# Practice-changing Progress from ASCO 2007

*Perspectives from an office-based oncologist* **by Cary A. Presant, MD**

The June 2007 meeting of the American Society of Clinical Oncology (ASCO) in Chicago, Ill., was the largest meeting ever—34,000 people in attendance, with approximately two-thirds from countries outside the United States. Many different research findings were discussed that will change my practice pattern in the coming years. From among the 2,000 papers that were accepted, here are 68 that will change the way you care for oncology patients.

## Breast Cancer: Adjuvant Therapy

In an unexpected finding, *Abstract 519* demonstrated that lumpectomy for ductal carcinoma in situ (DCIS) was superior to mastectomy in disease specific mortality. Therefore, lumpectomy is to be recommended above mastectomy for DCIS.

*Abstract 520* demonstrated that tamoxifen reduced in-breast recurrence from 32 percent for lumpectomy alone, to 15.8 percent for lumpectomy plus radiation, down to 12.5 percent with the addition of tamoxifen. Clinicians should add tamoxifen to radiation therapy and lumpectomy for DCIS.

*Abstract 1504* showed that that MRI was superior to mammography to detect DCIS—especially high-grade DCIS, ER negative DCIS, and HER2 positive DCIS. Bottom line: women at risk of breast cancer should be encouraged to have mammography *and* MRI.

In adjuvant therapy of invasive breast cancer, *Abstract LBA513* summarized the results of NSABP B-31, in which AC (adriamycin-cyclophosphamide) was followed by paclitaxel with or without trastuzumab. The study found that 3.8 percent had cardiotoxicity; however, 5 out of 33 were not reversible and continued to have symptoms for greater than 6 months and 12 out of 33 continued to have a reduced LVEF (left ventricular systolic function) less than 50 percent. Therefore, trastuzumab should be used with great caution in women over 50, women on treatment for hypertension, or women with a baseline LVEF of under 54 percent.

*Abstract 511* also reported on NSABP B-31 and surprisingly showed that trastuzumab decreased the risk of recurrence to a hazard ratio of 0.28 in women with previously unknown HER2 status who were subsequently found to be ICH 0-2+ and to 0.36 in patients found to have FISH HER2 negative breast cancer.

An important parallel study, *Abstract 1009*, demonstrated that in women with breast cancer with HER2 FISH less than 2.0, but with polysomy chromosome 17 greater or equal to 2.2 (19 percent of FISH negative woman), the response rate to paclitaxel alone was only 25 percent, but the response rate to paclitaxel plus trastuzumab was 63 percent (P=0.04). For patients with HER2 FISH negative tumors, clinicians should monitor the chromosome 17 copy number and consider trastuzumab therapy if the number is over 2.2.

*Abstract 516* summarized E1199, showing that the best taxane after AC adjuvant therapy was weekly paclitaxel with a 32 percent increased survival versus every 3 week paclitaxel or every week or every 3 week docetaxel. The study showed weekly paclitaxel to be the preferred adjuvant program.

*Abstract 517* compared AC followed by paclitaxel to doxorubicin and paclitaxel followed by weekly paclitaxel. The overall survival favored AP followed by P (P=0.054), indicating that AC need not be the only initial type of adjuvant therapy.

## Breast Cancer: Metastatic Disease

*Abstract LBA1005* looked at the Anglo Celtic IV trial. Weekly paclitaxel was found to be superior with a 29 week time to progression versus 22 weeks for every 3 week paclitaxel. Therefore, weekly paclitaxel is to be preferred for palliative therapy.

*Abstract 1008* summarized BCIRG-007, indicating equal overall survival and time to progression for TCH (docetaxel [T], carboplatin [C] and trastuzumab [H]) versus TH. The findings: less thrombocytopenia in TH, but more neutropenia and more anemia. It was concluded that TH was the preferred regimen.

*Abstract 514* gave the results of combining lapatinib plus trastuzumab indicating that it was safe, and with only 12 out of 238 patients demonstrating any cardiac side effects. The combination should be considered by clinicians.

