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ONCOLOGY ISSUES

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September | October 2017

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- Gina Clay, Integrated Director of Cancer Services, Central Region, Intermountain Healthcare

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Association of Community Cancer Centers

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The Journal of the
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FROM THE EDITOR

At ACCC—Content is King

BY CHRISTIAN DOWNS, JD, MHA



In January 2018, *Oncology Issues* will transition to a peer-reviewed journal under Taylor & Francis, increasing the visibility and reach of ACCC content. This offers our members more control over what's published in their journal by volunteering as peer reviewers. Interested? Simply go to accc-cancer.org/peer-review and fill out our short form. We look forward to working with you during this exciting time of transition and change.

On the subject of change: one thing that won't be changing is our unique content. *Oncology Issues* is one of the only non-clinical oncology journals and the only one that provides content for the entire multidisciplinary cancer care team, and we will continue this legacy under Taylor & Francis. One need look no further than this issue to experience the diversity and depth of our content.

Our cover article, "A Student Volunteer Program Takes Patient Satisfaction to the Next Level," offers a replicable (and cost-effective) model for extending your workforce using student interns—a strategy that benefits many members of the multidisciplinary cancer care team, including nurses, social workers, and administrators.

Next, we profile the Defeat GBM Research Collaborative, aimed at improving treatment of glioblastoma multiforme (GBM). Just as the collaborative is harnessing "the input and buy-in of many of the top minds in neuro-oncology—serving as a 'collective brain'—in the quest to overcome one of cancer's most challenging puzzles," ACCC continuously leverages the shared knowledge of its membership to improve care delivery and the patient experience.

On that note, in "The Role of the Oral Oncology Nurse Navigator," two ACCC member programs—one an oncology practice, the other a hospital-based cancer program—illustrate how navigation services can improve care coordination, as well as provider and patient satisfaction. Similarly,


"Painting a Brighter World in Cancer Care" shows how patients, caregivers, and providers can come together through art.

In closing this column, I want to draw your attention to two articles that address critical issues facing community oncology.

The first is the explosion in clinical data. We have yet to figure out how to manage these data in an effective manner for a busy community-based program. To make this even more challenging, the future will require clinicians to not only synthesize and process reams of clinical data, but also to integrate economic and outcomes-oriented information into a treatment plan.

So how does *Oncology Issues*—a non-clinical journal—help? One example is our "Best of ASCO" article, where Cary A. Present, a distinguished past president of ACCC, provides an overview of the research that may change how you practice oncology today and in the future. Written in clear, succinct language and organized by disease type, this information is accessible to the entire multidisciplinary cancer care team. We hear anecdotally how our members appreciate this curated information. In the future, we are going to need more—and frankly more sophisticated—means of synthesizing clinical information for the cancer care team.

A second major issue facing community oncology in the next decade is how to best leverage—and pay for—new technology. In this issue, we highlight one of many ACCC education programs in "Virtual Molecular Tumor Boards." This webinar series offers practical strategies for integrating "virtual" tumor boards and current trends in use of technology to advance patient care, including ongoing molecular testing issues in lung cancer.

Beyond the pages of this journal, one of our most important member resources is coming up right around the corner, Oct. 18-20, in Nashville, Tenn. Attend the 34th ACCC National Oncology Conference, and I guarantee you'll come away rejuvenated, re-energized, and ready to put the knowledge you've gained to work at your cancer program or practice. Register today at accc-cancer.org/OncologyConference. 

Building a Program from the Ground Up—Lessons Learned

BY MARK S. SOBERMAN, MD, MBA, FACS



On July 27, 2017, Frederick Regional Health System cut the ribbon on its beautiful new Cancer Institute, a culmination of five years of planning,

fundraising, design, and construction. Over the ensuing weekend, we moved into the new building and opened the doors for business on Monday, July 31.

The transition has gone smoothly—though not without a few hiccups. Overall, however, our physicians, staff, and patients are delighted with the new facility. As I look back and reflect on the process, there are several lessons learned on the journey that could benefit any cancer program.

First, a building is not a box into which you drop a program. We made a considered decision to approach the project from the perspective that “form follows function.” As part of our design process, we visited several cancer centers. Some had designed the facility around their workflow, and others had designed the building and plopped the program into the facility—without regard for the processes of care. You can guess which ones worked well and which ones didn't.


Before we undertook the building design process, we engaged in a redesign of our workflows and care processes. We also decided to work with the Samueli Institute (samueliinstitute.org) to create an Optimal Healing Environment. That process resulted in additional modifications to our workflow and informed some of the choices we made in the building design. Staff had significant input into the process and were extremely engaged.

Another lesson learned was to be flexible and unafraid of rethinking decisions. For example, we initially were going to build the new Cancer Institute on our hospital campus, attached to the main hospital building. This decision would have created a grand entrance to the campus and unified important inpatient and outpatient services. At the time, the decision seemed to make perfect sense.

But, as we studied the issue further, we began to think we had made the wrong decision. The cost and complexity of building on the main campus was greater than initially anticipated. Parking for employees and patients was problematic. Locating the center on the hospital campus meant that we would be charging hospital outpatient rates, making us a more expensive provider of cancer care.

