ASCO 2008 Roundup

A look at the latest advances in cancer care

by Cary A. Presant, MD, FACP

The 2008 ASCO meeting offered about 80 presentations or posters that, in my personal opinion, were of outstanding relevance to the field of oncology. Here is a list of those abstracts and results that I personally found to be most helpful—all of which will change the way I practice medicine.

General Care and Symptom Management

Abstract 9528 (H. Pfaff et al.) identified factors that increased patients' trust of their treating oncologist(s). The most important factor: the appearance of an organized office, with good communication between physicians and staff. Other important factors included understandable forms, physician(s) who provide a large amount of understandable information, and physician(s) who are accessible for patient questions. Of particular note, healthier patients and more educated patients had reduced trust, indicating a need for markedly increased communications in those patient populations.

Abstract 9513 (G. Lesser et al.) indicated that involuntary weight loss responds both to megestrol acetate or Oxandrin®. Clinicians should note, however, that Oxandrin produced an increase in lean body mass while megestrol acetate only produced an increase in fat.

Abstract 9512 (G. Morrow et al.) reported that modafinil increased patient strength and reduced cancer-related fatigue in severely affected individuals. Patients with mild cancer-related fatigue had no apparent benefit.

Breast Cancer

Abstract 511 (P. Goodwin et al.) highlighted the impact of low vitamin D, including an increased risk of distant breast cancer recurrence (HR 1.94 for deficient patients) and an increased risk of death with HR 1.73 for deficient patients. Overall, only 24 percent of the study's patients had sufficient levels of vitamin D; 38 percent had deficient vitamin D; and 39 percent were insufficient. The conclusion: every patient should have his or her vitamin D level measured and treated to restore them to normal levels.

Abstract 4 (M. Gnant et al.) discussed a trial of adjuvant Zometa® in premenopausal patients in a 2 x 2 comparison in which patients either received tamoxifen or LNRH plus Arimidex®. Astonishingly, the study showed an increased disease-free survival (DFS) at 3 years in patients receiving Zometa (HR 0.64), including reduced bone metastases, reduced non-bone metastases, reduced local regional recurrence, and even reduced contralateral new cancers. In addition, the overall survival (OS) was better if patients received adjuvant Zometa (HR 0.59).

Clinical trial participants were Stage I or Stage II and received Zometa 4 mg intravenously every 6 months for 3 years. Also important, the comparison of tamoxifen versus LNRH plus Arimidex indicated no significant difference in DFS (HR 1.10). Conclusion: premenopausal patients should receive adjuvant Zometa, and can receive LNRH plus Arimidex in place of tamoxifen.

In support of this result, *Abstract 1021* (R. Aft et al.) indicated that 40 percent of Stage II and III breast cancer patients have positive bone marrow micrometastases after completion of their adjuvant therapy. Although the impact of these micrometastases on DFS and OS is not yet known, patients without bone marrow metastases after adjuvant chemotherapy who received adjuvant Zometa following their chemotherapy every 3 weeks for 12 months showed a reduction in bone marrow metastases at 3 months. Zometa-treated patients showed only a 13 percent positivity at 3 months, compared to patients who had not received Zometa who had a 40 percent positivity.

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Abstract 1011 (D. Miles et al.) demonstrated that adding bevacizumab 5 mg/kg every 3 weeks to docetaxel increased progression-free survival (PFS) with an HR of 0.61.

Abstract 507 (H. Muss et al.) highlighted a cooperative group study, which indicated that in Stage I and II patients over the age of 65, Xeloda® was inferior to standard chemotherapy treatment (with either AC or CMF). Of note: in an unplanned subset analysis, the inferiority was in patients who were ER negative and PR negative. While we should await the final published data, it is possible that clinicians may consider Xeloda as an alternative to AC (adriamycin plus cyclophosphamide) or CMF (cyclophosphamide, methotrexate and 5-FU) in ER positive and PR positive patients over the age of 65. Clearly, risk

adjustment is appropriate if Xeloda is to be considered.

Abstract 1040 (Ibrahim et al.) highlighted a nomogram to predict subsequent brain metastasis in metastatic breast cancer patients. This tool will be important for increasing surveillance in these patients. Anyone interested in obtaining the nomogram should contact Nuhad K. Ibrahim, MD, FACP, through the University of Texas M.D. Anderson Cancer Center.

