

Perspectives

from an Office-based Oncologist

by Cary A. Presant, MD, FACP

The 2006 annual meeting of the American Society of Clinical Oncology (ASCO) was held in June in Atlanta, Georgia. As usual for the last five years, the meeting was large, requiring miles of walking to listen to presentations in frequently over-crowded rooms, making it difficult to talk to presenters or to find your friends and colleagues. But make no mistake about it, the meeting offered exciting breakthroughs and many presentations that will change the practice of oncology.

What follows are a few of observations of practice-changing presentations and discussions. For the complete text of these abstracts or discussions, I urge you to see the ASCO Virtual Meeting available at www.asco.org, or see the published meeting abstracts. Better still, attend a meeting of "The Best of ASCO." As for my list, long as it might seem, you might wish to consider the following results.

Lung Cancer

Discussions focused on the emerging technology of endoscopic ultrasound for staging of the mediastinum, and curative approaches to patients if there are only limited primary cancer or limited metastatic sites. Radio-frequency ablation and/or stereotactic beam radiation therapy were emphasized for local lesions, with nearly similar survival to surgery. Consider researching the following abstracts:

Adjuvant Therapy (Abstract 7007). An update of CALGB 9633 now shows no significant improvement for adjuvant therapy of stage 1B disease unless the tumors are over 4.0 cm. Therefore, adjuvant therapy should be given to large Stage 1B tumors, Stage 2, and Stage 3A tumors, and should concentrate on the combination cisplatin and vinorelbine (Navelbine).

Adjuvant Therapy (Abstract 7009). Elderly patients (ages 65-75) with non-small cell lung cancer showed no increased toxicity from adjuvant therapy compared to controls, but increased survival with a hazard ratio of 0.6. Therefore, elderly patients should always be offered adjuvant cisplatin and vinorelbine.

Screening (Abstract 1006). Semi-annual CT scans appear to decrease the stage of adenocarcinoma patients. Pending the results of large randomized trials in the United States, consider using semi-annual or annual CT scans in patients with a smoking history to try to reduce stage.

Advanced Non-Small Cell Lung Cancer (Abstract 8511). In patients with Stage 3B and 4 disease, depression was found in 23 percent of patients. More importantly, depressed patients had a survival at 6 months of 50 percent, compared to 80 percent in non-depressed patients. Consider screening newly diagnosed lung cancer patients for depression and treating that depression aggressively.

Renal Cancer

ASCO 2006 was a breakthrough year for renal cancer, a happening that might occur only once or twice in every century. In first-line treatment, sunitinib (Sutent) was found to be superior to interferon with a disease-free survival hazard ratio of 0.4. This treatment should be considered as the new standard of initial care for renal patients. See *Abstract 3* for the details.

Prostate Cancer

Three abstracts are particularly relevant for practicing oncologists.

Abstract 4513. Intermittent hormonal therapy appears to be equal to continuous therapy in patients treated with chemotherapy.

Abstract 4518. Intermittent chemotherapy shows equivalent outcome results to continuous treatment. Therefore, treatment holidays are safe to be considered for all patients with advanced prostate cancer.

Abstract 4515. In patients receiving monthly LHRH (luteinizing hormone-releasing hormones), there was bone loss of 3.1 percent per year if patients received no additional treatments, but an increase in bone density of 4 percent per year if patients received annual zoledronic acid (Zometa). Therefore, physicians should monitor bone density carefully and promptly treat emerging bone loss with addition of zoledronic acid.

Breast Cancer

In breast cancer prevention several significant observations were unveiled at ASCO 2006. They include:

Abstract 5. In the first presented results of the STAR (Study of Tamoxifen and Raloxifene) study, raloxifene (Evista) was found to be considerably less toxic than tamoxifen (Nolvadex), with equivalent reduction in invasive breast cancer, but with less beneficial effects on reducing non-invasive cancer.

