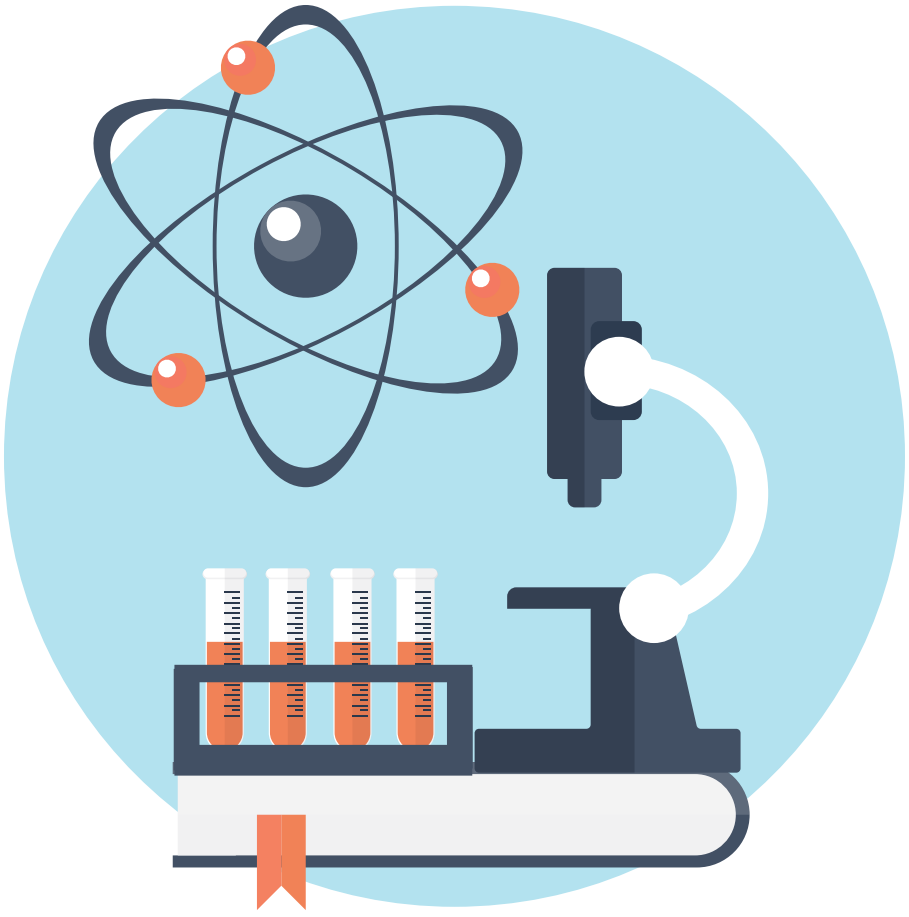
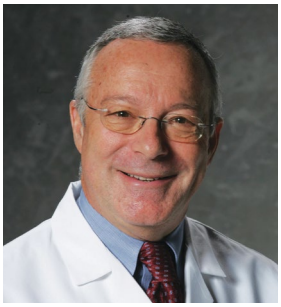


Best of ASCO 2016

BY CARY A. PRESANT, MD, FACP, FASCO



THE 2016 ASCO ANNUAL MEETING WAS FILLED WITH INFORMATION, practice advice, and exciting results that will change oncology for the coming year. Several themes emerged: genomics, immunotherapeutics, targeted oncology products, and practice management issues. Here are my thoughts about the best of ASCO 2016.

The impacts of sequestration and proposed ASP reductions in payment may be devastating for practices by pushing more oncology drugs "under water" and necessitating consideration of alternate sites of administration or alternative treatment plans.

Practice Management Issues

At the pre-ASCO session on Economics of Cancer Care, presentations focused on patient financial burdens and the impact of patient bankruptcy, which is associated with shortened survival; the new ASCO practice survey results; and experience with shared savings models.