After further analysis, we decided to build on one of our ambulatory sites adjacent to an imaging and lab facility. We would save millions of dollars on construction, allow easy access for our patients and staff, and provide care to the community at the same cost as a physician's office—while offering all of the coordinated and comprehensive services of a hospital-based Cancer Institute. Our Board of Trustees enthusiastically endorsed this new plan, and it was welcomed by our staff and the community.

My final pearl of wisdom: understand it won't be perfect when you open—despite meticulous planning and stakeholder engagement. Moving staff into a new building is never without a few hiccups. For us, it was a water pipe that broke at the end of the first week, necessitating a one-day closure for repairs. And remember, you will never please everyone. Despite staff involvement during all stages of the design process, on day one, some were less than enamored of their new digs. Yes, some clinic workflows and configurations probably need to be tweaked. While we plan to wait a full month before doing so, we are meeting with physicians and staff and letting them know that we hear and acknowledge their concerns.

The opportunity to conceptualize, plan, design, and build a new cancer center has been an amazing experience of learning, growth, and maturation as a cancer center director, leader, and physician executive. Most importantly, it has been an incredible privilege to be part of a team that has brought to our community a brand new, patient-centered, state-of-the-art cancer center that elevates the level of care and will benefit our patients, their families, our staff, and our physicians for years to come. 

Coming in Your 2017 ONCOLOGY ISSUES

- ▶ The Community Health Worker: A Cancer Program's Role in Population Health Efforts
- ▶ Enhancing Patient Satisfaction and Knowledge with the Patient Resource Navigator System
- ▶ Oncology Disease Site Process Mapping, Coordinating Care across the Continuum
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CMS Proposed 2018 OPPS & PFS Rules—What You Need to Know

CMS is proposing to reduce reimbursement for drugs purchased under the 340B Drug Pricing Program to ASP minus 22.5%. Learn about this and other proposed changes at: mynetwork.accc-cancer.org/viewdocument/2018-cms-oppo-pfs-proposed-rules.



An Acuity Tool to Optimize Nurse Navigation Caseloads

2017 ACCC Innovator Award winner University of South Alabama, Mitchell Cancer Institute, developed a homegrown tool to assess patient needs prior to caseload allocation and determine the level of navigation needed. youtube.com/watch?v=dol8QhrVgDU. Attend the 2017 National Oncology Conference, Oct. 18-20, Nashville, Tenn., to hear how they are using this tool in quality and process improvement efforts.



Building a Better Lung Cancer Model

Read how ACCC's Optimal Care Coordination Model initiative is addressing patient access to care, treatment team integration, physician engagement, survivorship care, and tobacco cessation through QI initiatives and metrics to help improve the care of lung cancer patients on Medicaid. onclive.com/publications/oncology-business-news/2017/september-2017/accc-seeks-to-build-a-better-lung-cancer-model?p=1.



Immunotherapy Updates On-Demand

Browse the ACCC Institute for Clinical Immuno-Oncology (ICLIO) webinar playlist. Just-added titles in this library of on-demand webinars include Post 2017 ASCO Immuno-Oncology Highlights and Therapeutic Approaches to Metastatic Melanoma. accc-icl.io/resources/webinar-archive.

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fast



Oncologists Share Top Concerns Around Genomic Testing

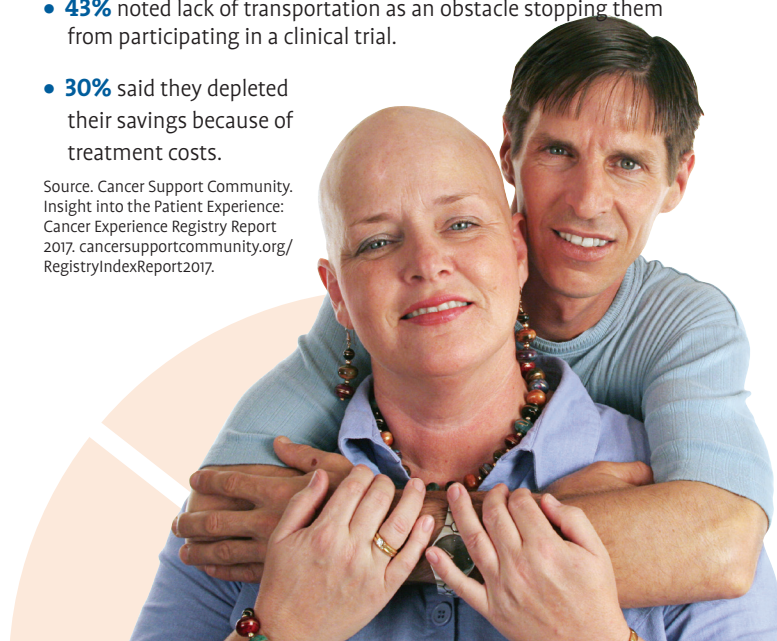
- More education is needed before widespread genomic testing can be advocated—**86%**
- Insurance coverage of genomic testing is poorly defined—**84%**
- Getting approval for an unapproved indication is too great a hurdle to use genomic testing results—**73%**
- The clinical utility of routine multiplex somatic genomic testing is unclear and too cost-ineffective to support widespread use—**73%**
- Concerns that genomic testing will be overused or misused by oncology—**65%**
- Concerns about the clinical reliability and validity of the test results provided by commercial genomic testing companies—**53%**

Source. West HJ, Miller G. Genomic testing and precision medicine in cancer care. *Medscape*; May 2, 2017. medscape.com/slideshow/genomics-and-oncology-report-6008655?faf=#1.

