Breast Cancer Chemotherapy: Adverse Effects Higher Than Reported in Clinical Trials

Breast cancer probably generates a higher than normal amount of informed decision-making on the part of consumers, largely because the disease generates a higher than normal number of clinical trials. And chemotherapy has been the topic of many, if not, most of these trials over the last two decades. A new study illustrates a major barrier to informed decision-making. It found that the incidence of serious adverse effects* is actually much higher in “the real world” than is reported in clinical trials.

The finding came from a new study that determined the prevalence of serious adverse effects by looking at the insurance claims of 12,239 women with breast cancer newly diagnosed between 1998 and 2002, aged 63 years or younger. Of these, 4,075 women were treated with chemotherapy within 12 months of their initial diagnosis. The study was led by Michael J. Hassett, MD, MPH, Center for Outcomes and Policy Research at Dana-Farber Cancer Institute, Boston, and published last month in the Journal of the National Cancer Institute.

Dr. Hassett and colleagues found that the women with breast cancer who received chemotherapy were more likely to be hospitalized or visit emergency rooms than those who had not (61% for those given chemo vs. 42% for those not given chemo). The more common types of serious adverse reactions were fever or infections, low blood counts, dehydration, nausea, vomiting, diarrhea, anemia, and deep-vein blood clots. This study was funded by a grant from the U.S. Agency for Healthcare Research and Quality.

Several explanations are offered for why this study revealed higher rates of serious adverse drug effects than are typically shown in breast cancer chemotherapy trials. For example, it has long been known that people who participate in clinical trials typically do better than people who do not. This is because they are usually healthier to begin with, and therefore less likely to experience a toxic reaction to chemotherapy. Most cancer trials would, for example, exclude people with other illnesses.

Furthermore, cancer trials are designed to determine the success of a treatment, such as disease-free survival or overall survival, rather than its toxicities. The trials do not usually have enough participants to fully explore the prevalence of adverse drug effects, wrote Hassett and colleagues. If only a few thousand people are given chemotherapy, then uncommon toxicities might be overlooked or they might be detected but inaccurately estimated to be rare.

Late Adverse Effects Go Unreported

In the editorial that accompanied the study, John K. Erban and Joseph Lau, MD, cite a 2001 study of breast cancer patients that found most would opt for chemotherapy, even when their oncologists inform them of the low odds of benefit, “…though the improvements in survival may be below 5%, women will often accept chemotherapy for as little as a 1%-2% survival advantage.” (It should be noted, however, that such women are unlikely to be informed of the treatment’s harms which might in some cases cancel the 1-2% survival advantage.)

Erban and Lau warned physicians to be vigilant about the potential for adverse effects of new drugs that might not show up until years after the treatment regimen is over. They are especially concerned about the growing use of so-called targeted drugs, such as Herceptin and Femara, which are prescribed for certain types of breast cancer to prevent recurrences. “These newer molecular drugs are increasingly effective against breast cancer and less toxic in the short term,” wrote Erban and Law.

The editorialists warn that this will encourage drug companies to “push them to market, and there will be few incentives for longer term toxicity studies.” Because clinical trials are designed to determine a drug’s benefits (e.g., prolonged survival), they suspect that there will be no incentive to track what is known as the “late adverse effects” of these newer drugs. ±

*The definition of a serious drug-related adverse effect is: Any untoward medical occurrence that is related to drug use and results in death or significant disability/incapacity; requires hospital admission or prolongation of existing hospital stay; or is life threatening