Abstract 1025 (G. VonMinkwitz et al.) demonstrated that after trastuzumab failure, patients treated with Xeloda or Xeloda plus trastuzumab showed an increased time to progression (TTP) if trastuzumab was included, 8.2 months versus 5.6 months without. This finding indicates continuation of trastuzumab is beneficial in this particular second-line treatment.

Abstract 522 (R. Chlebowski et al.) was a report on the WINS study (Women's Interventional Nutrition Study), which demonstrated that obesity decreased OS after regional breast cancer with a HR of 0.76. Importantly, in patients who were ER negative or PR negative, the HR was even lower, only 0.36. Conclusion: all obese women should be placed on an aggressive weight-reduction program.

Abstract 526 (W. Tester et al.) indicated that in Stage II or III patients with a median follow-up of 3.9 years, taking celecoxib for greater than 6 months (or any other COX-2 inhibitor) reduced bone metastases from 11 percent in the control group down to 2 percent, and this effect was sustained after multivariate analysis for other risk factors. Therefore, clinicians should consider the use of celecoxib after completion of adjuvant treatment.

Abstract 513 (R. Gray et al.) reported on the aTTom (adjuvant tamoxifen—to offer more) study, combining it with data from the ATLAS (adjuvant tamoxifen longer against shorter) study. The findings: continuation of tamoxifen for an additional 5 years (total 10 years) in patients appropriate for tamoxifen improved the progression-free survival to HR 0.90. Clinicians should therefore describe the risks of this treatment to all patients and consider longer therapy of tamoxifen (when appropriate).

Abstract 9538 (D. Barton et al.) found that citalopram 10 mg was very effective in hot flashes. At 20 mg, quality of life was also improved.

Abstract 528 (S. Jiralerspong et al.) indicated that in diabetic patients, those who were taking metformin had an increased complete response rate from 8 percent up to 24 percent. Conclusion: any diabetic patient with metastatic breast cancer should probably be taking metformin—to help control the diabetes and to improve breast cancer outcome.

Abstract 524 (P. Ismail-Khan et al.) showed that the use of the GnRH agonist triptorelin did not preserve ovarian function in premenopausal women on neoadjuvant chemotherapy.

Abstract 1014 (M. Bontenbal et al.) found that PFS in advanced breast cancer patients treated with trastuzumab monotherapy followed by docetaxel at progression was the same (9.8 months) as PFS for patients receiving the combination (9.1 months). Toxicity was less in the sequential arm, indicating that sequential therapy with these two drugs is a reasonable option for metastatic breast cancer patients.

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Abstract 1015 (J. O'Shaughnessy et al.) reported important results in HER2 positive patients progressing on trastuzumab. Namely, patients receiving lapatinib plus continued trastuzumab had better PFS (HR 0.77) and possibly better OS (HR 0.75) compared to patients receiving lapatinib alone.

Abstract 1030 (J. Thery et al.) demonstrated conversion of HER2 negative primary breast cancers to HER2 positive metastases in 6 of 60 patients. Serum HER2 predicted HER2 positive metastases with a sensitivity of 54 percent and specificity of 81 percent. Therefore, all HER2 negative patients should have metastases rebiopsied and serum HER2 measured to appropriately individualize therapy.

Abstract 530 (J. Vaselga et al.) indicated that RAD-001 in addition to letrozole improved response in the neoadjuvant setting.

Abstract 1016 (D. Slamon et al.) found that pazopanib increased lapatinib responses in patients with HER2 positive advanced or metastatic breast cancer.

Colorectal Cancer

Abstract 2 (E. Van Cutsem et al.) reported on two studies correlating KRAS before cetuximab treatment and found that only patients with wild type KRAS had improved PFS (HR 0.68). Patients with mutant KRAS had no improvement. Conclusion: clinicians should identify vendors that can supply KRAS evaluations and should measure KRAS in patients prior to using cetuximab or panitumumab.

