Best of ASCO 2012

PERSPECTIVES FROM A COMMUNITY ONCOLOGIST

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Presented by disease site, the following abstracts and presentations from ASCO 2012 most impressed me. Many will change my practice today; some will change my practice in the coming months or year. After reading this article, I encourage you to review the abstracts as published online by ASCO *(www.asco.org)* and then read carefully the final publications. Unless otherwise noted, all differences in response rates, progression free-survival, survival, and hazard ratios (HR) were statistically significant at $p<0.05$ or less.

Breast Cancer

☐ In *Abstract LBA 1,* K. Blackwell and colleagues presented the results of the EMILIA trial. The drug emtansine (previously known as T-DM1) was found to be superior to capecitabine plus lapatinib. The progression-free survival was increased from 6.4 to 9.6 months HR 0.65 and the two-year survival was increased from 47% to 65%, HR 0.621. Furthermore, there was less grade 3 toxicity on emtansine versus the combination, although there was a slight increase in liver function abnormalities and an increase in anemia.

☐ *Abstract CRA 1002* (H. Rugo et al.) reported on weekly paclitaxel compared to weekly nab-paclitaxel or ixabepilone in patients treated with first-line chemotherapy. This non-inferiority trial showed that paclitaxel was likely to be equal to or superior to other drugs in progression-free survival. This finding is important since paclitaxel is significantly less expensive. The occurrence of SN (sensory neuropathy) was greater in the nab-paclitaxel and ixabepilone arms compared to use of paclitaxel alone.

☐ In *Abstract 536* (G. King et al.), the use of statins in Stage II-III breast cancer patients decreased the frequency of bone metastases to HR 0.49, as well increased survival 66 months versus 59 months in non-users. Statins should be considered as additional therapy in any patients with dyslipidemia.

☐ In *Abstract 559,* M. Piccart-Gebhart and colleagues presented on the results of the Bolero trial. This trial showed that the combined use of everolimus plus exemestane, compared to exemestane alone, increased progression-free survival from 3.0 to 6.9 months HR 0.43, with maintenance of quality of life.

☐ *Abstract 600* examined the incidence of congestive heart failure with the use of trastuzumab in patients over 66 years of age. M. Chavez-Mac Gregor and colleagues reported that the risk of coronary artery disease, valvular heart disease, and/or chronic obstructive pulmonary disease was increased with a HR of 1.74 by the use of trastuzumab. This data is higher than reported in younger patients, and should result in identification of higher-risk patients in whom trastuzumab should be more carefully considered.

☐ In *Abstract 527* (R. Murthy et al.), the use of trastuzumab as an adjuvant therapy was associated with a reduced rate of tumor response when trastuzumab was later used in patients for first-line palliative therapy. The response rate if patients were trastuzumab naïve was 48%, versus only 32% if patients had received prior trastuzumab adjuvant therapy, and survival was longer if patients were trastuzumab naïve HR 1.8. In patients with prior trastuzumab, consideration must be given to use of pertuzumab or lapatinib with trastuzumab for first-line therapy in the recurrent disease setting.

Non-small Cell Lung Cancer

☐ *Abstract 7001* (R. Huber et al.) examined the use of maintenance chemotherapy in Stage IIIB patients following radiation plus chemotherapy. Study results indicated that there was no improvement in overall survival or in progression-free survival by continuing maintenance chemotherapy after completion of radiochemotherapy treatment, and maintenance therapy may be avoided in those patients.

☐ In *Abstract LBA 7500,* J. Yang and colleagues reported on the LUX-Lung 3 trial, which showed that afatinib was found to be superior to the use of pemetrexed plus cisplatin in patients with advanced adenocarcinoma with EGFR mutations. Patients had a prolonged progression-free survival (11.1 months versus chemotherapy 6.9 months, HR 0.58).

☐ In *Abstract LBA 7507,* L. Paz-Ares and colleagues studies the PARAMOUNT trial, reporting that the maintenance of pemetrexed after induction with pemetrexed and cisplatin showed improvement compared to placebo with a relapse-free survival HR of 0.6 and an overall survival HR of 0.78. The two-year overall survival was increased from 21% in placebo to 32% following pemetrexed.