In "Palliative Care Alongside Oncology: Better Care at a Cost We Can Afford," Thomas J. Smith, MD, FACP, FASCO, FAAHPM, reported that considerable healthcare savings were realized by implementing early palliative care, which may be important in programs that are participating in alternative payment models (APMs) where there are shared risk and savings arrangements.

In "Impacts of Changes in Part B Drug Payment Policy," Andrew Mulcahy, PhD, MPP, emphasized how much chemotherapy has shifted to the hospital outpatient site (now 41%). The impacts of sequestration and proposed ASP reductions in payment may be devastating for practices by pushing more oncology drugs "under water" and necessitating consideration of alternate sites of administration (e.g., hospital outpatient departments) or alternative treatment plans.

Acronym Legend

ACA: Affordable Care Act
ALL: Acute lymphoblastic leukemia
AML: Acute myeloid leukemia
APM: Alternative payment model
ASP: Average sales price
CIPN: Chemotherapy induced peripheral neuropathy
CLL: Chronic lymphocytic leukemia
CMS: Centers for Medicare & Medicaid Services
CR: Complete response
DFS: Disease-free survival
dMMR: Deficient mismatched DNA repair
EFS: Event-free survival
ESMO: European Society for Medical Oncology
GDP: Gross domestic product
HR: Hazard ratio
ICER: Institute for Clinical and Economic Review
MACRA: Medicare Access and CHIP Reauthorization Act of 2015
MIPS: Merit-Based Incentive Payment System
NCCN: National Comprehensive Cancer Network
NCI: National Cancer Institute
NSCLC: Non-small cell lung cancer
OS: Overall survival
PARP: Poly ADP ribose polymerase
PFS: Progression-free survival
PQRS: Physician Quality Reporting System
QOPI: Quality Oncology Practice Initiative
QRUR: Quality and Resource Use Reports
RR: Relative risk
TNBC: Triple negative breast cancer
TTP: Time to progression

ASCO was urging participation in the QOPI and PCOP programs, although it is unclear if these programs will be accepted in part—or at all—by CMS as quality measures or as APMs for 2017.

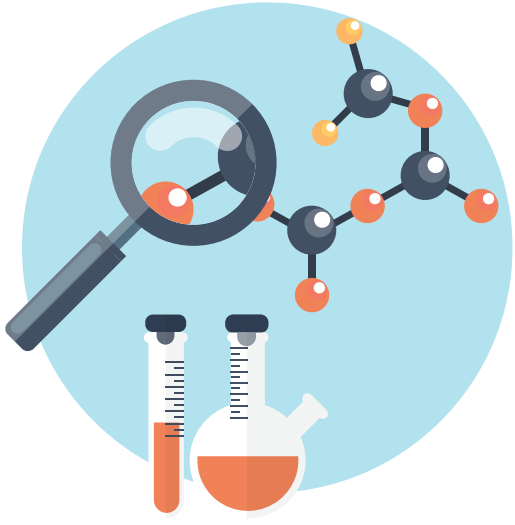
Ron Kline, MD, from the Center for Medicare & Medicaid Services (CMS), gave an update on the Oncology Care Model (OCM), which will impact many practices across the country.

In "The Economics of Cancer Care: The Impact of MACRA," Philip J. Stella, MD, Chair, Rapid Response Taskforce, reminded attendees that all oncology programs will, by law, be impacted by MACRA and MIPS starting in 2017. His takeaway: physicians and administrators must know *now* the metrics that are already being collected on physicians and practice patterns to determine what changes must be made. Know your PQRS, meaningful use, and QRUR scores, and review the cms.gov website to understand how you are doing.

At other education meetings, ASCO was urging participation in the QOPI and PCOP programs, although it is unclear if these programs will be accepted in part—or at all—by CMS as quality measures or as APMs for 2017.

Editor's Note: Proposed Medicare Outpatient Prospective Payment System and Physician Fee Schedule rules came out in July; final rules are expected in November 2016 for implementation in 2017. Be sure to read *Oncology Issues* and other journals, visit accc-cancer.org, reach out to your state oncology societies, and leverage ASCO resources to be fully prepared for new requirements.

