No Elevated Risk of Invasive Cancers Seen in JIA

BY AMY ROTHMAN SCHONFELD

PHILADELPHIA — Children followed for an average of 14 years after diagnosis of juvenile idiopathic arthritis showed no increased risk of invasive cancers, according to Dr. Ann Clarke.

Studies have shown an increased risk of malignancy—particularly lymphoma and lung cancer—in adult rheumatoid arthritis patients. This is the first assessment of cancer risk in children, she said at the annual meeting of the American College of Rheumatology.

In this study, the investigators analyzed juvenile idiopathic arthritis (JIA) registries maintained at two pediatric rheumatology centers located in Saskatoon, Sask., and Winnipeg, Man., between 1974 and 2006. Clinic patients were linked to regional tumor registries to determine any cancer occurrence. The observed malignancy incidence was compared with the expected incidence, based on general population cancer data, said Dr. Clarke of McGill University, Montreal.

The sample included 1,168 children with JIA (67.3% girls), most of whom were diagnosed when they were about 9 years old. Children were followed from the time of diagnosis until their death, their development of cancer, or the completion of the study interval at the end of 2006, for a total of 16,396 patient-years.

On the basis of regional age- and sex-specific general population cancer rates, the researchers expected six invasive cancers to be identified during the average 14 years of follow-up. In actuality, no cancers were found.

'The benefits of anti-TNF agents are very great and the risk to the individual child of developing a malignancy is almost vanishingly small.'

The investigators noted that the potential effect of medications on possible cancer risk is still not precisely known. In this cohort, about one-quarter of the children had been exposed to disease-modifying antirheumatic drugs, most commonly methotrexate. In all, 19 children had taken anti–tumor necrosis factor medications.

The U.S. Food and Drug Administration required stronger black boxed warnings in prescribing information that use of anti–tumor necrosis factor agents seemed to be associated with an increased risk for cancer among children

Dr. Thomas J.A. Lehman said in an interview that Dr. Clark's study illustrates that the risk of cancer in children receiving anti-TNF agents for JIA is very low. However, the anti-TNF warning by the FDA applies to children who received an anti-TNF agent for any reason not only children with juvenile arthritis.

A significant proportion of the children with reported malignancies noted by the FDA had inflammatory bowel disease, not juvenile arthritis. At the same time the FDA was able to draw on a much larger population of patients than the present study, said Dr. Lehman, chief of the division of pediatric rheumatology at the Hospital for Special Surgery in New York.

"Our obligation as physicians is to make sure families understand that the benefits of anti-TNF agents are very great and the risk to the individual child of developing a malignancy is almost vanishingly small. This study had no cases in all the children seen. We don't have adequate data to guarantee that there might not be a small increase in the risk of malignancies, but we do have adequate data demonstrating the dramatic benefits of anti-TNF agents.

Dr. Lehman, who is also professor of clinical pediatrics at New York Weill Cornell Medical Center, is on the speakers bureau for Wyeth Pharmaceuticals and Amgen Inc., which market etanercept, and Abbott Laboratories, manufacturer of adalimumab.

Dr. Clark noted that one limitation of the study was its predominantly white (80.5%) and First Nations/Inuit (16.9%) enrollment. She reported no conflicts. ■

Breast Cancer Survivors Often Report Persistent Pain

BY MARY ANN MOON

Nearly half of women with breast cancer report persistent pain, and 58% report sensory disturbances up to 3 years after surgery, according to Dr. Rune Gärtner of the University of Copenhagen and her associates.

In more than half of these cases, the women describe their pain as moderate to severe, Dr. Gärtner and her associates said (JAMA 2009;302:1985-92).

The researchers assessed persistent breast cancer pain in a nationwide study of 3,253 Danish women who underwent surgery for unilateral primary breast cancer in 2005-2006. They categorized the patients into 12 treatment groups according to the type of surgery, adjuvant radiotherapy, and adjuvant chemotherapy they received.

Surgeries included breast-conserving surgery with either sentinel node dissection or axillary node dissection and mastectomy.