Key Findings from Survey on the Cancer Patient Experience

- **93%** said QOL is very important when weighing treatment options.
- **73%** reported that they did not discuss the cost of care with their care team.
- **43%** noted lack of transportation as an obstacle stopping them from participating in a clinical trial.
- **30%** said they depleted their savings because of treatment costs.

Source. Cancer Support Community. Insight into the Patient Experience: Cancer Experience Registry Report 2017. cancersupportcommunity.org/RegistryIndexReport2017.



facts

Would More Survivors of Childhood Cancers Benefit from Genetic Screening?

Researchers found that **12%** of childhood cancer survivors carry germline mutations that put them or their children at increased risk of developing cancer. Their recommendation: expand genetic screening and counseling to include childhood cancer survivors diagnosed with second cancers and whose pediatric cancer treatment did not include radiation therapy.



Source: St. Jude Children's Research Hospital. multivu.com/players/English/7924753-st-jude-childhood-cancer-survivors-genetic-screening.



Researchers reviewed EHR data from 55 cancer centers in the U.S. and Canada and found that

adherence to distress screening protocols led to 18% fewer ED visits and 19% fewer hospitalizations in the two-month period following the screening.

Source: Zebrack, et al. A practice-based evaluation of distress screening protocol adherence and medical service utilization. *J Natl Compr Canc Netw*. 2017;15(7):903-912.

NCCN Surveys Providers About Federal Healthcare Changes

- **55%** say changes would likely have a negative impact on their practice, research programs, or patient outcomes.
- **11%** anticipate a positive impact.
- **34%** anticipate a neutral or mixed impact.

Those who anticipated a negative impact (55%) indicated that:

- Fewer patients will have access to health insurance—**71%**
- High deductibles will limit patient access to care—**69%**
- Cancer screening rates will decline due to higher co-pays and deductibles—**63%**
- Patients' pre-existing conditions could be excluded from coverage—**57%**
- Federal funding for cancer research will decline—**56%**
- There will be less support for mental health services—**50%**

Source: NCCN Trends Survey conducted March 23–24, 2017 at the NCCN 22nd Annual Conference: Improving the Quality, Effectiveness, and Efficiency of Cancer Care.



ISSUES

Holy OPPS!

BY LEAH RALPH

On July 13, 2017, the Centers for Medicare & Medicaid Services (CMS) released its CY 2018 proposed Hospital Outpatient Prospective Payment System (OPPS) and Physician Fee Schedule (PFS) rules. The proposed OPPS rule was the big news this year, signaling major changes may be in store for hospital reimbursement in 2018. The agency is proposing significant reduction in payment for drugs purchased under the 340B Drug Pricing Program and further reimbursement reductions for new off-campus provider-based departments (PBDs).

While the 340B Program has grown, and reform has been widely debated by policymakers over the past decade, CMS' rule proposes to fundamentally alter the program (notably a program that is not within CMS' purview). The agency is proposing to reduce Medicare reimbursement for separately payable drugs without pass-through status purchased through the 340B Program from average sale price (ASP) plus 6 percent to ASP minus 22.5 percent. Because CMS cannot currently identify 340B drugs in Medicare OPPS claims data, to better understand the breadth of the program, the agency also proposes to require that hospitals submitting claims for separately payable drugs *not* acquired through the 340B Program use a modifier on the claim in order to be reimbursed at ASP plus 6 percent. Significantly, as written, the agency's proposal would put the onus on all hospitals—340B *and* non-340B—to identify when drug claims should *not* be reimbursed at the reduced rate. ACCC continues to work through the details of the proposal and meet with policymakers and

other stakeholders to put forward meaningful, workable solutions for reforming the 340B Program. Join us at our National Oncology Conference, Oct. 18-20, in Nashville, Tenn., to learn more about CMS' proposal and ACCC's advocacy efforts around this issue.


CMS also proposes to double down on its site-neutral payment policy from last year and further reduce reimbursement for non-excepted PBDs. In general, these are entities that began billing Medicare as an off-campus PBD after November 2015. For these non-excepted PBDs, the agency is proposing to decrease payment from 50 to 25 percent of OPPS rates. CMS expressed concern that paying 50 percent of the OPPS rate might result in payments for items and services that are greater than would otherwise be paid to physician offices under the PFS. Early analysis by ACCC, however, shows that reimbursement at 25 percent of OPPS will be well below PFS rates for certain services.

Another significant change proposed relates to packaging of drug administration services. Currently, CMS excludes packaging of drug administration services (i.e., those costing less than or equal to \$100) from the ancillary services packaging policy. The agency is proposing to change that policy by packaging Level 1 and 2 drug administration services when these services are performed with another separately payable service, but paying for them separately when performed alone. CMS believes that conditional packaging of drug administration services will promote equitable payment between physician offices and hospital outpatient departments. ACCC disagrees with the agency's

rationale and will be urging CMS not to finalize this policy.