☐ *Abstract 7506* (R. Lilenbaum et al.) compared therapy of patients with performance status 2 with first-line pemetrexed versus carboplatin plus pemetrexed. In this, the first comparative trial in performance status 2 patients, use of the combination therapy produced an overall response rate of 24% versus only 10.5% with pemetrexed alone, and a longer progression-free survival of 5.9 compared to 3.0 months and a longer overall survival of 9.1 compared to 5.6 months (HR 0.57).

Surprisingly, the results were the same in adenocarcinoma and squamous cell carcinoma and in older patients compared to younger patients. This is the first trial indicating how therapy may be given to performance status 2 patients.

☐ In *Abstract LBA 7501,* patients with EGFR wild-type genetics, erlotinib was found to be worse than docetaxel. M. Garassino and colleagues showed that the progression-free survival was reduced to 0.69 when erlotinib was given.

☐ In *Abstract 7503,* P. Janne and colleagues examined second-line therapy in KRAS mutant patients. The use of selumetinib plus docetaxel was compared to docetaxel plus placebo. The results indicated that overall survival was longer with the additional selumetinib (9.4 months versus 5.2 months). The results of this drug may give an indication of how KRAS mutated non-small cell lung cancer can be treated.

Colorectal Cancer

☐ *Abstract 3507* (M. Faron et al.) examined patients with primary colorectal cancer and simultaneously detected unresectable liver metastases. The HR for death if primary tumor resection had been performed was 0.63, indicating a beneficial effect of removing the primary cancer. There was a decreased primary tumor resection rate if a CEA was over 600 or if the primary tumor was rectal rather than colon cancer.

☐ In *Abstract 3505,* C. Allegra and colleagues presented the VELOUR study using the VEGF trap medication aflibercept. FOLFIRI alone was compared to FOLFIRI and aflibercept. The combination increased progression-free survival from 4.7 months to 6.9 months, HR 0.76. The overall survival was also increased, HR 0.82.

☐ *Abstract LBA 3500* (C. Tournigand et al.) presented the results of the DREAM study. Patients who had received FOLFOX 7 or XELOX or FOLFIRI as first-line therapy of metastatic colorectal cancer were randomized to receive bevacizumab or bevacizumab plus erlotinib. The addition of the maintenance erlotinib produced an increased progression-free survival from 4.6 months to 5.8 months, HR 0.73. The overall survival was 25.4 months. The addition of erlotinib was associated with increased rash and diarrhea, but the improvement in progression-free and overall survival was a meaningful benefit.

☐ In *Abstract 3502,* E. Van Cutsem and colleagues presented findings on the CORRECT trial of the new drug regorafenib. When compared to placebo, the active drug increased overall survival from 5.0 to 6.4 months HR 0.77. This drug is active and should find its way into our treatment programs within the next year.

☐ *Abstract CRA 3503* (D. Arnold et al.) reported the results of chemotherapy with bevacizumab in second-line therapy compared to chemotherapy without bevacizumab. The overall survival was extended from 9.8 months to 11.2 months, HR 0.81. This data supports the use of bevacizumab in second-line and even third-line patients.

Prostate Cancer

☐ *Abstract 4* (plenary) by M. Hussain and colleagues summarized SWOG trial 9346 with continuous versus intermittent androgen deprivation. Continuous produced a 9% increase in survival from a median of 5.1 years to 5.8 years. While intermittent had fewer side effects, continuous produced a longer survival, suggesting that treatment was superior. These findings require discussion with patients who are being treated with palliative intent to balance outcomes with side effects.

☐ *Abstract 10503* (N. Vogelsang et al.) looked at circulating tumor cells (CTC) and prognosis in patients receiving docetaxel. After adjusting for PSA and other clinical characteristics, CTC >5 was associated with increased mortality HR 2.9, and increasing CTC on day 21 predicted worse survival HR 4.0. Therapy may have to be adjusted based on this poor-outcome monitoring method.

