

Finasteride Reduces Risk of Most Frequently Detected Intermediate- and High-grade Cancer

There is evidence from a randomized trial, reported in the May 1 issue of *Urology*, that finasteride significantly reduced the risk of prostate cancer relative to placebo across multiple Gleason scores (4–7). The Prostate Cancer Prevention Trial randomized 18,882 men 55 years and older with a prostate-specific antigen level of less than 3.0 ng/mL and normal digital rectal examination findings to receive finasteride 5 mg daily or placebo. Analysis of prostate cancer data from evaluable patients obtained within 7 years plus 90 or less days of randomization was performed. Polytomous logistic regression analysis of prostate cancer risk, which allows for simultaneous estimation of the probability of multiple diagnoses, was performed across individual Gleason scores using no prostate cancer as the reference group; no adjustment for multiplicity was made. Treatment, age, race, first-degree family history of prostate cancer, baseline prostate-specific antigen level, post randomization variables of prostate volume, and the number of biopsy cores at biopsy as covariates were evaluated. The results of the analysis showed that finasteride reduced prostate cancer risk, with a 58% reduction in Gleason score 5 prostate cancer risk ($P<.0001$), a 52% reduction in Gleason score 6 prostate cancer risk ($P<.0001$), and a 22% reduction in Gleason score 7 prostate cancer risk ($P=.0368$). Finasteride did not have a significant effect on the risk of Gleason score 2, 3, or 8–10 cancer.

Longer Progression-free Survival Seen with nab-Paclitaxel Compared with Docetaxel as First-line Therapy for Metastatic Breast Cancer

Results from a phase II study of metastatic breast cancer, reported in the May 26 issue of *Journal of Clinical Oncology*, show that nab-paclitaxel, a nano-sized albumin-bound form of paclitaxel, produces significantly higher antitumor activity compared with solvent-based paclitaxel. This randomized, multicenter study assigned 302 patients with previously untreated metastatic breast cancer to nab-paclitaxel 300 mg/m² every 3 weeks, 100 mg/m² weekly, or 150 mg/m²

weekly or docetaxel 100 mg/m² every 3 weeks. Study results demonstrated significantly longer progression-free survival (PFS) with nab-paclitaxel 150 mg/m² compared to docetaxel, by both independent radiologist assessment (12.9 vs 7.5 months; $P=.0065$) and investigator assessment (14.6 vs 7.8 months; $P=.012$). The 150 mg/m² and 100 mg/m² doses (49% and 45%, respectively) of nab-paclitaxel had a higher overall response rate compared with docetaxel (35%), but the difference was not statistically significant. PFS and overall response rate did not differ in patients receiving nab-paclitaxel given every 3 weeks versus docetaxel. The independent radiologist and investigator review determined that the disease control rate was significantly higher for patients receiving either dose of weekly nab-paclitaxel versus docetaxel. The incidence of grade 3/4 adverse events was less frequent in the nab-paclitaxel groups, except for peripheral neuropathy, which was similar in frequency and grade in all study arms. Study findings concluded that weekly nab-paclitaxel demonstrated superior efficacy and safety compared with docetaxel, with a significant prolongation of PFS in patients receiving nab-paclitaxel 150 mg/m² versus those receiving docetaxel 100 mg/m².

Immunotherapy Reduces Relapses and Improves Survival of High-Risk Pediatric Neuroblastoma

A phase III Children's Oncology Group study conducted in children with neuroblastoma found that the addition of an investigational immunotherapy, ImmRx, to standard treatment significantly reduced the risk of relapse and increased overall survival by 20%. Two years after treatment, approximately 2/3 of children in the immunotherapy arm were alive without relapse versus less than half of those who were given standard treatment alone ($P=.0115$). Each study arm consisted of 113 patients who had either complete response or a very good partial response to chemotherapy, surgery, and myeloblastic consolidation with stem cell rescue for newly diagnosed high-risk neuroblastoma. The control arm received a standard regimen of 13-cis-retinoic acid and the experimental group received retinoic acid plus ImmRx.

