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My name is Joscelyn Silsby and I am the Director of Programs at the Cancer Research Foundation of America, a national non-profit organization focused on cancer prevention through scientific research, education and early detection, and a former researcher at Georgetown University's Lombardi Cancer Center. I appreciate this opportunity to share with you our perspective on the value of tamoxifen and the great risk of labeling it "a substance known to be carcinogenic to humans" without further research.

The immediate impact of this decision would be negative and far-reaching: affected groups include breast cancer survivors many of whom are tamoxifen users, women at high-risk for breast cancer and women recently diagnosed with breast cancer for whom tamoxifen is prescribed as adjuvant therapy. Further implications include all women, their children, their families and their friends as in many instances tamoxifen is a lifeline, drastically increasing cancer survivorship.

History: Tamoxifen and Breast Cancer

This year more than 180,000 American women will be diagnosed with breast cancer and more than 43,000 American women will die from the disease. While mortality rates have declined over the last five years, there are far too many women dying from breast cancer. And, in the absence of a cure, women seek clinically effective methods of treating breast cancer.

Tamoxifen, the most widely prescribed breast cancer treatment in the world, has been a safe and effective method for treating breast cancer for over 14 years. The drug is used in 100 countries by millions of women and more than 100,000 women have participated in clinical trials testing tamoxifen. In fact, tamoxifen is considered to be the "most studied drug available for breast cancer." Studies have suggested that the drug is responsible for a 37-40 percent reduction in contralateral breast cancer. Some clinicians have suggested that the drug's best days are still to come as research determines the value of tamoxifen in preventing breast cancer in high-risk populations.

Messages about the possible carcinogenic properties of this drug will have a negative impact on the health of thousands of women currently taking

tamoxifen. Provoking unnecessary fear and creating anxiety throughout the breast cancer community may even cause women to discontinue the treatment without consulting their physicians. If women who are now breast cancer survivors and are benefiting from tamoxifen therapy suddenly stop taking it, they may suffer and die unnecessarily.

Research

Current research by Dr. Leslie Bernstein of the University of Southern California shows an *association* between tamoxifen and endometrial cancer. To be listed on the National Toxicology Program's *Report on Carcinogens*, there must be "sufficient evidence of carcinogenicity from studies in humans which indicates a *causal* relationship between exposure to the agent, substance or mixture and the human cancer." Without further research, we are not at a point where a *causal* relationship has been established. Furthermore, Dr. Bernstein found that the relationship between tamoxifen and endometrial cancer is duration-related and that other risk factors such as obesity and hormone replacement therapy are associated with increased risk of endometrial cancer. This may mean that specific groups of women taking tamoxifen are at increased risk, but not all women.

In addition, the Breast Cancer Prevention Trial (BCPT) is studying the chemoprotective effect of tamoxifen. This will provide valuable insight into the benefits and risks of tamoxifen. As noted by Peter Greenwald, acting NCI director of cancer prevention, "No intervention is totally without risk, and tamoxifen does have some potential side effects. It is important to keep in mind the dimensions of potential benefits."

Choice and Informed Consent

When women with breast cancer receive combination treatments of radiation and chemotherapy, they are told both orally and in writing that there is a three percent chance of developing a secondary malignancy. Similar information about treatment risks and potential for secondary malignancy is also provided for patients undergoing treatment for other types of cancer, (Karen Steakley, Clinical Trials Research Coordinator, The Lombardi Cancer Center).

Risk factors are a large part of treatment decisions that cancer patients, their families and doctors are faced with every day. These decisions almost always involve the patient assessing risks and potential benefits. For example, now that women can find out if they are genetically predisposed to breast cancer through genetic testing for the BRCA I and II genes, women who test positive face many questions about their risk and quality of life: *Should I have a prophylactic mastectomy so that the cancer never has a chance to develop?* Even women who do not have breast cancer or the BRCA I or II gene, but are at high risk for developing the disease, may face this type of decision: *Should*

I participate in a chemoprevention trial to take tamoxifen, even though there is also a slight risk of developing endometrial cancer?

These are decisions that women need to make for themselves in consultation with their families and doctors. If you make that choice more complicated for them by putting tamoxifen on the list of known human carcinogens before the results of pending studies are available, you are creating unnecessary fear and perhaps even denying women the opportunity to take control of and deal proactively with the risk that they face every day: the risk that this devastating disease will come back and be deadly.

The Public Health of Women with Breast Cancer

Putting tamoxifen on the list of substances "known to be carcinogenic to humans" could create fear and anxiety among the public BEFORE information is available about other possibly contributing factors. For example, obesity and hormone replacement therapy in combination with tamoxifen may increase risk of a second malignancy. Out of fear and lack of further information, women may end their treatment prematurely, without consulting their physician.

Given that tamoxifen is the only antiestrogen cleared by the Food and Drug Administration for adjuvant therapy of breast cancer, taking tamoxifen from women would put them at increased risk and they would not have the opportunity to make a choice through a careful process of examining all options or weighing the risks and benefits. This may unduly compromise "informed" consent and informed decision making among vast numbers of women, which in the long run compromises public health.

Conclusion

The data and my professional experience has convinced me and my colleagues at the cancer Research Foundation of America that the National Toxicology Program would be ill advised to classify tamoxifen as a human carcinogen. The drug's carcinogenic profile is well characterized and, more importantly, its benefit is well understood. Further research is needed before taking this valuable lifeline away from American women.