but it does supply the FDA with the safety data it mandates. In other words, as long as the patient dies of their cancer and not the new drug, it is now permissible to move on from Phase I to Phase II studies where a potentially effective dose of the anti-cancer drug can be given.

How the FDA perpetuates the cancer epidemic

It is clear that the bureaucratic process is incredibly long for the approval of anti-cancer and other therapies used in the treatment of life-threatening diseases. To add insult to injury, the very same approval process has geographic boundaries that create inhumane and unacceptable delays for approval of a critical drug in one country that may be a few miles away from a country where the drug is already studied, reviewed and accepted.

For example, it took years for Taxotere, one of the most impressive anti-cancer agents used to treat breast and prostate cancer, to finally gain FDA approval in the United States. This occurred despite hundreds of studies supporting its efficacy published in the European literature that were not acceptable to the FDA.

Ironically, now that Taxotere has gained FDA approval for the treatment of metastatic prostate cancer in the USA, countries such as Germany do not permit its use in the treatment of prostate cancer because no published papers on this subject have emanated from Germany. This becomes even more incredulous when one realizes that the pioneering research on Taxotere emanated from Germany's next-door neighbor France. The approval agencies such as the FDA here and its counterparts abroad are allowing bureaucratic ego, and perhaps economics, to interfere with the saving of life. Think about this! American and German physicians and scientists are engaged in a battle against a common enemy (cancer) while the respective regulatory agencies (those that approve the use of a drug) of each country use national borders to say "yes" or "no" to a live-saving drug or therapy. This is a violation of human rights within so-called civilized societies. People from all over the world should unite in protest to such atrocity.

people visiting this site are not part of any anti-FDA group, nor were they exposed to anti-FDA propaganda. These people were asked a simple question as to whether terminally ill cancer patients should have the right to any drug that might save their life. After 22,506 votes were tabulated, here are the results:

Terminally ill cancer patients

Should have access to any drug that might save their life: 89%

Should only have access to drugs approved by the FDA: 11%

We live in a constitutional republic where the people's wishes are supposed to be adhered to (as long as they don't infringe on the rights of others). If 89% of the American public thinks terminal cancer patients should have access to any drug that could save their life, then there is no reason for the law not to be changed to allow this. Companies that engaged in fraud could be prosecuted under consumer protection laws that already exist. The FDA could post its opinion about the safety and efficacy of purported cancer therapies on their website (www.fda.gov). The civil litigation risks to companies that knowingly sold bogus products would preclude large-scale unsavory activities that a minority of Americans fear. The greater fear Americans face is being diagnosed with cancer only to find out that a potential cure is too many years away to save their lives.

Of interest was an identical poll on Life Extension's website in which 98% of people voted to allow cancer patients to have access to any drug that might save their life. This is not surprising considering health conscious people's animosity towards the FDA.

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Not only do FDA policies delay life-saving drugs from being approved, but they often keep effective medications off the market forever! If a small company like Geron were to run out of money before they could conclude the expensive clinical trials, their vaccine research program could come to a grinding halt.

Contrast this with a libertarian policy of giving dying cancer patients the choice to try Geron's new vaccine immediately. Under this system, it could be possible to determine whether the vaccine worked within months, as opposed to the multi-year period currently mandated by the FDA. If it worked, then millions of cancer patients lives would be saved. If the vaccine failed, then these terminally ill cancer patients will have died, as they would have anyway.

The FDA does have a "compassionate use" exemption that allows cancer patients access to experimental therapies. The problem is that the FDA mandates that these cancer patients first fail so-called "proven" therapies. When cancer cells are exposed to "proven" therapies like radiation or chemotherapy, they mutate in a way that causes them to become super-resistant to future therapies. The patient's healthy cells (including dendritic cells of the immune system) are often seriously impaired when exposed to these "proven" therapies, thus making therapies like Geron's telomerase vaccine less likely to be effective.

Promising ovarian cancer drug

Ovarian cancer kills more than 14,000 women each year. What makes this type of cancer so insidious is that there are few early warning signs, meaning the disease is usually well advanced when diagnosed.

In May 2003, an announcement was made about a drug called phenoxodiol that induced cell death in 100% of ovarian cancer cells, including those cells resistant to chemotherapy drugs such as Taxol® and carboplatin. The tests were conducted on human cell lines at Yale University School of Medicine.

Phenoxodiol was discovered when scientists were studying the anti-cancer properties of isoflavonoid plant extracts. They used data collected from this research to synthesize phenoxodiol. This drug works by altering a signal pathway in cancerous cells that prevent them from undergoing apoptosis (programmed cell death). These findings indicate that the drug could be successful at treating other cancer types as well. The study was published in the May 1, 2003, issue of *Oncogene*.

As stated earlier in this article, FDA-mandated Phase I studies involve giving advanced cancer patients low doses of a new drug to verify safety. The dose is usually so small that the drug has no chance of curing end-stage cancer victims. In the case of phenoxodiol, five Phase I human trials have been completed with few if any side effects. Preliminary results of a trial conducted at the Cleveland Clinic found that more than half of the 10 patients tested on the experimental drug showed some response. Each of these patients had different types of advanced cancer that did not respond to chemotherapy.

It is very difficult to kill cancer cells once they have become resistant to chemotherapy. That is because the cancer cells not killed by chemo develop multi-survival mechanisms that make them extremely difficult to eradicate. What has surprised researchers at Yale was that phenoxodiol killed all ovarian cancer cells (in the laboratory setting), regardless of their immunity to chemo agents.