Abstract 4008 (D. J. Sargent et al.) presented a study that found patients with deficient mismatch repair in their primary tumors in Stage II or III did not benefit from adjuvant 5FU (plus leucovorin or levamisole) (OS HR = 1.26, p = 0.68; DFS HR = 1.41, p = 0.53). Patients with normal mismatch repair showed a definite benefit (OS HR = 0.69, p = 0.047). Microsatellite stability staining should help oncologist(s) select appropriate patients for adjuvant therapy.

Abstract 4009 (D. Nikcevich et al.) showed that IV calcium and magnesium significantly reduces neurotoxicity of oxaliplatin from 52 percent to 28 percent. Despite initial information to the contrary, clinicians should now understand that this adjunctive therapy will help protect patients.

Abstract 4005 (M. Wolmark et al.) reported the results of NSABP protocol C07, indicating that in Stage II and III colorectal cancer, adjuvant FLOX was borderline better than FU/LV with 5-year survival 80 percent versus 78 percent. For this very large study, this borderline outcome was surprising to many clinicians.

Abstract 4081 (B. Aussilhou et al.) found that patients receiving chemotherapy plus bevacizumab before hepatic resection had reduced liver regeneration. In 10 patients who received bevacizumab, only 2 showed regeneration with increases in liver size on CT scans. In contrast, 23 of 27 patients who were treated with chemotherapy without bevacizumab showed liver enlargement. Accordingly, bevacizumab should be reserved until after liver resection is performed.

Abstract 4049 (N. Love et al.) highlighted an interesting study on physician-patient communication. The study showed that only 70 percent of oncologists told patients their own personal choice for adjuvant therapy even after being asked. When shown adjuvant online data, oncologists changed their recommendations for low-risk Stage II cancer patients 69 percent of the time. In patients with high-risk colon cancer, oncologists often preferred for their own personal care untested, but exciting treatments, in 27 percent of instances. These results indicate that physicians should be more open with patients regarding their own personal choices; should consider all data, including adjuvant online data, before discussing recommendations with patients; and should be cautious in using chemotherapy treatments that are untested in the adjuvant setting.

Non-small Cell Lung Cancer

Abstract 1508 (R. V. van Klaveren et al.) reported on multi-detector CT screening for lung cancer in the NELSON trial of 15,800 patients. After the first two years of testing, the study showed a 92 percent sensitivity rate for detecting cancer and a 98 percent specificity rate. Only 0.7 percent of screened patients had cancer. While this study supports multi-detector screening, results are still not definitive. Instead, clinicians should look for results of an NCI-funded trial, which will be reporting in another two to three years. Clearly, patients with a 20-year smoking history can still be offered multi-detector CT screening even though it has not yet been proven to decrease the overall death rate from lung cancer in a large population. On an individual basis, multi-detector CT screening may offer important diagnostic information that can result in early detection of Stage I lung cancer.

Abstract 3 (R. Pirker et al.) showed results of the FLEX study. When cetuximab was added to carboplatin and Navelbine®, overall survival increased by one month. The cost per year of life saved, however, was over $500,000, indicating that while cetuximab has activity in initial treatment of non-small cell lung cancer, the activity is relatively limited.

Abstract 8011 (T. Ciuleanu et al.) evaluated maintenance pemetrexed and indicated an increased PFS of 4.3 months versus 2.6 months in the control group. Overall survival was 13.0 months versus 10.2 months in the control group with an HR 0.8. Accordingly, maintenance pemetrexed should be considered for patients with NSCLC.

Abstract 8012 (T. Hida et al.) studied patients who had received three cycles of chemotherapy. After randomizing to either an additional three cycles of chemotherapy or maintenance gefitinib, researchers found that maintenance gefitinib was advantageous in adenocarcinoma patients with an OS HR of 0.8.

Abstract 8013 (Y. Soon et al.) continued third-line chemotherapy and demonstrated an increased PFS with HR of 0.7. However, clinicians must carefully select patients who can tolerate considerably increased toxicity.

Abstract 8049 (F. Griesinger et al.) demonstrated bevacizumab to be safe in patients who were receiving anticoagulant or antihypertensive treatment, indicating that many patients who otherwise were thought possibly intolerant of bevacizumab can now receive that treatment if it is indicated.