*Abstract 1006* showed that ixabepilone plus capecitabine was superior to capecitabine alone with a progression-free survival of 5.8 months versus 4.2 months (HR-0.75). Once approved by the FDA, clinicians will be able to use this exciting new drug for palliative therapy for breast cancer patients.

*Abstract 1012* demonstrated that lapatinib in HER2 positive breast cancer patients with brain metastases after radiation therapy reduced the tumor volume by over 20 percent in 19 percent of patients with a 22 percent neurological progression-free survival at 6 months. Therefore, clinicians may consider using lapatinib after radiation therapy in patients with brain metastases.

*Abstract 1023* compared estrogen receptor and HER2 status in primary breast cancers with the status in metastases. The findings: 5 percent of initially HER2 negative patients became HER2 positive and 7 percent of ER negative patients became ER positive. All patients should now have ER status and HER2 status measured when metastases are seen.

*Abstract 598* summarized the aggressive treatment of

breast cancer patients at M.D. Anderson Hospital. Clinicians treated limited metastatic disease with chemotherapy, radiation therapy to bone lesions, surgical resection of metastatic lesions, radiofrequency ablation of liver metastases and lung metastases, and then compared whether or not a lumpectomy was also performed in those patients. At 8 years, the progression-free survival of patients with lumpectomy was 25 percent compared to 15 percent without, and the overall survival was 40 percent compared to 20 percent without lumpectomy. Accordingly, patients with limited metastatic disease should be treated aggressively with expectation of very good survivorship in a significant fraction of patients.

## Colorectal Cancer: Resectable Liver Metastases

*Abstract LBA5* presented the results of pre- and post-operative FOLFOX-4, and demonstrated an increase in 3 year progression-free survival by 7 percent with the addition of preoperative therapy. However, because of a 10 percent excess liver toxicities or abdominal complications with preoperative therapy, clinicians should only use postoperative chemotherapy in the setting of initially resectable liver metastases.

## Colorectal Cancer: Adjuvant Therapy

*Abstract 4019* demonstrated that patients with a higher Western diet (more red meat, higher fat, and more sweets) had an increased recurrence rate of 3.14 fold and an increased mortality rate of 3.75 fold compared to patients with a non-Western diet. Bottom line: all patients should be counseled regarding diet.

Multiple studies (*4099*, *4083*, *4029*, *4030*, and *4031*) showed that XELOX was equal to FOLFOX in adjuvant therapy.

*Abstract 4114* demonstrated that statins were associated with a reduction in relapse rate from 16 percent down to 6.7 percent in colorectal cancer patients.

*Abstract 4007* summarized the MOSAIC Trial, which indicated that in Stage III patients FOLFOX-4 was superior with 6 years overall survival of 73 percent compared to 68 percent for FU-5/LV-2; however, the results were equal in Stage II. These findings indicated that FOLFOX-4 is preferable in Stage III patients, while FU5/LV2 is preferable in Stage II patients.

*Abstract 4054* demonstrated that starting adjuvant therapy more than 56 days after surgery gave the same overall survival and disease-free survival as treating patients in less than 56 days. The take away message was that patients should be treated with adjuvant chemotherapy—even if they present late after surgery.

## Colorectal Cancer: Advanced Disease

*Abstract 4012* demonstrated that the sequential use of capecitabine followed by irinotecan followed by capecitabine plus oxaliplatin showed an equal survival compared to combination therapy with CAPIRI followed by CAPOX. Therefore, one can use sequential therapy in palliative therapy of advanced disease.

*Abstract 4013* summarized findings from the OPTIMOX-1 trial. Patients who had maintenance FU5/LV2 during holidays off FOLFOX showed a higher survival of 24.6 months compared to only 18 months in OPTIMOX-2 where there was no maintenance FU5/LV2. For patients intermittently discontinuing oxaliplatin, maintenance therapy with FU5/LV2 is preferred.

## Non-small Cell Lung Cancer: Early Disease

*Abstract 7512* showed that in Stage III patients the combination of cisplatin, etoposide, and radiation therapy gave only equal results to the same combination followed by docetaxel.