CMS is also soliciting comments on the "14-Day Rule," a policy that determines when a hospital may bill Medicare for a clinical diagnostic laboratory test versus when the laboratory performing the test may bill Medicare directly. CMS is considering potential modifications to the "14-Day Rule" that would allow labs to bill Medicare directly for molecular pathology tests and advanced diagnostic laboratory tests. ACCC played an active role in requesting that this policy be reopened for public comment.

With respect to payment for biosimilars, in the PFS rule, CMS is continuing its approach from 2016. Despite the expanding biosimilars market and promise of lower costs, the agency is maintaining its stance that biosimilars will generally share a single HCPCS code and that these products will be grouped into the same payment calculation for the purposes of determining a single ASP payment limit.

CMS is taking comments on both the OPPS and PFS CY 2018 proposed rules through Sept. 11, 2017, and seeking open-ended comments from the public on policies that would maintain flexibility and efficiencies in the Medicare program while reducing unnecessary burdens for clinicians and patients. ACCC is busy drafting its comments and we want to hear from *you*. Please contact Leah Ralph, Health Policy Director, at lralph@accc-cancer.org with your input. We also encourage you to submit comments directly to CMS at [regulations.gov](https://www.regulations.gov). 

Leah Ralph is ACCC Director of Health Policy.



compliance

Billing for Incarcerated Patients

BY CINDY PARMAN, CPC, CPC-H, RCC

As part of the judicial system, law enforcement officers are authorized by federal, state, and local lawmakers to arrest and confine individuals, either juveniles or adults, suspected of crimes. This confinement, whether before or after a criminal conviction, is called incarceration. According to the National Library of Medicine, the prison population of the United States has quadrupled in the past 25 years, and the country now incarcerates more people per capita than any other nation. Worldwide, imprisonment per 100,000 ranges from 30 in India to 75 in Norway, 119 in China, 148 in the United Kingdom, 628 in Russia, and 750 in the United States.

Healthcare Payments While Incarcerated

Currently, nearly 2.3 million U.S. inmates (about 1 percent of U.S. adults) must rely on their jailers for healthcare. However, there is little nationally available data on the health and healthcare of America's prisoners.

"Corrections Health Care Costs," published by The Council of State Governments, states:¹

There are two main reasons why states must pay for inmate health care. First, states are constitutionally mandated and court ordered to provide reasonable levels of care to inmates, including the provision for health care. Otherwise, states are subject to lawsuits brought on by mistreated inmates, which can cost millions of dollars. Secondly, thousands of prisoners are released back into communities each year. Inmates are more likely to acquire communicable diseases while

incarcerated and, likewise, share those diseases once released. The identification of diseases upon entry and the treatment of diseases during incarceration protect inmates and communities from the spread of infection, ultimately saving long-term costs and lives.

Today the most widely accepted policy is to provide inmates with a community standard of care. The community standard of care is based on the level of care someone in the community would normally receive. Despite attempts to regulate a community standard of care, states maintain definitions such as:

- Providing patients what they need medically, not what they want
- Providing care comparable to what a beneficiary of insurance, a government program such as Medicaid or Medicare, a health maintenance organization, or a private patient would medically receive
- Providing care that is medically necessary, not necessarily care that is medically acceptable, yet allowing practitioners to make exceptions to the policy on a case-by-case basis.

As a result, the provision of healthcare varies significantly across states and types of correctional facilities. Some larger prisons have infirmaries onsite, and many prisons hire independent physicians or contract with private or hospital staff to provide care with the majority of prisons, creating a hybrid system. In jails, healthcare is primarily provided through contracts with local healthcare providers, such as public hospitals or other safety-net providers, who come to the jails to provide services.² A

2009 study found that among inmates with a persistent medical problem, approximately 14 percent of federal inmates, 20 percent of state inmates, and 68 percent of local jail inmates did not receive a medical examination while incarcerated. For example, the state of Tennessee includes the following Q&A on its website:³

Does providing medical care include payment for the treatment? *Not necessarily. The county has fulfilled its constitutional obligation by seeing that the inmate is taken promptly to a hospital or other appropriate facility that provides the necessary treatment, and as long as the county ensures that the medical care is provided, the Constitution does not dictate how the cost of the care should be allocated as between the county and the medical provider. That is a matter of state law. See City of Revere v. Massachusetts General Hospital, 463 U.S. 239 (1983). The state statute requires only that the county ensures medical treatment is provided; it does not require that the county pay for the treatment. See Williams v. Anderson County, et al., an unpublished opinion of the Tennessee Court of Appeals issued December 20, 1988. The county's obligation is to ensure that the inmate receives the necessary medical treatment. If the only way the county can fulfill this obligation is to agree to pay for the services, then the county must do so.*

While correctional facilities must provide health services to people who are incarcerated, that does not mean that the care delivered is free of charge. According to the study, "Charging Inmates Perpetuates Mass Incarceration," inmates may owe copay-

ments ranging from a few dollars to as much as \$100 for medical care.⁴ At least 35 states authorize copayments and other fees for medical services at state prisons or county jails, according to the analysis by the Brennan Center for Criminal Justice at New York University School of Law.⁵

The Affordable Care Act (ACA) offers new opportunities to increase health coverage among individuals transitioning back into the community from prisons and jails. According to HealthCare.gov, special rules apply to healthcare options for individuals who are incarcerated, which is defined for the Marketplace as serving a term in prison or in jail.⁶ While incarcerated, individuals cannot buy insurance through the Marketplace, but once released there is a 60-day special enrollment period to sign up for private health insurance coverage. In addition, individuals who are in prison can apply for Medicaid coverage in their state, but Medicaid generally does not pay for any medical care for incarcerated individuals. Once released, however, these patients may be able to access healthcare quickly through the Medicaid program.