Abstract 8014 (J. Schiller et al.) noted that patients who had received two cycles of chemotherapy and who were then randomized to sorafenib had an increased PFS of 3.6 months compared to only 1.9 months with placebo. The HR was 1.3, indicating a possible beneficial use of this oral agent in cancer patients.

Abstract 8015 (D. Karp et al.) tested the not-yet-available anti-IGF-I receptor antibody CP751871, and indicated an increased response rate when combined with carboplatin and Taxol® in 51 percent of squamous cell carcinoma patients, compared to 36 percent without. In patients with small cell lung cancer, *Abstracts 8040* and *8041* indicated activity of amrubicin in refractory patients.

Ovarian Cancer

Abstract 5506 (S. Isonishi et al.) examined dose-dense paclitaxel and carboplatin versus conventional paclitaxel and carboplatin with an increased PFS of 27.9 months in dose-dense treatment versus 17.1 months in control.

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Abstract 5531 (S. Lewin et al.) evaluated ovarian cancer screening in patients who had BRCA1 or BRCA2 mutations. In 7 patients with persistently abnormal CA125 and/or transvaginal ultrasound, 4 patients had carcinoma; 60 percent of those were localized.

Abstract 5533 (A. Brown et al.) examined patients with abdominal masses, and tested both CA125 and a new test soon to be available called HE4. The study found that 35 percent of patients with normal CA125 levels had HE4 elevation. All of the patients tested were subsequently found to have ovarian cancer at the time of surgery.

A complementary study, *Abstract 5535* (J. Allard et al.), demonstrated an 84 percent concordance with CA125. This study also demonstrated that although CA125 was elevated both in endometrial cancer and in endometriosis; HE4 was only elevated in endometrial cancer. This finding indicates that HE4 may be helpful in screening and

diagnostically evaluating patients considered to have possible ovarian or endometrial cancer.

Abstract 5526 (M. Castello et al.) described an important desensitization program for patients who had allergic reactions to carboplatin, Rituxan®, or cisplatin. This program, initially taking place in the intensive care unit, may provide patients possible curative treatments with carboplatin, cisplatin, or Rituxan.

Abstract 5524 (D. Miller et al.) identified activity of pemetrexed in patients with recurrent ovarian cancer. The finding: 20 percent had complete or partial responses and 30 percent had stable disease for a median duration of response of 7 months.

Abstract 5556 (S. Rivkin et al.) added lapatinib to carboplatin and Taxol in patients with highly refractory ovarian cancer. The study found that 7 percent had complete remissions, 25 percent partial remissions, and 46 percent had stable disease with a median time to progression of 6 months. Most important, many of these patients had demonstrated previous resistance to carboplatin and Taxol.

Abstract 5551 (K. McGonigle et al.) used weekly topotecan and Avastin® in patients with refractory ovarian cancer and demonstrated a 35 percent partial response with an OS of 11.5 months. The progression-free survival in patients with more than two prior treatments was longer than 20 months.

Abstract 5510 (P. Fong et al.) examined the new poly-ADPRibose polymerase (PARP) inhibitor AZD2281. In patients who had BRCA1 deficient ovarian cancer, 21 partial responses were observed in 92 patients.

Soft Tissue and Bone Sarcoma

Abstract 10512 (M. Park et al.) indicated a 79 percent partial response and 14 percent stable disease in patients with hemangiopericytoma/malignant solitary fibrous tumor if they were treated with temozolomide plus bevacizumab.

Abstract 10500 (D. Thomas et al.) showed that denosumab therapy produced responses in 87 percent of patients with recurrent or unresectable giant cell tumors of bone.

Renal Cell Carcinoma

Abstract 5026 (R. Motzer) indicated that in patients with recurrent renal cell carcinoma after VEGF/TKI inhibitor therapy, RAD-001, a new agent, produced a progression-free survival HR of 0.3 compared to placebo.

Hematological Malignancies

Abstract 7004 (S. Verstovsek et al.) found that an oral JAK inhibitor, INCBO-18424, reduced spleen size dramatically in five months in patients with myeloproliferative syndrome.

