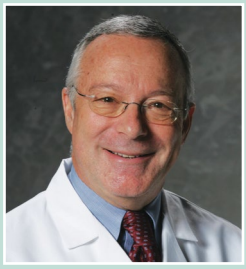

Highlights of ASCO 2014

Thoughts from a community oncologist

BY CARY A. PRESANT, MD, FACP, FASCO

From May 30-June 3, 2014, I made my yearly pilgrimage to ASCO's annual meeting. And some of you are probably thinking—why do you keep going every year? The answer is simple: the meeting offers attendees important updates on scientific advances and the opportunity to get a feel for the state of the art in oncology. Personally, I view the meeting as a "must attend" because I can catch up with colleagues from around the country and share perspective about where we think oncology is going.

This year, I was able to network with Dr. James Holland, who was important in my formative years, and who is still offering wonderful advice. I also caught up with Drs. Peter Wiernik and Charles Balch—peers with whom I published my early manuscripts. And I talked with Drs. Douglas Blayney and Craig Henderson who were important colleagues later in my career. There were many others, too numerous to mention, and the opportunity to share impressions and current goals is always important in a field that changes as rapidly as medical oncology.

For those of you unable to attend or for members of the multidisciplinary team who are interested in brief highlights from ASCO 2014, I offer this round-up—which I have been writing annually for *Oncology Issues* since 2006.

But before we get into individual scientific papers, I must mention some important themes at ASCO 2014. First, there was an increasing emphasis on the value of oncologic care to the patient—where value equals the improvement in outcomes divided by the costs of care. (For example, Drs. Jennifer Malin and Lowell Schnipper's discussion of abstracts 8520 in lymphoma, 9007 in melanoma, and 8517 in myeloma.)

ASCO 2014 also saw a focus on immunotherapy, with trials of several different drugs to influence the T-cell immune response being presented for multiple diseases.

Third, ASCO 2014 was a year of molecular correlates of prognosis and therapeutic outcome. As molecular assays become more ubiquitous, our need to understand their relevance and value to patients will become important. It will also be critical to understand which assays we will endorse when payers ask us questions about their value, and which are of interest, but not necessarily value-enhancing.

Lastly, at the 2014 meeting, ASCO presented its recommendations for payment revisions for physicians—recommendations that represent more patient-centric values. Keep in mind, however,

that these are just "recommendations." It is uncertain if these will be implemented, and whether any reimbursement changes will be adequate to maintain the current infrastructure of oncology practices. Be sure to read updates in *Oncology Issues* and listen to discussions at future ACCC meetings to understand the response to ASCO's innovative initiative.

And now for the science behind ASCO 2014.

Prevention & Epidemiology

In the Science of Oncology Award and Lecture, Dr. Harald zur Hausen described his theory that many human cancers (e.g., colon cancer) are produced by infectious agents from domestic cattle. He emphasized that 21% of human cancer is caused by infections, a high number, which I had not previously realized. Included in this are H. Pylori, HPV, hepatitis B and C, HIV, EB virus, and parasitic infections. His lecture is worth reading when published in the *Journal of Clinical Oncology*.

Abstract 1501 (P. Ramakrishnan et al.) described how navigation programs for African-Americans resulted in increased use of colonoscopy. This session is important to cancer programs that serve this patient population and others where use of colonoscopy is below average.

Abstract 1502 (N. Beri et al.) described screening programs in rural young women, and noted that the increased availability of healthcare from the Affordable Care Act (ACA) should increase the frequency of use of mammograms.

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Abstract 1503 (R. Chlebowski et al.) investigated the impact of obesity and BMI (body mass index) on breast cancer survival. In African-Americans, use of estrogens decreased risk of breast cancer with a hazard ratio of 0.32 (p=0.04).