Robin Zon, MD, vice president and senior partner at Michiana Hematology-Oncology, PC, in South Bend, Indiana, emphasized several important preparations that oncology practices should make over the next months. Her suggestions:



- Participate in PQRS (the CMS quality reporting system)
- Improve your meaningful use performance by having patients use your portal
- Reduce hospitalizations when possible
- See when you can use generics in place of single-source drugs
- Code for all ICD-10 comorbidities in each patient so that CMS knows the complexity of your patients
- Have a practice leadership team (physician, nurse, administrator, and medical assistant) to get ready for 2017.

Value continued to be an underlying theme at ASCO 2016. In "Quality and Value: Measuring and Utilizing Both in Your Practice," Lowell E. Schnipper, MD, PhD, discussed the ASCO equation for value determination. Net health benefit was equal to clinical benefit (80% of the benefit as measured by Phase III studies of survival, PFS, response plus extended survival plus symptom control minus toxicity) divided by cost to the system and the patient. Examples were provided. No corrections are made according to the perceived value to the individual patient, although adjuvant-treated patients value individual therapies differently from palliative-treated patients. Of course the ASCO model is not the only value framework; ESMO, NCCN, ICER, and the DrugAbacus are others. Bottom line: we do not know how insurers and health systems will respond to these innovative value determinations, but they likely will affect which treatments will be available for our patients, and how we and our profession will be viewed by patients and the public.

Health Science Research

- ***Abstract LBA6500,*** Goldstein et al. showed that in the U.S., the retail price of patented drugs was $8,694 per month, compared to $654 per month for generic drugs. But in other countries, the retail price of patented drugs was $1,500-$3,100 per month, while generic drugs were $120-$530 per month. Looking at a percent of GDP per capita, patented drugs were 192% in U.S. vs. 288% in China and 313% in India.
- Kehl and colleagues ***(Abstract 6503)*** found that after the ACA, while 94% of networks covered by the ACA nationally had a CoC-approved hospital in network, only 40% had at least one NCI-approved comprehensive cancer center. Only two-thirds of states with ACA national networks had an NCI-approved comprehensive cancer center located in the state. Only 30% of HMO networks had an NCI-approved comprehensive cancer center in their network.
- ***Abstract 6505,*** Neubauer et al. showed that in practices that used value-based NCCN pathways compared to practices not using such pathways, there was adherence to pathways in

84% with 93% patient satisfaction, increased use of hospice of 57%, and savings of 20% in chemotherapy, 15% in inpatient care, and overall savings of 18.5%.

- Wong and colleagues ***(Abstract 6506)*** evaluated the time costs of getting oral anticancer drugs approved by insurance. Financial assistance was necessary in 43%, with 5 calls per patient, and 5 days (range 0-45 days) to get authorization, and 11.6 days (range 1-66 days) to actually receive the drugs.
- ***Abstract 6507,*** Patel showed that using lay health workers to help patients navigate a VA health system resulted in cost savings of $11,000 (9%) per patient and increased use of hospice 40% vs. 23%, with equal survival.
- Veenstra and colleagues ***(Abstract 6508)*** reported that 55% of working patients lose their jobs while receiving chemotherapy for stage III colorectal cancer. This percentage was less in patients with employer-provided health insurance, who were men, Caucasian, or married, and who had fewer co-morbidities.