Abstract 7005 (F. Huget et al.) reported on a new standard of care option. In brief: patients with adolescent or adult ALL showed improved responses to increased chemotherapy doses similar to those used in pediatric ALL. The study (GRAALL 2003) showed a 93 percent complete response rate with a DFS at 42 months of 57 percent.

Prostate Cancer

Abstract 5014 (S. Yao et al.) looked at older patients with localized carcinoma of the prostate who were treated without any chemotherapy. In 19,271 patients from the SEER database, use of PADT (primary androgen depletion therapy) produced no increased survival except in patients with poorly differentiated tumors. In patients with these tumors, the OS was HR 0.9 after PADT with median survival of 88 months compared to 81 months without PADT. Conclusion: PADT may be most beneficial for patients who elect watchful waiting and who have more aggressive tumors.

Abstract 5016 (W. Figg et al.) evaluated patients after PSA recurrence. After an initial treatment with an LHRH agonist plus thalidomide, PFS was not statistically prolonged. However, after the second PSA recurrence, thalidomide plus LHRH improved PFS to 17.1 months versus 6.6 months in patients treated with only placebo plus LHRH.

Abstract 5068 (M. Taplin et al.) examined KHAD regimen (ketoconazole, hydrocortisone, and dutasteride) in castration-resistant patients with prostate cancer. The study round that 56 percent of patients had a greater than 50 percent fall in PSA. TTP was 13.8 months and MDR (median duration of response) was 15 months.

Abstract 5166 (K. Chi et al.) demonstrated a more than 50 percent reduction in PSA in 47 percent of patients with docetaxel-resistant refractory prostate cancer when treated with patupilone.

Abstracts 5005 (D. Danila et al.), *5017* (C. Logothetis et al.), *5018* (C. Ryan et al.), and *5019* (D. Danila et al.) found that abiraterone showed significant anti-tumor activity.

Abstract 5003 (Sartor et al.) showed anti-tumor activity for satraplatin and prednisone.

Non-Hodgkin's Lymphoma

Abstract 8530 (F. Cabanillas et al.), described the new GROC Program (gemcitabine, Rituxan®, and oxaliplatin combination) in patients with diffuse large cell lymphoma, B-cell type. The study produced results that were at least equal to ESHAP or DHAP, with a three-year survival of 33 percent, and a CR (complete response) and PR (partial response) rate of 84 percent. Most important, patients exhibited markedly less toxicity with GROC, and so it should become the preferred treatment program for such individuals.

Abstract 8515 (P. Reimer et al.) examined four cycles of CHOP followed by two cycles of ESHAP, followed by autologous stem cell transplant in patients with PTCL, (peripheral T-cell lymphoma). The 3-year OS was 71 percent versus only 11 percent without transplant.

Abstract 8513 (G. Hess et al.) found that in patients with mantle cell cancer recurrence after standard therapy, temsirolimus demonstrated increased PFS with HR 0.44 compared to the investigators' choice of other therapy.

A complementary presentation, *Abstract 8514* (S. Smith et al.) showed temsirolimus had activity in patients with DLCL or follicular lymphoma.

Pancreatic Cancer

Abstract 4508 (U. Pelcer et al.) demonstrated that oxaliplatin plus 5-FU and leucovorin was better than 5-FU plus leucovorin in overall survival (26 weeks versus only 13 weeks without oxaliplatin).

Abstract 4507 (W. Veverne et al.) compared gemcitabine

plus erlotinib and bevacizumab to gemcitabine and erlotinib alone in the AVITA trial. The addition of bevacizumab increased progression-free survival to 4.6 months compared to 3.6 months in the control group.

Abstract 4504 (P. Neuhaus et al.) described the CONKO-001 trial. In patients after whipple surgery, adjuvant treatment with gemcitabine produced an improvement in disease-free survival of 13.4 months compared to only 6.9 months in control patients with a Whipple resection alone. Conclusion: clinicians should consider adjuvant treatment gemcitabine.

Abstract 4506 (P. Loehrer et al.) compared gemcitabine alone versus gemcitabine plus radiation therapy in pancreatic patients who were not resectable. Overall survival was improved to HR 0.54 with the addition of the combination.

Abstract 4638 (D. Oh et al.) described the use of erlotinib plus gemcitabine and capecitabine. This combination produced a 26 percent partial response with a PFS of 7 months and an OS of more than 8 months.