Abstract 9509 (F. Joly et al.) investigated cognitive decline. Elderly patients reported a 66% subjective decrease in cognitive ability, while physicians measured a 49% objective decrease in cognitive ability. Remarkably there was no correlation between subjective feelings of cognitive decline and objective measures of cognitive decline. There was a high correlation of fatigue with cognitive decline, which suggests a potential benefit of exercise in protecting against this important complication.

Abstract 9510 (C. Kamen et al.) examined the EXCAP exercise program. It demonstrated that with exercise, there was a reduction in depression, confusion, and distress. As clinicians, we should be encouraging this intervention.

Abstract 1507 (K. Metcalfe et al.) demonstrated that oophorectomy was beneficial in estrogen receptor negative patients with BRCA1 positivity. This procedure was best performed at ages less than 50. The hazard ratio for death was 0.59 (p=less than 0.05) for BRCA carriers, but was not significant in women with BRCA2 tumors (0.81, p=0.61).

That said, *Abstract 1508* (D. Domchek et al.) demonstrated in the FORCE study that oophorectomy increased patient symptoms, including sleeplessness, increased vasomotor changes, increased stress, and reduced sexual function. Hormone replacement therapy for these individuals restored sexual satisfaction and decreased vasomotor changes.

Using state registry data *Abstract 1506* (T. Pal et al.) found that African-American women under 50 had a remarkably high frequency of mutations, 9.9%. There was also a 33% discovery of mutations of uncertain significance in this population of women. This number is remarkably high, and should increase our likelihood of doing gene testing in these patients.

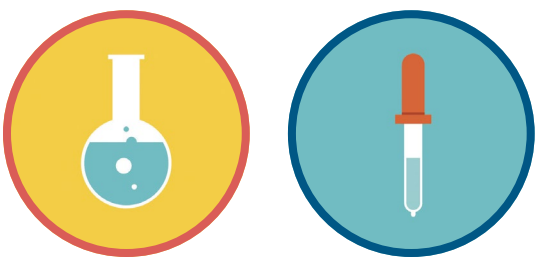
Ovarian Cancer

Abstract LBA 5500 (Late Breaking Abstract, J. Liu et al.) demonstrated that a non-chemotherapeutic approach to ovarian cancer using cediranib plus olaparib reduced risk of recurrence to only 48% compared to 80% recurrence in patients receiving combination chemotherapy. The progression-free survival was improved significantly. This was a three-fold increase in progression-to-free survival in patients without BRCA mutations.

Abstract 5503 (S. Pignata et al.) demonstrated that in platinum-resistant patients, pazopanib plus weekly paclitaxel was better than paclitaxel alone, with a progression-free hazard ratio of 0.4 (p=0.002) with a borderline improvement in overall survival, hazard ratio 0.6 (p=0.056).

Pediatric Oncology

Abstract 10000 (E. Mullen et al.) dealt with pathology review. In 3,000 patients with renal tumors, second pathology opinions resulted in a 40% discrepancy in pathologic impressions, which would affect selection of chemotherapy. This finding suggests it is very important to get pathology second opinions in many patients with pediatric malignancy.



Breast Cancer

Abstract LBA 505 (H. Moore et al.) discussed the POEMS study. In patients less than 50 years old, the use of chemotherapy versus use of chemotherapy plus goserelin showed that ovarian failure was markedly reduced by the use of goserelin. Patients on chemotherapy had a 45% incidence of ovarian failure at two years after therapy, compared to only 20% with addition of goserelin (p=0.006). Most importantly, overall survival was improved with the addition of goserelin, hazard ratio at four years 0.43 (p=0.05) and successful pregnancies were increased by addition of goserelin (12 pregnancies in 18 attempts after chemotherapy, versus 22 pregnancies in 25 attempts with addition of goserelin). These findings have a major impact for our premenopausal patients who wish to continue the possibility of pregnancy after therapy.

Abstract 506 (L.A. Carey et al.) looked at the results of CALGB study 40601. Tumors after therapy achieved more normal subtype or more luminal A-like subtype. This finding indicates that there are genomic changes with chemotherapy and retesting is important.