Medicare Coverage

According to MedicareInteractive.org:⁷

Medicare generally will not pay for your healthcare while you are incarcerated. Instead, your correctional facility will typically provide and pay for medical care while you are in custody. Once you are released, Medicare will cover your care as long as you remain enrolled in Medicare and follow Medicare's rules.

According to the CMS publication, "Medicare Coverage of Items and Services Furnished to Beneficiaries in Custody Under a Penal Authority" (July 2016), beneficiaries in custody (or incarcerated) include, but are not limited to, those individuals who are:

- Under arrest
- Incarcerated
- Imprisoned
- Escaped from confinement
- Under supervised release
- On medical furlough

- Required to reside in mental health facilities
- Required to reside in halfway houses
- Required to live under home detention
- Confined completely or partially in any way under a penal statute or rule.

Healthcare for incarcerated patients has been an ongoing problem; the Office of Inspector General (OIG) published a special report, *Review of Medicare Payments for Services Provided to Incarcerated Beneficiaries*, in October 2002.⁸ Medicare acknowledged the overpayments detected in that report, which were attributed to the fact that incarceration data from the Social Security Administration was not contained in the CMS records, and Medicare contractors did not have controls in place to detect claims submitted on behalf of incarcerated patients.

This report was followed by the January 2013 OIG document, "Medicare Improperly Paid Providers Millions of Dollars for Incarcerated Beneficiaries Who Received Services During 2009 Through 2011."⁹ According to this publication, CMS controls were adequate to prevent payment of Medicare services when the data systems indicated that the beneficiary was incarcerated. However, when the systems were not updated until after a claim had been processed, CMS controls were not adequate to detect and recoup the improper payment.

A recent HHS OIG semiannual report to Congress (October 1, 2016 – March 31, 2017) includes the following area of concern:¹⁰

"Medicare Improperly Paid Providers Millions of Dollars for Incarcerated Beneficiaries Who Received Services During 2013 and 2014." The Medicare Access and CHIP Reauthorization Act of 2015 (MACRA) requires CMS to establish policies and implement claim edits to ensure that payments are not made for Medicare services rendered to incarcerated beneficiaries. Our audit found that CMS's policies and procedures did not allow CMS to detect and recoup improper payments to beneficiaries who were incarcerated. CMS has not taken steps to determine

whether any of the \$34.6 million in potentially improper payments (for claims for incarcerated beneficiaries) made in 2013 and 2014 should have been denied.

CMS concurred with our recommendations to review the \$34.6 million in claims to determine which portion, if any, was not claimed in accordance with Medicare requirements; direct the Medicare contractors to recoup any ensuing improper payments; and identify improper payments made on behalf of incarcerated beneficiaries after our audit period to ensure that Medicare contractors recoup those payments.

This echoes information in the 2017 OIG Work Plan, which adds that Medicare does not pay for services rendered to incarcerated beneficiaries because they do not have a legal obligation to pay for medical care (Social Security Act, §1862).¹¹ However, the Code of Federal Regulations [42 CFR § 411.4(b)] allows Medicare payment when an incarcerated beneficiary has an obligation for the cost of care. This means that services furnished for incarcerated beneficiaries are covered by Medicare when *both* of the following criteria are met:


- State or local law requires those individuals or groups of individuals to repay the cost of medical services they receive while in custody.
- The state or local government entity enforces the requirement to pay by billing and seeking collection from all such individuals or groups of individuals in custody with the same legal status (for example, not guilty by reason of insanity), whether insured or uninsured. It must also pursue collection of the amounts owed in the same manner and with the same vigor that it pursues the collection of other debts. This includes the collection of any Medicare deductible and coinsurance amounts and the costs of items and services that are not covered by Medicare.

When both criteria are satisfied, the healthcare services are billed with modifier:

- **OJ.** Services provided to a prisoner or patient in state or local custody, however, the state or local government, as applicable, meets the requirements of 42 CFR § 411.4(b).

Closing Considerations

Individuals moving into and out of the criminal justice population are a low-income population, often with significant physical and mental health needs. Historically, this population has had high uninsured rates and very limited access to Medicaid coverage given the program's limited eligibility for adults prior to the ACA. The ACA's Medicaid expansion and Marketplaces, coupled with targeted outreach and enrollment efforts, provide opportunities to increase coverage among this population that should improve their ability to access needed care and contribute to greater stability in their lives.

Now is a good time for all cancer program providers to revisit policies, procedures, and billing protocols for incarcerated patients; and to review, revise, or implement contracts and set payment rates with local law enforcement authorities regarding these patients. Lastly, all providers should ensure that their billing staff remain aware of the special rules regarding incarcerated patients so that these services are not billed to insurance in error. 