> ...**ASCO 2008** produced a number of advances in **many different types of diseases.**

Gastric Cancer

Abstract 4511 (Y. Kang et al.) looked at serosa positive gastric cancer patients. Intraperitoneal cisplatin, oral FUDR, and intravenous mitomycin were found to be better than IV mitomycin and oral FUDR (without intraperitoneal therapy). The relapse-free survival was HR 0.7 and 3-year DFS was 60 percent compared to only 50 percent in the control groups. The 3-year OS was 71 percent compared to 60 percent in controls.

Head and Neck Cancer

Abstract 11007 (C. Blau et al.) looked at the presence of EPO receptor MRNA in patients' serum. Those who were positive had a poor prognosis if treated with EPO. Increased local regional recurrence emphasized warnings about using EPO to cure patients with head and neck cancer.

Abstract 6000 (A. Paccagnella et al.) demonstrated that in patients with locally advanced squamous cell carcinoma, neoadjuvant docetaxel, platinum, and 5-FU (TPF) for 2 cycles followed by simultaneous chemotherapy and radiation therapy produced a DFS of 30 months compared to only 19.7 months with simultaneous chemotherapy and radiation therapy alone.

Melanoma

Abstract 9003 (K. McMasters et al.) described the Sunbelt trial. If a single sentinel lymph node was positive at the time of primary melanoma surgery, the study found no need for adjuvant interferon or completion lymph node dissection.

Abstract 9005 (P. Gimotty et al.) showed that all patients who had a sentinel lymph node biopsy had an increased survival compared to those patients who did not have any sentinel lymph node biopsy. The melanoma specific survival was HR 0.4.

Abstract 9522 (C. Alvarado et al.) demonstrated that in patients with melanoma and brain metastases and the presence of venous thrombosis, use of anticoagulants did not produce any increased intracranial bleeding. Only 4 out of 61 patients with brain metastases showed intracranial hemorrhage after anticoagulant therapy, compared to 3 out of 20 who had bleeding without anticoagulant treatment for their venous thromboses.

Endometrial Cancer

Abstract 5503 (R. Nout et al.) compared adjuvant vaginal brachytherapy to external beam pelvic radiation therapy and demonstrated increased pelvic recurrences following vaginal radiation therapy of 3 percent compared to 0.7 percent with external beam pelvic radiation, but markedly reduced vaginal recurrences and increased quality of life if patients received vaginal brachytherapy.

Abstract 9539 (R. Muecke et al.) reported on a study where 80 percent of the patients were selenium deficient. Use of selenium plus radiation therapy reduced diarrhea from 40 percent in the control group down to 20 percent if selenium was given, and overall survival increased from 85 percent to 90 percent.

Central Nervous System Tumors

Abstract 2026 (A. Desjardins et al.) described treatment with bevacizumab plus irinotecan in patients with recurrent glioblastoma. The 6-month disease free survival was 65 percent.

In a complementary study, *Abstract 2021* (S. Wagner et al.), the same treatment program used in the same type of patients demonstrated a 1-year overall survival of 20 percent in glioblastoma multiforme and a 40 percent 1-year year overall survival in patients with anaplastic astrocytoma or anaplastic oligodendroglioma.

Abstract 2006 (E. Shaw et al.) compared adjuvant radiation alone, or with PCV (procarbazine, CCNU, and vincristine) in patients with adult low-grade glioma. PCV was found to increase PFS. Overall survival was also increased in those patients who survived more than two years HR 0.52.

For practicing oncologists, ASCO 2008 produced a number of advances in many different types of diseases. Some of these findings were significant advances; others represented baby-steps in improvements in care. I advise readers to review the 2008 ASCO Abstracts, or to subscribe to the ASCO Virtual Meeting and form your own judgment about these new treatments.

Cary A. Presant, MD, FACP, is with the Wilshire Oncology Medical Group; past president of the American Cancer Society; chairman of the board of the Medical Oncology Association of Southern California; professor of clinical medicine, University of Southern California KECK School of Medicine; medical columnist, HealthNews.com. Dr. Presant served as ACCC President, 2003-2004.