☐ *Abstract 4555* (S. Rudman et al.) showed an increased mortality HR of 2.12 in patients who had prostate cancer and metabolic syndrome. Therapy may have to be adjusted according to this increased risk.

☐ In *Abstract 4553,* D. Bianchini and colleagues examined continuing abiraterone beyond PSA progression. An average of 5.7 months of continued abiraterone was seen until there was actual evidence of objective progression in bone metastases by scan or X-ray. These data suggest that changing therapy based upon PSA changes can reduce length of abiraterone benefits in some patients.

☐ *Abstract LBA 4512* (C. Parker et al.) reported findings from the ALSYMPCA trial of Radium-223 versus placebo. Data indicated that use of Ra-223 in patients with castration-resistant prostate cancer increased survival from 2.8 months with placebo to 3.6 months, with a HR of 0.70. Use of Radium-223 is not only palliative but has a survival advantage as well.

Non-Hodgkin Lymphoma

☐ In *Abstract 3* (plenary), M. Rummel and colleagues compared rituximab plus bendamustine to rituximab plus CHOP. In indolent mantle cell lymphomas, progression-free survival was improved with rituximab plus bendamustine, HR 0.58. Importantly, no alopecia was observed with bendamustine.

☐ *Abstract 8007* (M. Williams et al.) showed that in indolent lymphomas, maintenance rituximab every three months in lymphomas other than follicular lymphoma showed a treatment advantage.

☐ *Abstract 8006* (M. Federico et al.) showed that R-CHOP and R-FM were superior to R-CVP, but R-FM had an increase in second cancers, resulting in a superiority of R-CHOP in patients with advanced follicular lymphoma first-line therapy. The time-to-treatment failure was prolonged.

Brain Tumors

☐ In *Abstract 2* (plenary), M. Van Den Bent and colleagues presented the results of EORTC 26951. The use of PCV in anaplastic oligodendroglial tumors showed a significant advantage when combined with radiation therapy if the patient had a 1p19q deletion. However, if there was no deletion, there was no advantage in using PCV with radiation therapy. The increase in overall survival showed an HR of 0.75 and progression-free survival of HR 0.66.

Myeloma

☐ *Abstract 8010* (J. Mikhael) presented the results of the CYCLONE trial (cyclophosphamide, carfilzomib, thalidomide, plus dexamethasone). There was a complete response rate of 35% after four cycles, with 83% achieving a very good partial response. This combination is active and the drug should find its way into the clinic in the next year.

☐ In *Abstract 8014,* P. Rodon and colleagues presented the results of the BVD trial (bendamustine, bortezomib, plus dexamethasone) in elderly patients. After four cycles, there was an 11% complete response rate plus a 47% very good partial response or partial response. In elderly patients this combination is highly active.

Gynecologic Cancers

☐ *Abstract LBA 5001* (A. Oza et al.) presented the results of olaparib plus paclitaxel and carboplatin followed by olaparib maintenance treatment or placebo in patients with recurrent ovarian cancer. The use of olaparib maintenance therapy resulted in an increased progression-free survival of HR 0.51. However, there was no change in overall survival.

☐ *Abstract 5003* (M. Katsumata et al.) reported the results of the JGOG 3016 trial. In this trial, the use of dose-dense carboplatin plus paclitaxel was shown to be superior to standard carboplatin plus paclitaxel. The progression-free survival increased from 17.5 months to 28.2 months with a dose-dense HR of 0.76. The overall survival at three years was different with an HR of 0.79, median survival not yet reached in the dose-dense versus 62 months in the standard arm. Bottom line: Dose-dense therapy should become an option for patients with ovarian cancer.

☐ In *Abstract LBA 5002,* E. Pujade-Lauraine and colleagues presented the results of the AURELIA trial. This trial showed that the addition of bevacizumab in patients with recurrent platinum-resistant ovarian cancer was associated with an increased progression-free survival of 3.3 months. The bevacizumab was combined with either liposomal doxorubicin, topotecan, or paclitaxel.