*Abstract 7520* demonstrated that neoadjuvant chemotherapy with paclitaxel and carboplatin gave a possibly increased progression-free survival of 33 months compared to 21 months without the neoadjuvant chemotherapy (P=0.07). The conclusion would be to use chemotherapy before or after surgery in Stage II or III non-small cell lung cancer.

Once approved by the FDA, vinflunine represents another drug to be added to the armamentarium of non-small cell lung cancer management.

## Non-small Cell Lung Cancer: Advanced Disease

*Abstract 7511* found that vinflunine showed equal efficacy to docetaxel in second-line treatment. Once approved by the FDA, vinflunine represents another drug to be added to the armamentarium of non-small cell lung cancer management.

*Abstract LBA7514* compared gemcitabine-cisplatin with or without bevacizumab in first-line therapy. Bevacizumab increased the progression-free survival from 6.1 months to 6.7 months, a significant hazard ratio of 0.75; however, this 0.6 month prolongation is thought possibly to be of marginal use by this author and I will not be using this combination in my practice despite its favorable combination with paclitaxel and carboplatin therapy.

*Abstract 7517* demonstrated that gemcitabine plus carboplatin was equal to pemetrexed plus carboplatin. However, the pemetrexed combination was much gentler with reduced toxicity so this doublet is a possible preferred treatment program for certain patients.

*Abstract LBA 7516* compared gemcitabine plus carboplatin for four cycles followed by docetaxel for six cycles versus no maintenance therapy. With docetaxel maintenance, the study demonstrated an increase in progression-free survival from 2.8 months to 6.5 months; overall survival was possibly increased from 9.1 months to 11.9 months. After gemcitabine plus carboplatin, clinicians should probably use docetaxel as maintenance therapy.

## Small Cell Lung Cancer

*Abstract 4* looked at prophylactic cranial irradiation (PCI) in patients who have had a response to induction chemotherapy for widespread SCLC. The study showed a decrease in symptomatic brain metastases from 41 per-

cent in the control group down to 17 percent in those who received radiation, with an increase in the overall survival at 12 months from 13 percent to 27 percent. Accordingly, PCI should be used in any patient with a response in advanced SCLC.

*Abstract 7523* looked at the combination of irinotecan plus carboplatin (IC) compared to etoposide and carboplatin (EC). The mean survival time was 8.5 months for IC versus 7.1 months for EC. Although the carboplatin dose was low and the etoposide was given orally, it is possible that the irinotecan combination is better than an etoposide platinum combination.

## Prostate Cancer

*Abstract 5019* looked at a new medication, satraplatin plus prednisone, and demonstrated an increase in progression-free survival from 6 weeks on prednisone alone to 16 weeks on satraplatin plus prednisone. When approved by the FDA, this combination will be a much needed new treatment for a common widespread malignancy.

*Abstract 5014* compared androgen deprivation therapy for 3 years to androgen deprivation therapy for 6 months, both following radiation therapy. The overall survival at 5 years was 85 percent for the 3-year treatment versus 80 percent for a 6-month treatment. To maximize survival, these findings suggest that longer ADT is necessary after radiation therapy.

*Abstract 5068* looked at the combination of irofulven plus prednisone, compared to irofulven plus capecitabine plus prednisone, compared to mitoxantrone and prednisone. The irofulvin combinations showed increased overall survival in time to progression. Once approved by the FDA, irofulven will be an exciting new drug for prostate cancer therapy.

*Abstract 1510* looked at flaxseed. Although the study demonstrated a decrease in cancer cell proliferation in patients, it caused significant nausea, vomiting, and even impotence. Based on these results, flaxseed should be discouraged in patients until more data are obtained.

Once approved by the FDA, irofulven will be an exciting new drug for prostate cancer therapy.

## Hepatocellular Cancer

*Abstract LBA1* compared sorafenib to placebo. Overall survival increased from 7.9 months to 10.7 months, indicating a new possible first line treatment. Physicians should work with payers to try to obtain authorization for sorafenib in appropriate patients.

