Biomedicine

Elizabeth Pennisi reports from Orlando, Fla., at the annual meeting of the American Society of Clinical Oncology

Yew drugs show their mettle

Taxol, a compound derived from the bark of the Pacific yew, may be a useful first chemical defense against tumors as well as a last-resort cancer treatment. Five studies conducted in recent years show that taxol can cause remission of breast and ovarian tumors unresponsive to other drugs (SN: 2/22/92, p.124; 4/18/92, p.244). Now, researchers are finding that for ovarian cancer, taxol works better than the standard drug treatment.

In a study involving 388 women with ovarian cancer, tumor tissue shrank or disappeared in 73 percent of women taking taxol and cisplatin, compared with 59 percent of those receiving cytoxan and cisplatin, reports William P. McGuire III of the Johns Hopkins Oncology Center in Baltimore. On average, tumors took three months longer to reappear in women treated with taxol than in those receiving the other regimen. "This should become the standard of care for this group of patients," he concludes.

Some have expressed concern about side effects — notably numbness or tingling in toes and fingers and a reduction in infection-fighting blood cells — due to taxol's toxic effect on bone marrow. But McGuire and others point out that these effects can be managed with other medications and that taxol is often tolerated better than many cancer drugs now in use.

For example, in a new study conducted by Charles Link and his colleagues from the National Cancer Institute in Bethesda, Md., bone marrow in 48 women fared better after prolonged treatment with taxol when the patients received a growth factor at the same time. These women suffered from ovarian cancer that did not respond to other drugs. The growth factor, a protein called granulocyte colony stimulating factor, protected bone marrow, so the women maintained adequate numbers of white cells and platelets despite a near doubling of the taxol dose and more than a year of taxol therapy, says Link.

Several groups are testing another yew compound, this one derived from the harvested needles. Pierre Fumoleau of the Nantes (France) Cancer Center and his colleagues observed a 73 percent response in 33 patients with advanced breast cancer who received this experimental drug, known by the brand name Taxotere. Dutch and Canadian researchers also report that Taxotere proved very active against breast cancer.

Mixed reviews for growth factors

In addition to malignant cells, many cancer-killing drugs also destroy some normal cells — in particular, those in the bone marrow that develop into blood cells. Scientists are assessing how to use growth factors to help the body recover from these and other damaging effects of chemotherapy, but a new analysis suggests the compounds may not be worth the cost.

Researchers at Indiana University Medical Center in Indianapolis reviewed results from two studies, one conducted by them, the other conducted at Duke University Medical Center in Durham, N.C. Both studies focused on the effects of a bone marrow growth factor administered to people with small-cell lung cancer. The growth factor increased treatment costs — in some cases more than sixfold — but did not improve the overall survival rate of those in the study, says Indiana's Edward P. Fox.

Other studies by the two research groups have now determined safe doses of a newer growth-factor product, human stem cell factor, which is produced by genetically engineered bacteria. When given to women undergoing drug therapy for breast cancer, this growth factor led to modest increases in infection-fighting blood cells and in other types of blood cells, but it also stimulated allergic reactions, report Michael S. Gordon and his colleagues at Indiana University. Jeffrey Crawford and his co-workers at Duke observed similar changes when they gave the compound to patients undergoing therapy for non-small-cell lung cancer.

Another growth factor, called PIXY321, is two molecules in one. It contains granulocyte-macrophage colony stimulating factor linked with interleukin 3. In patients who have undergone an autologous bone marrow transplant, this "fusion" molecule speeds the replacement of red blood cells by about two weeks and of platelets by three days, compared to those receiving no growth factor or treated with the granulocyte-macrophage colony stimulating factor alone, reports Julie M. Vose of the University of Nebraska Medical Center in Omaha.

Soluble cancer drugs: Just add phosphate

Many anticancer drugs fail to live up to their potential simply because they do not dissolve well in water. Only by mixing these fat-soluble compounds in oils, detergents, and other substances that cause unwanted side effects can pharmacologists keep them in the bloodstream long enough to reach the tumor targets.

Now, by adding a phosphate side group to a commonly used anticancer compound called etoposide, researchers have managed to get rid of all other chemical baggage. As a result, cancer specialists can explore different and possibly more effective treatment regimens involving this compound, says Daniel R. Budman of North Shore University Hospital-Cornell Medical College in Manhasset, N.Y. The phosphate imparts a charge to the molecule so that it readily dissolves in water.

Budman and his colleagues administered the water-soluble version to 25 people whose solid tumors had not responded to other treatments. The researchers proved they could deliver the drug faster (in five, instead of 45, minutes) and in higher doses with fewer complications than is possible with etoposide in its original form, says Budman. After injection, enzymes in the blood chop off the compound's phosphate group and, within 10 minutes, restore the drug to its original, active form. "Then it [follows] the same pharmacology as the older drug," Budman explains. "[This form] is a lot more convenient."

The new version must undergo further evaluation, but Budman and others predict that pharmaceutical companies will soon begin making water-soluble versions of other drugs.

Dissecting breast cancer treatments

The improved technology and expanded use of mammography have led to an increase in the detection of abnormal cell division in women's breasts. But not all of these abnormalities require the aggressive treatment that is typical for most breast cancers, caution experts in the field.

In the United States, mammograms detect noninvasive breast cancer in 25,000 women a year, but up to four times as many women may have these microscopic tumors, says Melvin J. Silverstein of the Breast Center in Van Nuys, Calif. Only half of these tumors become invasive, he adds.

Called ductal carcinoma *in situ*, this disease does not require removal of the breast or lymph nodes in the adjacent armpit, two studies confirm. In one, Silverstein treated 285 women whose tumors remained confined to the ducts and 47 whose breasts contained cancer cells outside the affected ducts. He removed the cancerous cells but not the adjacent lymph nodes and saw no difference in the rates at which tumors reappeared.

The second study, involving 819 women, suggests that radiation treatment should follow the removal of the affected part of the breast. After four years, tumors developed in 57 of the 403 women who underwent lumpectomy but in only 20 of the 409 women who underwent lumpectomy plus radiation treatment, reports Donald L. Wickerham of the University of Pittsburgh Medical Center.

However, Silverstein cautions that radiation might only delay the return of disease and that over a longer period, the difference between the two groups might diminish.

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