Abstract 561. Also in the STAR study, raloxifene was found to produce 6 to 10 percent less hot flashes than tamoxifen, but showed 7 percent worse patient sexual activity compared to tamoxifen. Therefore, patients starting either on tamoxifen or raloxifene can be switched over to the alternative treatment if side effects are being seen.

Abstract 6. In the Women's Health Initiative, calcium and vitamin D overall did not reduce breast cancer. However, if patients had not previously been on calcium and vitamin D, addition of calcium and vitamin D produced a decrease in breast cancer. Significantly, there was also a decrease in estrogen receptor negative and progesterone receptor negative cancer. As calcium and vitamin D offer no side effects, women should be advised to begin calcium and vitamin D. Notably, since tamoxifen and raloxifene reduce



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hormone receptor positive cancer, and calcium and vitamin D reduce hormone receptor negative breast cancer, this combination potentially offers a broad spectrum of breast cancer prevention.

Abstract 1006. Exercise was found to decrease breast cancer by 9 percent.

Abstract 1003. In women with BRCA2 mutations, removal of fallopian tubes and ovaries reduced breast cancer by 72 percent. In both BRCA1 and BRCA2 mutation positive patients, gynecologic cancer (mostly ovarian) decreased by 90 percent.

Abstract 508. In women with triple negative tumors, estrogen receptor negative, progesterone receptor negative, and HER2 normal, 11 percent of patients had BRCA1 mutations. Women with this phenotype should be offered BRCA1 testing.

Adjuvant Therapy

Abstracts that warrant a close look by practicing oncologists include:

Abstract 550. After adjuvant tamoxifen has been

completed, later addition of letrozole (Femara) is effective in reducing recurrence of breast cancer even if the drug is given months to years from the end of tamoxifen. The disease-free survival in treated patients was a hazard ratio of 0.3, indicating that patients should consider adding letrozole even if women have been off tamoxifen for some time.

Abstract 523. In women receiving adjuvant trastuzumab (Herceptin), radiation therapy can be added without increasing cardiotoxicity.

Abstract 561. In women receiving adjuvant trastuzumab following AC-T (Adriamycin and Cytosin followed by Taxol), the cardiotoxicity rate was 4.1 percent. This toxicity was seen mostly in patients with a pre-Herceptin LVEF (left ventricular ejection fraction) of 50 to 54 percent, however, or in patients on anti-hypertensive medications.

Abstract 8500. Chemobrain, or cognitive dysfunction, was found in 20 percent of patients receiving adjuvant chemotherapy. In long-term follow-up, if patients had a normal cognitive testing before chemotherapy, only 2 percent had persistent cognitive impairment at 6 months. If patients had abnormal cognitive testing results prior to chemotherapy, this number increased 8 percent.

Abstract 554. In women receiving adjuvant hormonal therapy, 88 percent of patients had vitamin D deficiency. This finding was confirmed in the Women's Health Initiative (*Abstract 6*), where 79 percent of patients had vitamin D deficiency. Therefore, in all women, physicians should be testing for vitamin D levels and administering at least 1,000 units of vitamin D daily.

Abstract 537. For women who are started on neoadjuvant chemotherapy, continuous AC (Adriamycin and Cytosin) followed by Taxol was found to be better than standard AC followed by Taxol. The pathologic complete remission rate was 27 percent within continuous versus only 17 percent with standard therapy. Accordingly, continuous therapy should be considered in women needing neoadjuvant therapy.

Metastatic Disease Therapy

Several key findings were released at ASCO 2006, including:

Abstract 516. Carboplatin did not add to docetaxel plus trastuzumab, and is not needed for women receiving trastuzumab chemotherapy combination therapy.

Abstract 574. Weekly docetaxel was found to be superior to every-three-week docetaxel.

Abstract 571. Combination chemotherapy with capecitabine (Xeloda) and docetaxel (Taxotere) was found to be superior to sequential capecitabine and docetaxel

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with a hazard ratio of 0.5 in survival. Unless the patient is fearful of toxicity, women should be started on combination therapy rather than sequential therapy.