Breast Cancer

- ***Abstract LBA1,*** Goss et al. reviewed hormonal adjuvant trial MA.17R. After 5 years of letrozole (+/- tamoxifen for the first 5 years), patients continuing letrozole for 5 more years had improved DFS HR 0.66 (p=0.01). Contralateral cancer diagnosis was reduced HR 0.42 (p=0.001). OS was equal. Distant recurrence was reduced 1.1%. However, fractures were increased to 14% vs. 9% in placebo control (p=0.001), and osteoporosis was 11% vs. 6% (p=0.001). Discussant Ian Smith pointed out that if letrozole was continued, an IV bisphosphonate should be given, and that continued therapy might be best used for high risk patients (e.g., larger tumors).
- Hurwitz and colleagues ***(Abstract 500)*** showed in neoadjuvant therapy, TCH pertuzumab was superior to trastuzumab emtansine plus pertuzumab CR 56% vs 44% (p=0.01), but was more toxic.
- ***Abstract 504,*** Urreticoechea et al. showed addition of pertuzumab to trastuzumab plus capecitabine resulted in non-significant increased PFS by 2 months and OS by 8 months in patients progressing on trastuzumab.
- Blum and colleagues ***(Abstract 1000)*** reported on the adjuvant combination ABC trial (USOR 06-090 + NSABP 46 + NSABP 49). Four-year invasive DFS favored doxorubicin combination (TaxAC) compared to TC; 90.7% vs 88.2% (p=0.04), HR 1.20. Leukemia so far has been seen in 0.24% of TaxAC patients, none in TC. Four-year OS was equal. This may change therapy, especially in ER positive 4+ nodes positive patients.
- ***Abstract 1002,*** Bergh et al. showed dose dense epirubicin cyclophosphamide was superior to Q3W FEC with 5-year EFS, HR 0.79 (p=0.04).
- ***Abstract 1005,*** Soran et al. showed that mastectomy improved survival in patients presenting with de novo stage IV breast cancer; OS HR 0.66 (p=0.005).
- Giuliano and colleagues ***(Abstract 1007)*** showed in patients with 1-2 positive sentinel nodes, complete axillary node dissection was not necessary, 10-year OS equal.
- Adams and colleagues ***(Abstract 1009)*** found a CR+PR rate of 71% in patients with ≤ 3 prior regimens with atezolimumab plus nab-paclitaxel.
- ***Abstract 1012,*** Zhimim et al. showed that adding capecitabine to docetaxel + FEC in adjuvant breast cancer produced better distant DFS; 94.3% vs 89.3% (p=0.02) in TNBC.
- Freedman and colleagues ***(Abstract 1024)*** showed that in adjuvant Alliance breast cancer trials, there were only 17% of patients over 65, and only 7% over 70.
- ***Abstract 11578,*** Reinbolt et al. showed genetic mutations in 100 breast cancer patients having comprehensive genetic profiles. There was a median of 5 mutations per patient (0-13 range). Other than for drugs already FDA-approved for breast cancer, researchers found a drug, which had already been FDA-approved for other cancers to be associated with the mutations found in breast cancer genes in 77/100 patients; 41% of reports suggested a change in therapy, and in half of those the physician followed the change advice.

Colorectal Cancer

- ***Abstract 3503,*** Morris et al. reported a 24% RR in patients with squamous cell cancer of the anus with nivolumab.
- Venook and colleagues ***(Abstract 3504)*** found that right-sided cancers had better outcomes when bevacizumab was given, but left-sided cancers had better outcomes when cetuximab was given (if KRAS wild type).
- ***Abstracts 3505*** (Schrag et al.) and ***3506*** (Lee et al.) reported outcomes of right-sided colon cancer were better than left-sided.

Gastrointestinal & Pancreatic Cancer

- ***Abstract 103,*** Le et al. found that PFS from pembrolizumab was longer in patients with deficient mismatched DNA repair (dMMR) vs. those with no dMMR HR 0.135 (p<0.0001); OS was also longer HR 0.25 (p-0.001).

- Strosberg and colleagues *(Abstract 4005)* showed that treatment of recurrent midgut neuroendocrine tumors had longer PFS with 177-Lu-DOTATATE compared to octreotide LAR; RR was 18% vs 3% (p=0.0008).
- *Abstract LBA 4006,* Neoptolemos et al. reported on ESPAC-4. OS for gemcitabine/capecitabine was superior to gemcitabine alone median survival time (MST) 28.0 months vs 25.5 months; HR 0.82 (p=0.032).