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spotlight

Georgetown Cancer Center Georgetown, Kentucky



In 2009 Georgetown Community Hospital partnered with nearby University of Kentucky Markey Cancer Center to establish a cancer program that serves Scott County and neighboring areas of the Bluegrass State, providing close-to-home cancer care to a larger population. In August of this year, Georgetown Cancer Center became a Commission on Cancer-accredited program, expanding its outreach and screening services further into the community.

The cancer center, which is conveniently situated inside the 75-bed hospital, offers medical oncology services, including chemotherapy and infusion services (six treatment chairs and one treatment room), as well as pharmacy, rehabilitation, and laboratory services. Currently, the cancer center is staffed by one medical oncologist, five nurses, three PRN (per diem) nurses, and a full-time nurse navigator.

Not only is the cancer center's location on the Georgetown Community Hospital campus convenient for patients, it allows

cancer center staff to coordinate directly with the hospital for additional services or referrals. "We make sure the transition is pretty seamless. We're located in the same place, so conversations are encouraged between inpatient and outpatient staff," said Dianna Kouns, RN, BSN, community outreach coordinator at Georgetown Cancer Center. All cancer patients have access to psychosocial services with a social worker, nutrition services with a registered dietitian, financial counseling, and a rehabilitation services team at Georgetown Community Hospital.

As part of the affiliate network of the University of Kentucky Markey Cancer Center, located only 12 miles away in Lexington, Georgetown Cancer Center can refer patients for clinical trials, genetic counseling, radiation oncology, and surgical oncology.

Connection with the Community

The cancer center serves an especially tight-knit community. "The small-town atmosphere makes it more personal. Everybody knows everybody, and I have not seen that anywhere else I have worked. There is something to be said about a community hospital where these nurses live and work in our community," said Erin Collins-Buchanan, MSW, CTR, oncology program director for Georgetown Cancer Center.

To help the cancer program better meet the needs of the patient population it serves, cancer registry staff leveraged results from the Georgetown Community Hospital Community Needs Assessment to plan screening and outreach priorities. One important finding from the report was the

prevalence of lung cancer in the community due to high smoking rates. In fact, lung cancer is the most common cause of cancer death for both men and women in the state of Kentucky.

To combat this finding, Georgetown Cancer Center offers smoking cessation classes year-round via the Freedom from Smoking program, an American Lung Association initiative. The cancer center also partners with the local health department to provide nicotine replacements for patients and community members who are trying to quit smoking.

Patients in the catchment area can be screened at Georgetown Community Hospital via its Low-Dose CT Lung Cancer Screening Clinic. Going forward, the program seeks to educate and promote these screenings to primary care providers and the public through its partnership with the Markey Cancer Center.

Cancer center staff and hospital staff also participate in a monthly general tumor board to discuss complex cases.

Outreach Efforts & Supportive Care

In 2016 the cancer center expanded its outreach efforts, participating in numerous activities to make the public aware of the services it offers, as well as to educate the community on cancer prevention and screening practices. In addition to events like Relay for Life and an annual Cancer Survivor Dinner, the cancer center continued to build meaningful relationships with its community with a "Dinner with a Doc" held during Colon Cancer

Select Support Services

- Financial counseling
- Support groups
- Look Good, Feel Better
- Cancer rehabilitation services


Number of new analytic cases seen in 2016: 125

Awareness Month. At this event, the public could attend and have a discussion with a gastroenterologist about colon cancer screening and early detection.

Over the past months, Georgetown Cancer Center has also worked to address the need for additional cancer support groups. The cancer center now partners

with Hospice of the Bluegrass for a Living with Loss support group, a grief-based group available to family members affected by cancer or patients grieving their own cancer diagnosis.

Responding to patients' need for reliable transportation to and from appointments, the cancer center partners with the American

Cancer Society Road to Recovery program to provide rides, and has two transit buses run by volunteers to help shuttle patients between counties. "Our hospital mission is to make communities healthier," said Kouns. "Our cancer center is contributing to that mission with our community outreach initiatives." 



tools



Approved Drugs

- The Food and Drug Administration (FDA) has approved Pfizer's (Pfizer.com) **Besponsa® (inotuzumab ozogamicin)** for the treatment of adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).
- Amgen (amgen.com) announced that the FDA has approved the supplemental biologics license application (sBLA) for **Blinicyto® (blinatumomab)** to include overall survival (OS) data from the Phase III TOWER study. The approval converts the drug's accelerated approval to a full approval. The sBLA approval also included data from the Phase II ALCANTARA study supporting the treatment of patients with Philadelphia chromosome-positive (Ph+) relapsed or refractory B-cell precursor ALL. The approval expands the indication of Blinicyto for the treatment of relapsed or refractory B-cell precursor ALL in adults and children.
- Celgene Corporation (celgene.com) and Agios Pharmaceuticals, Inc. (agios.com) announced that **Idhifa® (enasidenib)** was granted FDA approval for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (R/R AML) with an isocitrate dehydrogenase-2 (IDH2) mutation as directed by an FDA-approved test.
- The FDA approved **Imbruvica® (ibrutinib)** (PharmacyClics LLC, pharmacyClics.com) for the treatment of adult patients with chronic graft versus host disease

after failure of one or more lines of systemic therapy.