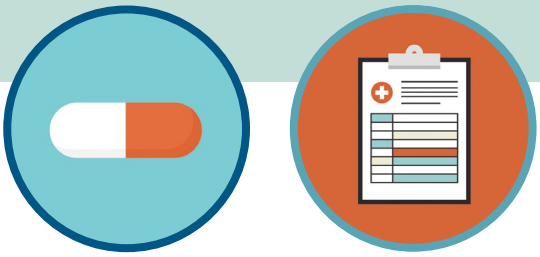
Abstract 511 (N. Turner et al.) looked at liquid biopsy. Plasma DNA was collected in 20 patients receiving neoadjuvant therapy, and circulating tumor DNA was positive in 90% of the patients who developed stage 4 disease. This marker may be important, and appeared to have a median eight-month lead time before clinical relapse. In four patients who had circulating tumor DNA, all relapsed by 24 months, compared to 95% non-relapsers in the 16 patients with no circulating tumor DNA (p=0.01).

Abstract 503 (H. Pan et al.) studied the impact of obesity. In ER positive premenopausal patients, obesity increased mortality. The hazard ratio was 1.36 (p=0.0001), but survival was no worse in ER positive postmenopausal patients or in any ER negative patients. This finding should increase our surveillance in obese ER positive premenopausal patients.

Abstract LBA 1 (Plenary Session, O. Pagani et al.) looked at patients with ER positive breast cancer. The use of ovarian function suppression (OFS) plus exemestane was superior to OFS plus tamoxifen. The five year disease-free survival was 91% with OFS plus exemestane versus 87% with OFS plus tamoxifen, hazard ratio 0.72 (p=0.002).

Abstract LBA 4 (M. Piccart et al.) examined the ALTTO study. Unfortunately, the addition of lapatinib to trastuzumab did not increase the disease-free survival or overall survival at four years. This is the first study examining a combination that had been positive in neoadjuvant therapy trials (with increased response rate), which has thus far failed to show improvement in a randomized adjuvant comparative trials.

Abstract LBA 9500 (G. Hortobagyi) examined the use of



zoledronic acid. After one year of monthly therapy, use of the drug every 4 weeks was equal to its use every 12 weeks.

Abstract 9507 (D. Barton et al.) studied vaginal DHEA (dehydroepiandrosterone) and found increased sexual desire, increased sexual arousal, and increased sexual function with decreased pain in breast cancer survivors with those symptoms.

Multiple Myeloma

Abstract 8515 (A. Palumbo) examined duration of therapy. Continuous chemotherapy, compared to fixed length therapy with drug holiday, showed improvement in progression-free interval number one with continuous therapy; 16 months for fixed length up to 32 months for continuous treatment (p=0.001). There was an increase in progression-free interval number 2 from 40 months for fixed length up to 55 months for continuous (p=0.001) with a suggestion of increased 4-year overall survival up from 60% to 69%. This finding indicates improvement with continuous therapy.

Abstract 8517 (G. Singh et al.) looked at Medicare SEER data and demonstrated increased cost effectiveness of transplant in eligible patients. Patients with transplant had increased survival of 4.9 years compared to 3.6 years without. This treatment had a cost of $72,852 per year of life saved, indicating the value of the transplant experienced.

Non-Hodgkin Lymphoma

Abstract 8500 (F. Cavalli et al.) reported on the LYM 3002 study. This looked at RCHOP versus VRCAP in which vincristine was replaced by bortezomib. The overall disease-free survival with VRCAP was 25 months, compared to 14 months with RCHOP, hazard ratio 0.63 (p=0.001). These data are very promising.

Abstract 8501 (M. Pfreundschuh et al.) presented on the SEXIE trial. This trial showed an increase in progression-free survival with high-dose RCHOP in men compared to standard dose RCHOP, but no difference in women. This suggests increased rituximab dosing in men may be appropriate.