Abstract 8505. For women receiving radiation therapy, yoga was found to increase quality of life and reduce fatigue. I believe this finding may be relevant to other cancer patients.

Abstract 8507. For women with reduced libido, transdermal testosterone was found to be ineffective.

Abstract 564. In women on bisphosphonates, a reduction of glomerular filtration rate by over 25 percent was observed in between 24 percent and 27 percent of patients, emphasizing the need for careful monitoring of creatinine levels in women on these drugs.

In a *Review Session Discussion*, Julie Gralow, MD, of the University of Washington and the Fred Hutchinson Cancer Center in Seattle, found that for women receiving aromatase inhibitors, a normal bone density before aromatase inhibitor was associated with a 53 percent progression only to osteopenia. In contrast, if women had osteopenia prior to aromatase inhibitor therapy, only 15 percent progressed to osteoporosis. Bone mineral density determination should then be performed before aromatase inhibitor therapy, and patients should be advised and treated appropriately.

Colorectal Cancer

In women receiving FOLFOX7, the stop-and-go technique with periods off oxaliplatin (Eloxatin), was found to produce a marked reduction in neurotoxicity without any reduction in therapeutic effects. This finding (*Abstract 3504*) will likely represent the new standard of chemotherapy for patients with metastatic cancer.

Gastric Cancer

Possibly the best chemotherapy for advanced gastric cancer (*Abstract 4017*) appears to be epirubicin (Ellence) plus oxaliplatin plus capecitabine. Capecitabine can replace 5-fluorouracil (5FU) and oxaliplatin can replace cisplatin.

A new option for standard care (*Abstract 4018*) for advanced gastric cancer may be capecitabine plus cisplatin, which was found to be equivalent to 5FU plus cisplatin, and was much easier to administer.

Ovarian Cancer

In consideration of bevacizumab (Avastin) therapy of ovarian cancer (*Abstract 5006*), bowel perforations were observed in 11 percent of patients. This finding was mostly in patients with evidence of bowel obstruction at some point prior to bevacizumab therapy. Accordingly, this drug must be used with extraordinary caution, if at all, in women with ovarian cancer.

Head and Neck Cancer

For patients with head and neck cancer (*Abstract 5506*), docetaxel plus cisplatin and 5FU was found to be superior to cisplatin and 5FU with median survival of 70 months with the three drugs, versus only 30 months with the two drugs. This finding represents a new standard of care in head and neck cancer.

Myeloma

For patients ages 65 to 75 (*Abstract 1*) the addition of thalidomide to melphalan and prednisone increased overall survival from 32 months to 54 months, representing a new standard of care for this disease site.

Drugs in the Pipeline

Of particular note were:

Abstract 512. In patients with bone metastases and breast cancer, denosumab (AMG162) reduced skeletal related events and reduced N-telopeptide excretion in urine. This drug may be extraordinarily helpful in women with persistent elevation of N-telopeptide despite bisphosphonate therapy.

Abstract 7014. In patients with non-small cell lung cancer with brain metastases, addition of motexafin gadolinium to radiation therapy increased the time to neurologic progression from 10.0 months to 15.4 months with a hazard ratio of 0.78. If approved by FDA, this drug will be a new standard for treatment of brain metastases.

Abstract 4. In patients with poor prognosis renal cancer, temserolimis was found to be superior to interferon.

In ASCO's *Clinical Science Symposium*, lead researcher Charles Geyer, MD, of Allegheny General Hospital, in Pittsburgh, described a study adding lapatinib to capecitabine after trastuzumab progression in patients with metastatic breast cancer. The time for progression was increased from 20 weeks with capecitabine alone, to 37 weeks with lapatinib plus capecitabine.

Although this list is lengthy, for many patients at risk of cancer, or with diagnosed cancer, the findings and research presented at ASCO 2006 will improve the quality of care and improve patient outcomes. As members of the healthcare team, we should all remain dedicated to implementing the newest results of definitive trials, many of which were described above, if we are to reach the goal of reducing the impact of cancer on patients in the near future. ☐

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