## Endometrial Cancer

*Abstract 5504* reported that radiation therapy following surgical hysterectomy did not increase overall survival, but did decrease pelvic recurrence from 7 percent to 4 percent. These findings support a possible role for radiation therapy, as has been conventional in the past.

*Abstract 5503* looked at Stages IC, II, and III comparing radiation therapy versus radiation therapy plus any chemotherapy (drugs used were either docetaxel, epirubicin, cisplatin, carboplatin, or paclitaxel). The five-year overall survival with chemotherapy was 88 percent versus 78 percent for those patients having only radiation therapy. Therefore, appropriate therapy following higher risk endometrial cancer would be radiation therapy plus chemotherapy.

## Urothelial Cancer

*Abstract LBA5030* compared gemcitabine plus carboplatin plus paclitaxel to gemcitabine and carboplatin alone in urothelial cancer. Survival was improved in bladder cancer, but not in ureteral or urethral cancer. Careful consideration of this three-drug regimen seems appropriate for practicing oncologists.

## Ovarian Cancer

*Abstract LBA5506* compared gemcitabine with liposomal doxorubicin in recurrent ovarian cancer. There was a trend to better quality of life in the gemcitabine group, with equal overall survival in time to progression. Clinicians can use either treatment equally, and the preferred sequence would appear to be gemcitabine, then liposomal doxorubicin, and then topotecan.

*Abstract 5505* demonstrated that after six cycles of platinum plus paclitaxel, maintenance paclitaxel for six cycles produced the same overall survival and time to progression as no maintenance at all. At this time, therefore, it seems appropriate to not treat patients with maintenance paclitaxel.

## Head and Neck Cancer

*Abstract 6013* compared 5-FU plus cisplatin with or without cetuximab. The addition of cetuximab increased overall survival from 7.4 months to 10.1 months in first-line therapy. Accordingly, cetuximab should be added to 5-FU and cisplatin therapy.

## Non-Hodgkin's Lymphoma

*Abstract 8004* demonstrated in follicular carcinoma patients that cyclophosphamide and fludarabine showed a high incidence of toxic deaths, so CVP or CHOP plus Rituxan seems to continue to be the standard at the present time.

In diffuse large B-cell lymphoma, *Abstract 8011* indicated that in patients over 60 years of age further rituximab after R-CHOP is no better than R-CHOP alone, so maintenance rituximab is not necessary in older patients.

In chronic lymphoid leukemia (CLL), *Abstract 7008* demonstrated that at 5 years following FCR (fludarabine, cyclophosphamide, and rituximab), 70 percent of patients achieving complete remission remained in complete remission at 5 years. Therefore, FCR should be the first-line treatment. There was only 3 percent myelodysplastic syndrome.

*Abstract 7004* demonstrated that dasatinib at 100 mg per day was the optimal dose, and, therefore, this dose should

be used in further treatment of CML (chronic myelogenous leukemia).

## Multiple Myeloma

*Abstract LBA8025* compared lenalidomide plus high-dose dexamethsone with low-dose dexamethsone, and demonstrated that lenalidomide plus low-dose dexamethsone showed a 98 percent survival at 1 year compared to 90 percent for high-dose decadron. In older patients above 65 years of age, low-dose produced a 95 percent survival at 1 year versus 83 percent for high-dose. Accordingly, low-dose decadron is recommended in combination with lenalidomide.

*Abstract 8018* reported that patients with Waldenström's macroglobulinemia who were treated with nucleosides had an increased transformation to diffuse large B-cell lymphoma (4 percent) and MDS or AML (1.7 percent). Therefore, non-nucleoside treatment of Waldenström's is preferred.

*Abstract 8017* also studied Waldenström's macroglobulinemia in patients treated with thalidomide and rituximab. The response rate was 78 percent with a time to progression of 35 months. This combination seems to be an appropriate one for consideration in first-line use in patients with Waldenström's.