Abstract 8520 (G. Nowakowski et al.) examined lenalidomide plus RCHOP (called R2CHOP) in diffuse large B-cell lymphoma. The two-year progression-free survival was 28% with RCHOP in non-germinal center lymphomas compared to 60% with R2CHOP, and in germinal cell tumors was 46% with RCHOP and 83% with R2CHOP. These data are very promising.

Prostate Cancer

Abstract 5008 (R. DeWit et al.) looked at orteronel with prednisone compared to prednisone 5 mg b.i.d. alone. The progression-free survival was improved, hazard ratio 0.7 (p=0.001 with addition of orteronel). There was considerable fatigue, however.

Abstract LBA 2 (C. Sweeney et al.) presented on the CHAARTED study ECOG 3805, specifically the early addition of docetaxel with ADT (androgen deprivation therapy) versus ADT in castration sensitive prostate cancer. Overall survival with docetaxel addition was 58 months, compared to 44 months with ADT alone, hazard ratio 0.61 (p=0.0003). The overall survival was also improved to 49 months, compared to 32 months, hazard ratio 0.6 (p=0.0006). These findings are highly significant for patients with metastatic prostate cancer initiating therapy.

Abstract 5003 (X. Garcia-Albeniz et al.) examined PSA recurrence. Patients who received immediate ADT in the CaPSURE study had equivalent overall survival to patients who had delayed ADT, with a hazard ratio for survival of 1.06.

Bladder Cancer

Abstract 5011 (T. Powles et al.) showed that with treatment aimed at suppressing PD-L1 with the drug MPDL 3280A, patients whose tumor expressed PD-L1 had a response rate of 43% compared to only 11% in patients whose tumors did not express PD-L1.

Renal Cell Cancer

Abstract 5010 (A. Amin et al.) looked at the PD-L1 suppressor nivolumab with PEGF inhibition. The response rate was 52%. The combination of nivolumab plus pazopanib was considered too toxic, but the combination of nivolumab with sunitinib was found to be tolerable and gave durable responses.

Abstract 4504 (H. Hammers et al.) studied nivolumab plus ipilimumab. The response rates were 29% to 39%, depending on dose.

Colon Cancer

Abstract LBA 3 (A. Venook et al.) presented on the LEAP study, SWOG trial 80405 performed with CALGB. The LEAP study compared the use of bevacizumab versus use of cetuximab used in conjunction with FOLFOX or FOLFIRI. They found no difference in progression-free survival or overall survival. Quality of life was better in patients who received bevacizumab, (p=0.054). The overall survival of 29 months represents a new standard of therapy, and 10% of patients were alive over five years.

Rectal Cancer

Abstract 3500 (I.C. Rodel et al.) demonstrated that the addition of oxaliplatin to 5-FU in neoadjuvant and adjuvant therapy was better than use of 5-FU alone in localized rectal cancer, disease-free survival hazard ratio 0.8 (p=0.03).

Abstract 3502 (Y. Hong et al.) showed that adjuvant FOLFOX increased disease-free survival at three years compared to adjuvant 5-FU alone, hazard ratio 0.66 (p=0.04).

Gastric Cancer

Abstract 4003 (S. Qin et al.) looked at apatinib, which increased overall survival and progression-free survival compared to use of placebo in third-line or later therapy. Progression-free survival was increased (p=0.001) and also overall survival (p=0.01).

Head and Neck Cancer

Abstract 6004 (M. Ghi et al.) showed that neoadjuvant chemotherapy with TPF (paclitaxel, cisplatin plus 5-FU) increased progression-free survival, hazard ratio 0.73 (p=0.02) and overall survival of 53.7 months versus 30.3 months, hazard ratio 0.72 (p=0.03). This finding may set a new standard for neoadjuvant therapy in head and neck cancer.