- The FDA approved **Nerlynx™ (neratinib)** (Puma Biotechnology, Inc., pumabiotechnology.com) for the extended adjuvant treatment of adult patients with early stage HER2-overexpressed/amplified breast cancer, following adjuvant trastuzumab-based therapy.
- Bristol-Myers Squibb Company (bms.com) announced that the FDA has approved **Opdivo® (nivolumab)** injection for intravenous use for the treatment of adult and pediatric (12 years and older) patients with microsatellite instability-high or mismatch repair deficient metastatic colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.
- The FDA has approved a combination of Genentech's (gene.com) **Rituxan® (rituximab)** and Halozyme Therapeutics, Inc.'s (halozyme.com), hyaluronidase human enzyme **Enhaze™ drug delivery** technology for subcutaneous injection in multiple blood cancer indications.
- Novartis (novartis.com) announced FDA approval of **Tafinlar® (dabrafenib)** in combination with **Mekinist® (trametinib)** to treat patients with metastatic non-small cell lung cancer (NSCLC) whose tumors express the BRAF V600E mutation.
- The FDA approved **Vyxeos™ (cytarabine and daunorubicin)** (Jazz Pharmaceuticals,

jazzpharma.com) for the treatment of adults with two types of acute myeloid leukemia (AML): newly-diagnosed therapy-related AML or AML with myelodysplasia-related changes.

- Bristol-Myers Squibb Company (bms.com) announced that the FDA has expanded the indication for **Yervoy® (ipilimumab)** injection for intravenous use to now include the treatment of unresectable or metastatic melanoma in pediatric patients 12 years of age and older.

Approved Devices

- The FDA cleared the expanded use of a cooling cap, **DigniCap® Cooling System** (Dignitana, Inc., dignitana.se), to reduce hair loss during chemotherapy.
- Varian Medical Systems (varian.com) has received FDA 510(k) clearance for its **Halcyon™** system.
- Royal Philips (philips.com) announced it has received 510(k) clearance from the FDA to market **IntelliSpace Portal 9.0** and a range of radiology applications for longitudinal brain imaging multi-modality tumor tracking and lung nodule assessment.
- The FDA has granted premarket approval to Thermo Fisher Scientific, Inc. (thermofisher.com) for its **Oncomine Dx Target Test**, a next-generation sequencing (NGS)-based test that simultaneously screens tumor samples for biomarkers associated with three FDA-approved

therapies for NSCLC. Following FDA approval, results from analysis of three of these genes can be used to identify patients who may be eligible for treatment with one of the following: the combined therapy of **Tafinlar® (dabrafenib)** and **Mekinist® (trametinib)**, **Xalkori® (crizotinib)**, or **Iressa® (gefitinib)**.

Drugs in the News


- Eli Lilly and Company (lilly.com) announced that the FDA has accepted and filed its new drug application (NDA) for **abemaciclib**, a cyclin-dependent kinase (CDK)4 & 6 inhibitor, and given the NDA a priority review designation. The NDA includes the company's submission of abemaciclib for two indications: abemaciclib monotherapy for patients with hormone-receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) advanced breast cancer who had prior endocrine therapy and chemotherapy for metastatic disease; and for abemaciclib in combination with fulvestrant in women with HR+ HER2- advanced breast cancer who had disease progression following endocrine therapy.
- Amgen (amgen.com) and Allergan (allergan.com) announced the submission of a BLA to the FDA for **ABP 980**, a biosimilar candidate to Herceptin® (trastuzumab).
- AstraZeneca (astrazeneca.com) announced that the FDA has granted breakthrough designation to **acalabrutinib (ACP-196)** for the treatment of patients with mantle cell lymphoma.
- Genentech (gene.com) announced that the FDA has accepted the company's supplemental NDA and granted priority review for **Alecensa® (alectinib)** as first-line treatment for people with anaplastic lymphoma kinase (ALK)-positive, locally advanced or metastatic NSCLC as detected by an FDA-approved test.

- Astellas Pharma, Inc. (astellas.com) announced that the FDA has granted orphan-drug designation to **gilteritinib (ASP2215)** for patients with AML.
- AstraZeneca (astrazeneca.com) announced that the FDA has granted breakthrough therapy designation for **Imfinzi™ (durvalumab)** for the treatment of patients with locally-advanced unresectable NSCLC whose disease has not progressed following platinum-based chemoradiation therapy.
- Eisai, Inc. (eisai.com) has submitted a supplemental NDA to the FDA for the first-line use of **Lenvima® (lenvatinib)** in patients with hepatocellular carcinoma.
- Bristol-Myers Squibb (bms.com) announced that the FDA has accepted its sBLA to update **Opdivo® (nivolumab)** dosing to include 480 mg infused over 30 minutes every four weeks for all currently approved monotherapy indications.
- Bristol-Myers Squibb Company (bms.com) announced that the FDA accepted its sNDA to include an indication for **Sprycel® (dasatinib)** to treat children with Philadelphia chromosome-positive chronic phase chronic myeloid leukemia (CML), as well as a powder for oral suspension formulation of Sprycel.
- The FDA has awarded orphan drug designation to MimiVax LLC (mimivax.com) for its vaccine, **SurVaxM**, for the treatment of glioblastoma.
- Syros Pharmaceuticals (syros.com), announced that the FDA has granted orphan drug designation to **SY-1425**, an oral selective retinoic acid receptor alpha (RAR) agonist, for the treatment of AML.
- Amgen (amgen.com) announced that the FDA has approved the sBLA for **Vectibix® (panitumumab)** for patients with wild-type RAS (defined as wild-type in both KRAS and