## Malignant Melanoma

*Abstract 8511* looked at Stage IV patients, and demonstrated an increased progression-free survival with a combination of DTIC (dacarbazine) plus sorafenib of 21 weeks compared to 11.7 weeks with DTIC alone. Physicians should begin to obtain authorizations for sorafenib for use in melanoma patients in first-line Stage IV therapy.

## Gastric Carcinoma

*Abstract 4500* looked at patients with familial gastric carcinoma, a condition associated with the CDH-1 mutation and lobular breast cancer. Prophylactic gastrectomy was performed in patients, and 80 percent were found to have occult carcinomas not yet widely invasive. Therefore, patients with familial gastric cancer should have a CDH-1 mutation test and prophylactic gastrectomy if indicated.

*Abstract 10016* presented the results of the American College of Surgeons Study Z9001. In patients with GIST tumors, imatinib for 1 year was compared to no imatinib following resection. While the 1-year relapse-free survival was 97 percent with imatinib compared to 83 percent without treatment, overall survival was equal. For patients with large tumors, over 6.0 cm, the relapse-free survival still seems to provide an advantage for patients with imatinib. Therefore, adjuvant imatinib therapy seems to be appropriate for patients with high mitotic index, large tumor over 6.0 cm, or a primary in the small intestine.

## Symptom Management

*Abstract 9006* looked at tetracycline 500 mg twice per day to prevent the onset of rash in patients treated with EGFR inhibitors. This treatment prophylactically was found to reduce the incidence of rash from 55 percent down to 17 percent. Immediate institution of tetracycline therapy now seems appropriate in those patients treated with EGRF inhibitors.

*Abstract 9001* was a study of various doses of ginseng to increase strength. At a dose of 1,000 mg per day, 25 percent of patients reported an increase in strength and 33 percent reported a high satisfaction with ginseng use. Based on these findings, ginseng should be considered for treatment of cancer-related fatigue.

*Abstract 9004* studied modafinil 200 mg daily in patients with cognitive problems. Based on increased attention, increased memory, and increased speed of memory, this drug seems to have an appropriate use for these patients.

*Abstract 9005* demonstrated that gabapentin was effective in controlling hot flashes in men at a dose of 900 mg per day.

*Abstract 9114* looked at vitamin E 400 mg per day, and demonstrated reduced neurotoxicity and ototoxicity from cisplatin. Clinicians should now consider use of this vitamin.

## The Practice of Oncology

*Abstract 4135* demonstrated that bevacizumab can be given over 10 minutes safely, with only 1.6 percent minor adverse events.

*Abstract 6505* showed that participation in ASCO's QOPI (Quality Oncology Practice Initiative) produced improvement over time in the lowest quartile of practices in terms of compliance with QOPI criteria.

*Abstract 6535* also demonstrated that, in an academic center, participation in QOPI can result in improved performance over time.

*Abstract 6637* indicated that an EMR can be used to track NCCN guideline compliance for every patient in a practice. Practice costs annually were $265 per patient, or $0.28 per/member, per/month in capitated programs.

*Abstract 6538* demonstrated that telemedicine can be used for oncology consults and oncology visits in remote areas. Organized medical societies should now begin to try to obtain payments for telemedicine oncology care to increase the acceptability of telemedicine care.

*Abstract 6589* found that if there was a delay in breast cancer treatment of over 3 months, overall survival was reduced by 34 percent.

*Abstract 6591* demonstrated that a delay in radiation therapy of 12 weeks after surgery for breast cancer, or 16 weeks after adjuvant chemotherapy, produced a decreased disease-free survival with a hazard ratio of 4.66.

## Conflict of Interest in Authors and Planners

*Abstract 6530* indicated that author conflict of interest was associated with highly positive conclusions and use of "superlatives" in articles published in *JCO* (*Journal of Clinical Oncology*).

*Abstract 6633* indicated that authors of clinical trials in *JCO* had a conflict of interest in 58.3 percent of papers.

*Abstract 6635* demonstrated a conflict of interest in 67.4 percent of ASCO meeting planners. This finding indicates a need for ethical improvement in clinical trials, publications, and major meeting planning.

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