Central Nervous System

Abstract 2000 (J. Buckner et al.) studied patients with low-grade gliomas. Use of radiation therapy alone was inferior to radiation plus PCV (procarbazine, CCNU and vincristine) adjuvant chemotherapy. Overall survival without PCV was 7.8 years and with PCV was 13.3 years, hazard ratio 0.56 (p=0.001).

Non-Small Cell Lung Cancer

Abstract 7500 (K. Park et al.) looked at patients who were inoperable after induction chemotherapy for six weeks with radiation therapy. Those patients with stable disease, partial, or complete response were randomized to either every three week docetaxel plus cisplatin or to no additional therapy. There was no change in overall survival or progression-free survival by an additional two cycles of chemotherapy.

Abstract 7501 (K. Kelley et al.) presented on the RADIANT trial. In patients with stage 1B through 3A disease who had received four cycles of a platinum doublet, use of continuation erlotinib was superior to no erlotnib. The disease-free survival was 46 months compared to 29 months in patients with EGFR mutations, hazard ratio 0.61 (p=0.04). There was no difference in patients who did not have an EGFR mutation or who were not tested.

Abstract 8002 (T. Mok et al.) studied patients with ALK mutations. This trial compared chemotherapy with pemetrexed doublet versus crizotinib. Progression-free survival was 10.9 months in patients with ALK-positive mutations with crizotinib, compared to 7.0 months with chemotherapy. The hazard ratio was 0.45 (p=0.0001).

Abstract 8003 (D. Kim et al.) looked at progression-free survival with ceritinib in patients with crizotinib-resistant cancer and ALK mutation. The progression-free survival was 8.2 months.

Abstract 8004 (J. Yang) compared standard chemotherapy versus afatinib. Results in patients with EGFR mutations (DEL19) showed a progression-free survival of 31.7 months with afatinib versus 20.7 months with chemotherapy, hazard ratio 0.59 (p=0.001).

Abstract 8007 (N. Rizvi et al.) studied patients receiving a PD-L1 inhibitor if they had PD-L1 positive lung cancer. In 45 patients, the observed response rate was 26%, disease control rate 64% with a progression-free survival of 37 weeks.

Abstract 8019 (N. Schuler et al.) looked at paclitaxel plus afatinib compared to physician choice of chemotherapy. Progression-free survival with afatinib was 5.6 months versus physician choice 2.8 months, hazard ratio 0.6 (p=0.003).

Abstract 8020 (E. Garon et al.) studied the PD-L1 inhibitor pembrolizumab. Observed response rate was 26% and progression-free survival was 11 weeks with a significantly long "tail."

Abstract 8023 (S. Antonia et al.) looked at nivolumab plus ipilimumab. The observed response rate was 22%, and the median duration of response has not yet been reached.

Abstract 8024 (S. Gettinger et al.) studied nivolumab with a response rate in PD-L1 positive squamous cell cancer of 67%, and 36% in non-squamous cell cancer. The median duration response has not yet been reached.

Small Cell Lung Cancer

Abstract 7502 (B. Slotman et al.) studied patients who had received chemotherapy plus prophylactic cranial radiation. Patients who received radiation therapy to the chest had an overall survival at 24 months of 13% compared to only 3% without chest radiation therapy, hazard ratio 0.84 (p=0.07). Progression-free survival had a hazard ratio of 0.73 (p=0.011).

Abstract 7504 (K. Goto et al.) looked at either cisplatin plus etoposide plus irinotecan (CEI) compared to topotecan alone in patients who had a relapse of more than 90 days after prior chemotherapy. Progression-free survival was improved by CEI, hazard ratio 0.5 (p=0.001) with an improvement also in overall survival 18.2 months compared to 12.5 months, hazard ratio 0.67 (p=0.008).

Melanoma

Abstract 9002 (F.S. Hodi et al.) presented on a Phase I trial of nivolumab. The overall response rate was 32%. Overall survival at the dose of 3 mg/kg was 20.3 months. In PD-L1 positive tumors, response rate was 44%.