A phase II trial using phenoxodiol is under way at Yale for women with chemo-resistant ovarian cancer. In this Phase II study, a therapeutic dose of the drug is given with the hope of improving survival or achieving a complete response. The researchers also tested phenoxodiol in mice and found that when dosed at 20 mg/kg every day for six days there was a three-fold reduction in tumor mass compared to a control group. No side effects were noted.

Phenoxodiol functions via several unique mechanisms to induce cancer cells to undergo programmed cell death (apoptosis). Normal cells undergo apoptosis in a controlled manner so they can be replaced with healthier functioning cells. Cancer cells, on the other hand, have gene mutations that prevent them from self-destructing. The ultimate goal of a cancer therapy is to induce malignant cells to undergo apoptosis, instead of indefinitely proliferating out of control.

Under today's antiquated system, a new drug cannot be marketed until it has been thoroughly investigated in clinical trials. These trials can take many years to complete. The results of these numerous trials are then submitted in a new drug application to the FDA. The FDA sends these results to a committee for review. The committee may ask for more studies, reject the application or recommend the drug be approved. The FDA then takes the committee's report and decides whether to approve the drug as safe and effective. This can happen quickly, or it can become bogged down in the FDA's regulatory quagmire. Until the FDA reaches its final verdict, no marketing can take place. It can take 10 or more years after a promising cancer drug has been

discovered before the FDA is even in a position to approve it. One reason for this long delay is that after the drug as been discovered, money has to be raised to fund the clinical studies and negotiations with the FDA have to be completed to get approval for the study design itself.

Every month, more than 1,000 women succumb to ovarian cancer. Phenoxodiol was discovered in April 2002. If this drug turns out to be even partially effective, the delay in getting it into cancer victims' hands would have caused thousands of needless deaths.

Saving cancer patients' lives

Large amounts of monies have been spent on cancer research, yet the findings from this research are not being incorporated into clinical oncology practice. To help remedy this problem, The Life Extension Foundation searches the peer-reviewed scientific literature in order to interpret and compile this data into life-saving protocols.

We have completely updated our reference book, Disease Prevention and Treatment. This 1,500-page "edifice" contains an abundance of information about better ways to treat cancer that are often overlooked by oncologists. While this book provides novel guidance about many different disorders, there are 295 pages dedicated to informing cancer patients of what they should do to improve their chances of achieving a remission or complete response.

It is sad to think of how many cancer patients die when potential solutions to their disease are already published in the scientific literature. The new Disease Prevention and Treatment reference book breaks down the barriers of ignorance that causes those with cancer and other life-threatening diseases to die while effective therapies already exist to better treat their disease.

The research, writing and editing of the 2003 edition of Disease Prevention and Treatment consumed tens of thousands of hours at a cost of over one million dollars. Commercial publishers do not spend this kind of time or money producing health books. It is our intense dedication to finding solutions for our members' health problems that motivated us to publish such a comprehensive text.



For longer life,

William Faloon.

Editor's Note: Just as we were going to press, the FDA released news of an initiative to speed the identification and development of new cancer drugs. It appears that the FDA is in the beginning stages of a long overdue reform of Byzantine bureaucracy in order to properly fulfill its public service mission. We have printed the news release in its entirety on this page. As you will read, what the FDA proposes is not nearly enough. The FDA, in essence, is trying to put out a forest fire with a garden hose.

NCI and FDA Announce Joint Program to Streamline Cancer Drug Development

Under an agreement between the Food and Drug Administration (FDA) and the National Cancer Institute (NCI), which is part of the National Institutes of Health (NIH), the two agencies will share knowledge and resources to facilitate the development of new cancer drugs and speed their delivery to patients.

FDA Commissioner Mark McClellan, M.D., Ph.D., and NCI Director Andrew von Eschenbach, M.D., said today that they will establish a multi-part Interagency Agreement to enhance the efficiency of clinical research and the scientific evaluation of new cancer medications. The planned agreement, to be announced formally at this week's meeting of the American Society of Clinical Oncology in Chicago, will enhance existing programs and add new joint programs to the existing close cooperative relationship between NCI and FDA, both of which are part of the Department of Health and Human Services (HHS).

"This new collaboration between two key HHS agencies means that federal researchers and regulators will be working together more effectively than ever before," said HHS Secretary Tommy Thompson. "The result will be a more unified, integrated, and efficient approach to the technology development and approval process at a critical time for a disease that affects too many lives," Secretary Thompson said.

The agreement offers potential benefits for the more than one million Americans who are diagnosed with cancer each year. "The FDA is committed to finding better ways to get safe and effective treatments to patients with life-threatening diseases as quickly as possible," said McClellan. "At a time when the opportunities to reduce the burden of cancer are greater than ever, sharing tools and resources with our colleagues at the National Cancer Institute will help us fulfill that mission," he said.

"The effort between NCI and FDA in cancer therapies is a prototype that should inform and eventually be applied across all areas of research," said NIH Director Elias A. Zerhouni, M.D. "Dr. McClellan and I are committed to NIH and FDA working closely to find innovative ways to more rapidly make the fruits of our discoveries available to the public."

"The collaboration will help the two agencies take full advantage of their combined knowledge base at a time when many new kinds of anti-cancer agents are in the pipeline," said von Eschenbach. "Molecularly targeted drugs and other novel agents offer great promise, but they also present new challenges that require more collaboration between those involved in their discovery and development," he said.

References

1. Wang Z, Ramin SA, Tsai C, et al. Telomerase activity in prostate sextant needle cores from radical prostatectomy specimens. *Urol Oncol* 6:57-62, 2001.
2. A Life-Saving Drug Discovered In the United States Over 20 Years Ago Is Saving Lives Around the World...But Not Yet Here. *Life Extension* magazine, July 2001, p. 54-62.

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