☐ *Abstract 5007* (S. Mahner et al.) reviewed patients with vulvar cancer, reporting that if patients had lymph node positivity, the addition of adjuvant radiation therapy increased overall survival with an HR of 0.68.

☐ In *Abstract 5004* (S. Dowdy et al.), patients with endometrial cancer at low risk of recurrence by Mayo Clinic criteria (low-grade, less than 50% of myometrial invasion) did not benefit by the addition of lymph node dissection. Without node dissection, cost was reduced, lymphedema was reduced, and length of surgery was reduced. No pelvic recurrences were observed if lymphadenectomy was avoided.

Genitourinary Tumors

☐ In *Abstract 4500* (N. Haas et al.), the use of sunitinib or sorafenib was associated with evidence of decreased left ventricular ejection fraction in a small number of patients, 1.8 to 2.3%. This small but real risk should be discussed with patients, and patients with renal cell carcinoma who have preexisting cardiac disease should be cautioned regarding the use of those agents.

☐ In *Abstract CRA 4502* (B. Escudier et al.), patients were found to prefer pazopanib over sunitinib in the PISCES study with 48% showing a strong preference for pazopanib.

Gastrointestinal Tumors

☐ In *Abstract 4018* I. Trouilloud and colleagues presented the results of the FIRGEM study for patients with pancreatic cancer. This study, which compared alternating the combination of FOLFIRI with gemcitabine, versus use of gemcitabine alone, demonstrated that the FIRGEM regimen produced 73% disease control compared to 52% in gemcitabine alone. The FIRGEM regimen is useful, and gives comparable results to FOLFIRINOX.

☐ In *Abstract LBA 10008* (G. Demetri et al.), the use of regorafenib as third-line therapy for patients with GIST tumors was found to be superior to placebo. The progression-free survival showed an HR of 0.27, indicating significant activity of this new medication, which should find its way into clinical use soon.

Melanoma

☐ In *Abstract LBA 8500,* A. Hauschild and colleagues showed that in BRAF-mutated patients, treatment with the medication dabrafenib was superior to treatment with dacarbazine. This indicates a new medication that may be used in patients with BRAF mutations.

☐ *Abstract LBA 8509* (C. Robert et al.) reported findings from the METRIC trial. Specifically, the use of the MEK inhibitor trametinib increased the progression-free survival with a HR of 0.44 compared to DTIC plus paclitaxel. In addition, overall survival showed a HR of 0.53. This is the first activity of a MEK inhibitor in this study.

☐ In *Abstract 8507,* F. Hodi and colleagues reported that an anti-PD-1 antibody showed a 28% response rate with 12 out of 20 responses lasting over 12 months. This new immunotherapy was extremely exciting, and remissions persisted after discontinuation of the anti-PD-1 antibody. This anti-PD-1 antibody is referred to as BMS-936558, or MDX-1106.

☐ *Abstract 8501* (J. Kirkwood et al.) found that brain metastases in patients with BRAF-mutated melanoma respond to dabrafenib. There was a 39% response rate.

☐ In *Abstract 8510,* J. Weber and colleagues found that the combination therapy of dabrafenib plus the MEK inhibitor trametinib showed a response rate of 60% with a progression-free survival of 10.8 months in a Phase I/II study. These results suggest progressive improvement in treatment of BRAF-mutated patients.

☐ *Abstract 8511* (P. Ascierto et al.) reported the results of patients treated for NRAS mutations. Seven out of 24 patients with NRAS mutations responded to MEK162, an oral medication. This news is encouraging for patients who harbor this less common mutation (15 to 20% of melanoma).

Liposarcoma

☐ *Abstract 10002* (M. Dickson et al.) studied patients with liposarcoma, finding that 90% of liposarcomas show CDK4 amplification. In second-line treatment after chemotherapy, the treatment with the CDK4 inhibitor PD0332991 showed a progression-free survival at 12 weeks of 65%, an impressive response. The median progression-free survival was 18 weeks. This new medication targeting a molecular abnormality in liposarcomas shows promising results.