Abstract LBA 9003 (M. Sznol et al.) looked at nivolumab plus ipilimumab. The response rate with the combination was 40%, and two year overall survival with the combination was 82% compared to only 43% with nivolumab alone.

Abstract LBA 9000 (A. Ribas et al.) studied the drug pembrolizumab in patients who were PD-L1 positive; there was a 49% response rate. Overall survival is over 28 months, and was 62% at 18 months. This represents the largest PD-L1 trial with 411 patients.

Abstract 9007 (C. Chang et al.) compared the value of different chemotherapy regimens in melanoma. The cost of the targeted drug vemurafenib was less than the cost of ipilimumab. The monthly healthcare cost was $17,000 on vemurafenib versus $65,000 on ipilimumab (compared to $16,000 on DTIC and $17,000 on temozolomide). Monthly toxicity cost was $2,200 on vemurafenib, $4,600 on ipilimumab, $9,000 on DTIC, and $3,000 on temozolomide. This cost-effectiveness study was important as we consider value-based therapy.

Abstract LBA 9008 (M. Eggermont et al.) compared ipilimumab versus placebo as adjuvant therapy in stage 3 patients. Patients receiving ipilimumab had increased progression-free survival of 26.1 months versus 17.1 months with placebo, hazard ratio 0.75 (p=0.001).

Abstract 9008a (H. Kaufman et al.) looked at the oncolytic herpes virus therapy TVEC versus GMCSF alone in patients with stage 3B, 3C, or 4 melanoma. TVEC increased overall survival to 23.3 months compared to 18.9 months with GMCSF alone, hazard ratio 0.79 (p=0.05), suggesting a possible role for immunotherapy. There was considerable fatigue and chills with this intratumoral injection therapy.

Abstract 9011 (G. Long et al.) looked at dabrafenib plus trametinib compared to dabrafenib alone in patients having a BRAF V600E mutation. The doublet had a longer progression-free survival of 9.3 months compared to 8.8 months with dabrafenib, hazard ratio 0.75 (p=0.04) and a longer overall survival of 93% at six months compared to 85% at six months with dabrafenib alone, hazard ratio 0.66—this was not significant. Interruption of therapy was 49% on the doublet and 33% on the dabrafenib.

Supportive Care

Abstract LBA 9513 (J. Dionne-Odom et al.) randomized patients to palliative care immediately or delayed for 12 weeks. There was increased quality of life, decreased depression (p=0.003) in patients, and decreased depression in caregivers. This suggests a benefit of palliative care beyond the patient alone, extending to caregivers and suggests starting early is important.

Abstract LBA 9514 (A. Abernethy et al.) showed that discontinuation of statins at point of tumor and patient deterioration was associated with improvement in the quality of life (p=0.04). Stopping statins (given to prevent cardiovascular events) did not increase the frequency of cardiovascular events and survival was equal whether statins were continued or discontinued.

Chronic Lymphocytic Leukemia

Abstract LBA 7008 (J. Byrd et al.) studied ibrutinib compared to ofatumumab in second or later lines of therapy. Use of ibrutinib improved progression-free survival, hazard ratio 0.2 (p=0.001), and improved overall survival, hazard ratio 0.4 (P=0.005), with an improved response rate of 43% compared to 4% on ofatumumab (p=0.0001).

General Oncology

Abstract 6506 (K. Takahashi et al.) examined the use of the IBM super computer Watson. The accuracy was found to be 82.6% compared the standard oncologist recommended therapy. There was a significant communication challenge using Watson. This was observed when physician notes were difficult to automatically incorporate into the Watson database.

In summary, ASCO 2014 was an exciting meeting with lots of take-home information. I encourage readers to read the abstracts on the ASCO website, and to read the completed manuscripts when they are published in order to completely understand the final data and final interpretations. See you at ASCO 2015!

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