Genitourinary Cancer

- McDermott and colleagues *(Abstract 4507)* showed that renal cell cancer patients on nivolumab had a 5-year OS of 41% and 5-year OS of 34%.
- *Abstract 4515,* Dreicer et al., showed that atezolizumab had RR of 28% in bladder cancer patients with high PDL1 levels, with 15% CR, and 12-month OS of 37%. 19% of progressing patients had responses after progression.
- Nelson and colleagues *(Abstract 5009)* found that in metastatic prostate cancer, 11% of patients had deficient DNA repair mutations in germline analysis, suggesting increased use of olaparib or other PARP inhibitors.

Glioblastoma

- *Abstract LBA2,* Perry et al., showed that patients over age 65 treated with RT 40 Gy over 3 weeks with temozolamide had 9.3 months survival and 10% 2-year survival, vs 7.6 months and 2% 2-year survival without temozolamide.

Gynecologic Cancer

- *Abstract 5501,* Ledermann et al. showed that olaparib maintenance after response to platinum-based induction chemotherapy in ovarian cancer patients with 2 or more prior therapies offered longer PFS 8.4 months vs. 4.8 months compared to control patients, HR 0.35 (p<0.0001), with better OS 29.8 months vs. 27.8 months, HR 0.73 (p=0.02), and best in BRCA mutated patients 34.9 months vs. 30.2 months, HR 0.62 (p=0.02).
- Gershenson and colleagues *(Abstract 5502)* found that hormonal maintenance therapy after surgery for low-grade serous cancer was better than no therapy after surgery; TTP 81 months vs. 29.9 months (p<0.001).
- *Abstract 5505,* Pignata et al. showed that in patients with ovarian cancer relapsing in 6-12 months, platinum re-induction therapy was better than non-platinum; OS 24.5 months vs. 21.8 months, HR 1.38 (p=0.06).

Head and Neck Cancer

- *Abstract 6007,* Zhang reported that patients with nasopharyngeal cancer showed superiority of gemcitabine/cisplatin vs. 5FU/cisplatin with PFS 7.0 months vs. 5.6 months, HR 0.55, and OS 29.4 months vs. 20.9 months, HR 0.62 (p=0.0002).
- Soulieres and colleagues *(Abstract 6008)* showed that after 1 prior line of platinum taxane therapy, buparlisib (an oral PIK3 inhibitor) plus paclitaxel was better than paclitaxel with PFS 4.6 months vs. 3.5 months, HR 0.65, and OS 10.4 months vs. 6.5 months, HR 0.72 (p=0.04). RR in HPV-negative patients was 39% vs. 11%.

Leukemia, Myelodysplastic Syndrome

- Turtle and colleagues *(Abstract 102)* showed CAR-T responses in ALL at 100% CR; NHL at 44% CR, and CLL at 45% CR. Cytokine release syndrome was common with 70-90% needing hospitalization.
- *Abstract 7000,* Lancet et al., showed that liposomal cytarabine + daunorubicin was superior to standard therapy in patients with AML age 60-75, CR (complete response) 37% vs 25%, and increase OS HR 0.69 (p=0.005).
- Frey and colleagues *(Abstract 7002)* and Park and colleagues *(Abstract 7003)* reported successful results of CA19 CAR-T cell therapy of ALL; CR 70-90%.
- Lin and colleagues *(Abstract 7007)* showed venetoclax in relapsed AML showed CR 54% and 1 year OS 58%.