The findings, which were presented at the 2009 American Society of Clinical Oncology meeting, demonstrated a 2-year overall survival rate of 86% in patients

receiving standard care plus immunotherapy versus 75% in patients receiving standard treatment alone ($P=.0223$). The event-free survival at 2 years was also significantly higher for patients randomized to ImmRx (66% vs 46%; $P=.0115$). Based on the benefits seen in the interim analyses, randomization was stopped after 226 patients and the study was continued as an open-label trial. Dr. Yu, a professor at the University of California in San Diego, stated that the 20% improvement in overall survival has affirmed the immunotherapy as the new standard of care. This immunotherapy, which consisted of an antibody-based vaccine-chimeric anti-GD2 antibody ch14.18, targets a specific glycolipid on neuroblastoma cells called GD2 to a standard cis-retinoic acid treatment in the trial. Presently, it is not approved by the U.S. Food and Drug Administration. The children who were given the vaccine were also given granulocyte-macrophage colony stimulating factor and interleukin-2 to stimulate immune cells to attack the cancer. Although the standard therapy was well tolerated, there were side effects with the immunotherapy: grade 3 pain (21%), vascular leak syndrome (7.3%), and allergic reactions (7.2%) were observed.

The immunotherapy is also being studied in other cancers such as melanoma and sarcoma; it is the first to demonstrate that combining human monoclonal antibodies with cytokines can be an effective treatment of cancer.

Stem Cell Protein Offers a New Target for Drug Development

Dr. George Daley and colleagues from the Stem Cell Program at the Children's Hospital Boston found that a protein found in embryonic stem cells called LIN28 offers a possible new target for cancer drug development. The protein regulates a group of tumor-suppressing micro-RNAs called let-7. Increasing LIN28 production in a cell prevents let-7 from maturing and therefore makes the cell more immature and stem-like. These characteristics also make a cell more cancerous, and because low levels of mature let-7 have been linked with breast and lung cancer, this finding suggests that LIN28 may be oncogenic. These results, reported in the May 31 issue of *Nature Genetics*, showed that LIN28 can transform cells to a cancerous state and that it is abundant in various cancers such as liver cancer, ovarian cancer, chronic myeloid leukemia, germ cell tumors, and Wilm's tumor. The researchers believe that LIN28 and LIN28B, a related protein, may be

involved in approximately 15% of human cancers. Blocking or suppressing LIN28 may make it possible to restore the let-7 family's natural tumor-suppressing action. This discovery provides a new target to attack, particularly in the most resistant cases of cancer. Daley and colleagues are currently searching for ways to inhibit LIN28, which would provide novel treatments for advanced cancer.

Standard Adjuvant Chemotherapy is Best for Breast Cancer Patients Over 65 Years of Age

According to a report in the May 14 issue of the *New England Journal of Medicine*, standard adjuvant chemotherapy is superior to capecitabine (Xeloda, Roche) in patients with early-stage breast cancer who are 65 years or older. The investigators, led by Dr. Hyman Muss, observed that breast cancer in older women is not always managed according to treatment guidelines, and many oncologists prefer less aggressive adjuvant chemotherapy for this type of patient population. The researchers compared the efficacy of 2 standard chemotherapy regimens with that of capecitabine in women 65 years or older who had operable adenocarcinoma of the breast and an expected survival time of more than 5 years. The enrollment was stopped after 624 participants because an interim data analysis showed the inferiority of capecitabine. At the time, 133 patients were given cyclophosphamide, methotrexate, and fluorouracil (CMF), 184 were given doxorubicin plus cyclophosphamide, and 307 were randomly assigned to receive capecitabine. After a median follow-up of 2.4 years, the rates of relapse and death were almost twice as high in patients receiving capecitabine versus those receiving either standard chemotherapy. The superiority of standard chemotherapy was seen most prominently in the subgroup of women with hormone-receptor-negative tumors. In this subgroup of patients who received capecitabine, the relapse risk was more than 4 times higher and the risk of death was more than 3 times as much when compared with other patients. The incidence of adverse events was higher in the standard chemotherapy regimen groups with at least one grade 3 or grade 4 toxicity observed in 70% of the CMF group, 60% of the doxorubicin plus cyclophosphamide group, and 34% of the capecitabine group. Two deaths were related to capecitabine. Dr. Muss and colleagues stated that their findings are in line with the belief that adjuvant chemotherapy improves survival in patients over 65 years of age.