☐ In *Abstract 10009,* W. Van Der Graaf and colleagues presented the results of the PALETTE study. In second-line therapy of sarcoma patients after chemotherapy progression, the use of pazopanib versus no therapy demonstrated an increased progression-free survival with a HR of 0.31. Pazopanib was approved by the U.S. Food and Drug Administration on April 26, 2012, for treatment of patients with sarcoma.

Head and Neck Cancer

☐ *Abstract 5500* (R. Haddad et al.) reported on the DeCIDE trial, which found that induction chemotherapy with TPF (docetaxel, cisplatin, and 5-fluorouracil) followed by chemotherapy (cisplatin, 5-fluorouracil, and hydroxyurea) plus radiation therapy did not show any improvement in overall survival compared to treatment with chemotherapy plus radiation therapy without initial TPF. The overall survival and performance in progression-free survival were equal and the toxicity was higher within induction chemotherapy. Based on these data, induction chemotherapy is not needed.

☐ In *Abstract 5504,* J. Stoehlmacher-Williams and colleagues reported on the SPECTRUM study. In this study, chemotherapy alone was compared to chemotherapy plus panitumumab. These results demonstrated that there was an increase in progression-free survival in patients who were negative for p16, HPV-negative tumors. There was no difference in progression-free survival with the addition of panitumumab if patients were p16 positive. Therefore, evaluating patients for the presence of p16 expression is necessary if this drug is to be considered.

Symptom Control

☐ *Abstract CRA 9013* (E. Smith et al.) reported on the use of duloxetine in patients with chemotherapy-induced neuropathy. The results of use of duloxetine, compared to placebo, showed an improvement in pain score. The most commonly reported side effect was fatigue, 11% on duloxetine versus 3% on placebo. However, the improvement in pain control was not different based on which chemotherapy had produced the neuropathy. Takeaway message: this therapy should be able to be used immediately in patients with painful drug-induced neuropathy.

Prevention and Epidemiology

☐ In *Abstract CRA 1505,* M. Wood and colleagues reported on the evaluation of family history as reported in the QOPI database. Family history was reported in 81% of entries, but age of occurrence of cancer was only reported in 45%. Furthermore, when genetic counseling was indicated based upon family history, patients were referred to genetic counselors in only 57% of instances of breast cancer and only 24% of patients with colon cancer. Clearly, family history and genetic evaluations need to be addressed more comprehensively.

Patient Survivor Care and Symptom Management

☐ *Abstract 9000* (Q. Khan et al.) examined patients with Stages I through III breast cancer with vitamin D levels under 40 ng/ml. Patients received letrozole plus placebo versus letrozole plus vitamin D 30,000 units per week. There was a reduction in disability, pain, or fatigue from 72% to 42% by use of vitamin D. Monitoring vitamin D levels and instituting vitamin D supplements may be useful in patients receiving aromatase inhibitors.

☐ In *Abstract 9001,* D. Barton and colleagues examined the use of American ginseng (from Wisconsin) at a dose of 1,000 mg twice a day versus placebo. Fatigue was reduced by 50% at both four and eight weeks in patients who were receiving ginseng.

☐ *Abstract 9003* (C. Zimmermann et al.) looked at the use of early palliative care consultations. There was an increase in quality of life at four months, reduced pain at four months, and increased satisfaction as expressed by the patient.

☐ In *Abstract 9002,* S. Yennurajalingam and colleagues examined the use of dexamethasone 4 mg twice a day compared to placebo. There was a reduction in fatigue and a reduction in physical distress—both significant findings.

☐ *Abstract 9005* (D. Amadori et al.) looked at the ZOOM trial. Breast cancer patients had all received over 12 months of prior monthly zoledronic acid for bone metastases. There was no change in frequency of skeletal events when zoledronic acid was subsequently used every 12 weeks compared to every 4 weeks. OI

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