The mean interval between the surgery and this pain assessment was 26 months (range, 13-41 months). Very few of these patients were receiving aromatase inhibitors when they were assessed, which are known to cause muscular and joint pain.

A total of 1,543 women (47%) reported pain in the area of the affected breast, the axilla, the arm, or the side of the body. Eighteen percent reported pain in one of these areas, 28% in two areas, 28% in three areas, and 26% in all four areas.

Thirteen percent of the women reported severe pain and 39% reported moderate pain, while 48% reported light pain. Among the women who reported severe pain, 77% had pain every day, Dr. Gärtner and her colleagues said.

One-fifth of the study subjects had consulted a physician about the pain during the preceding 3 months. A total of 28% had taken analgesics, and 26% had received other therapies, such as physiotherapy or massage.

Fifty-eight percent of women reported persistent sensory disturbances. The rate was lowest (31%) among women who had breast-conserving surgery with sentinel node dissection, and it was highest (85%) among women who had breast-conserving therapy with axillary node dissection and radiotherapy.

"The most important determinant of persistent pain and sensory disturbance was young age (less than 40 years)," they noted. Radiotherapy also was an independent and significant risk factor for persistent pain.

Taken together with the results of previous research, these findings indicate that "chronic pain after breast cancer surgery and adjuvant therapy may predominantly be characterized as a neuropathic pain state and [is] probably related to intraoperative injury of the intercostal-brachial nerve," Dr. Gärtner and her colleagues said.

In the future, using nerve-sparing surgical and radiotherapy techniques may reduce the risk of persistent breast cancer pain, they added, but larger, more detailed studies are needed.

No conflicts of interest were reported. The work was supported by grants from the Danish Cancer Society, Breast Friends, and the Lundbeck Foundation. ■

Polypharmacy Found Common Among Breast Cancer Survivors

BY DOUG BRUNK

SAN DIEGO — Breast cancer survivors take an average of eight medications or supplements, results from a survey of nearly 400 women showed.

"This study shows that there is a need to evaluate medications women are taking prior to the start of cancer treatment to promote discussion and education about drug-drug interactions that can impact treatment," Julie L. Otte, Ph.D., said in an interview after her poster presentation at the annual meeting of the North American Menopause Society.

The majority of research has focused on diseases and medications that are related to the prevalence of cancer, said Dr. Otte, a nurse who is a postdoctoral fellow focusing on behavioral oncology at Indiana University School of Nursing, Indianapolis. "However, there is little research in the field of pharmacogenetics regarding drug-drug interactions and cancer treatment and survivorship," she said.

To investigate the association, she and her associates reviewed prescription, herbal, and over-the-counter medications reported in baseline questionnaire data from the COBRA (Consortium on Breast Cancer Pharmacogenomics) randomized clinical trial that evaluated the pharmacogenetics and toxicities of exemestane and letrozole for the treatment of breast cancer. The sample included 389 female breast cancer survivors with a mean age of 59 years and a mean body mass index of 37 kg/m^2.

The top five noncancer comorbid conditions reported by the study participants were drug allergies (50%), high or low blood pressure (41%), high cholesterol (38%), a history of bone fracture (34%), and arthritis (29%).

The women reported that they were taking an average of eight medications or supplements per day. The five most common therapeutic categories represented were vitamins and herbal supplements (39%), cardiac drugs (16%), medications for pain and inflammation (13%), other (9%), and drugs for psychological conditions (6%).

"Although we expected the number of comorbid conditions to increase with age, requiring several prescription medications, it was interesting that the majority of medications reported were over-the-counter" herbals or supplements, and not prescriptions, Dr. Otte commented. Because these data were collected before the patients started a clinical trial, it is unclear whether patients would divulge the same information to their practitioners. The extent of polypharmacy is unclear.

"All of these questions prompt the need for further investigation and study to better educate patients on the possible harm of certain drug interactions," Dr. Otte said.

She noted that there was potential for underreporting of prescription and over-the-counter medications by some participants.

Dr. Otte reported that she had no conflicts of interest. The study was funded by the National Cancer Institute. ■