Lung Cancer

- *Abstract 100,* Antonia et al. reviewed the results of Checkmate 032 nivolumab plus ipilimumab in patients with recurrent NSCLC. Only 24% of patients were PDL1 positive. Depending on dose, 1 year OS was 33% to 43% with some long survival in the follow-up "tails."
- Rudin and colleagues *(Abstract LBA8505)* showed patients with SCLC, treated with the DLL-3 targeted antibody drug conjugate rovalpituzumab teserine, had an RR of 25%, but RR was 91% if they were DLL-3 positive. In third line DLL-3 positive patients, RR was 70%.
- Wakelee and colleagues *(Abstract 9001)* showed that in 36% of NSCLC patients the EGFR mutation T790M was present in urine but not in tumor tissue, so urine, plasma, and tumor tissue should all be tested.
- *Abstract 9004,* Gomez et al., treated patients with oligometastatic NSCLC (3 or fewer metastases) without progression on chemotherapy, with either local surgery and RT or continued chemotherapy. PFS was longer with local therapy, 11.9 months

vs. 3.9 months, HR 0.36 (p=0.01). OS is being evaluated but patients on the chemotherapy arm are crossing over to local therapy.

- Nokihara and colleagues ***(Abstract 9008)*** showed that in patients with ALK- positive NSCLC, alectinib was better than crizotinib, PFS 20.3 months vs. 10.2 months, HR 0.34 (p<0.0001).

Melanoma

- ***Abstract 9505,*** Wolchok et al. updated the Checkmate 067 trial. Nivolumab plus ipilimumab gave longer PFS than nivolumab alone or ipilimiumab alone, 11.5 months vs 6.9 vs. 2.9 months.

Multiple Myeloma

- ***Abstract LBA4,*** Palumbo et al., showed that in the CASTOR trial daratumumab with Vd (bortezomib plus decadron) was better than Vd with PFS >12 months vs 7.2 months (p<0.0001), 1 year PFS 67% vs. 26%.
- Cavo and colleagues ***(Abstract 8000)*** showed early transplant was superior to late transplant PFS HR 0.76 (p=0.01).
- ***Abstract 8002,*** Lacy et al., showed a 77% response rate with all oral therapy ixazomib, cyclophosphamide, and dexamethasone (ICd).

Precision Medicine

- Zill and colleagues ***(Abstract LBA11501)*** found that circulating tumor DNA showed agreement with tissue analyses in 87% of 15,000 patients. They found actionable changes in patients with insufficient tumor tissue for analysis, patients with tumor progression without tissue biopsies, and patients with TNBC but mutations in HER2 on tumor progression.
- ***Abstract LBA11511,*** Hainsworth et al., showed a RR of 14/74 in patients (with non-trastuzumab approved tumors) who showed alterations in the HER2 pathway and who were treated with anti-HER2 therapy. Also, 7/31 RR occurred in the patients found to have a BRAF mutations treated with anti-BRAF therapy.

Patient & Survivor Care

- ***Abstract 10001,*** Hershman et al. reported that risk for chemotherapy induced peripheral neuropathy (CIPN) from paclitaxel was worse in diabetics (25%) vs. 12% without diabetes. It was less in patients with autoimmune disease 10% vs. those without autoimmune disease 20%.
- Greenlee and colleagues ***(Abstract 10002)*** found that CIPN was increased in obese patients and less if patients had 5 hours per week of exercise, suggesting a therapy, or preventive strategy. Kleckner and colleagues ***(Abstract 10000)*** also showed reduced CIPN with exercise.
- ***Abstract 10006,*** Knestrick et al. showed use of physician orders for scope of treatment vs. standard advanced directives resulted in increased hospice use 54% vs. 27%, and reduced in-hospital deaths 11% vs 30%.
- Hanai and colleagues ***(Abstract 10022)*** reported on reduced paclitaxel CIPN by use of frozen gloves and socks. Objective CIPN was reduced from 81% in controls to 28% in contralateral extremities treated by frozen gloves or socks (p<0.01).

Pediatric Cancer

- ***Abstract 10507,*** Minard-Colin et al. found that adding rituximab to standard chemotherapy in high-risk non-Hodgkin's lymphoma patients resulted in increased PFS at 1 year 94% vs. 81% without rituximab (p<0.001). OI

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