NRAS as determined by an FDA-approved test for this use) metastatic colorectal cancer as first-line therapy in combination with FOLFOX and as monotherapy following disease progression after prior treatment with fluoropyrimidine, oxaliplatin, and irinotecan-containing chemotherapy. As part of this new indication, the FDA approved the first multigene, NGS-based test to identify the RAS mutation status of a patient's tumor.

- Roche (roche.com) announced that the FDA has granted breakthrough therapy designation for **Venclexta® (venetoclax)** in combination with low dose cytarabine for elderly patients with previously untreated AML who are ineligible for intensive chemotherapy.

Genetic Tests and Assays in the News

- The FDA authorized the marketing of Clear Lab Reagents (**T1, T2, B1, B2, M**) test to aid in the detection of several leukemias and lymphomas, including chronic leukemia, acute leukemia, non-Hodgkin lymphoma, myeloma, myelodysplastic syndrome (MDS), and myeloproliferative neoplasms (MPN).
- The FDA granted marketing approval to the **Praxis™ Extended RAS Panel** (Illumina, illumina.com), an NGS-test to detect certain genetic mutations in RAS genes in tumor samples of patients with metastatic colorectal cancer. The test is used to aid in the identification of patients who may be eligible for treatment with Vectibix (panitumumab). This is the first FDA-approved NGS test that can detect multiple RAS gene mutations for colorectal cancer in a single test. 



A Student Volunteer Program Takes Patient Satisfaction to the Next Level

Rural cancer programs face unique and challenging barriers ranging from limited healthcare access to scarcity of health-care providers.¹ The Providence St. Joseph Health Cancer Program in rural Eureka, California, is one such program. Eureka is situated in the heart of the majestic redwoods in Humboldt County, 272 miles north of San Francisco, with a population of 135,727.² The nearest cancer program is 150 miles southeast, making Providence St. Joseph Health Cancer Program the only option for three rural Northern California counties. St. Joseph created a fully accredited Commission on Cancer (CoC) cancer program in 1992. Throughout the years we began to more fully understand the unique barriers facing this cancer program, and in 2007 St. Joseph Health Humboldt requested that a local task force propose significant expansion of the program to include support services and additional oncology staff. Their vision was “to ensure the enhancement and modernization of the existing cancer program to best meet the needs of the community.”³ The task force’s goal was to improve the facility so that it would be recognized as “a source of coordinated, comprehensive, state-of-the-art cancer care, delivered with respect and compassion.”³

The Vision for a Rural Cancer Program

According to the Providence St. Joseph Health Cancer Program’s 2014 needs assessment, about 60 percent of its patients received some type of cancer care outside of Humboldt County.¹ Prominent breast surgeon and medical director of the Providence St. Joseph Health Cancer Program Ellen Mahoney, MD, championed the vision of delivering state-of-the-art medical care comparable to any large urban cancer center, such as Stanford Medical Center in Palo Alto, Calif., eliminating the need for patients to travel

The addition of volunteers would help provide higher quality of care for the patients and reduce tasks for the oncology nurses while also improving quality of care for patients.

hours for treatment. Thus, a main programmatic goal was to increase patient quality of life (QOL) by enabling patients to receive their cancer treatment close to home. The cancer program has been actively pursuing this goal with excellent outcomes while seeing exponential market growth.

To help meet this goal, Providence St. Joseph Health Cancer Program expanded its radiation oncology service line with the recent acquisition of two new linear accelerators and a 3D mammography machine. Cancer program staff and clinicians include experienced, certified medical and radiation oncologists, certified oncology nurses, oncology and clinical social workers, mental health clinicians, a financial counselor, nurse navigators, and a registered dietitian. Additionally, the cancer program has STAR (Survivorship Training and Rehabilitation) certified physical therapists, oncology nurses, and social workers. Providence St. Joseph Health Cancer Program has an ongoing partnership with Stanford University to do telemedicine conferencing and patient case consults. In short, patients can be confident that they are receiving the quality of cancer care they would receive at a large university medical center.



Beautiful Eureka Marina on Humboldt Bay.

Barriers to Care in the Rural Setting

A long-term goal of Dr. Mahoney's was to leverage volunteers and student interns from the local university, Humboldt State University. In the absence of a large university medical center in the area, a collaboration with the local state university was an attractive option for creating an oncology learning environment for students. April Alexander, MSW, ASW, was the first student to intern for the program. She obtained her undergraduate and graduate degrees in social work from Humboldt State University while interning in Cancer Support Services at Providence St. Joseph Health Cancer Program. Her master's project was a collaboration with oncologists to create a psychosocial intervention manual for patients in treatment for cancer. The manual included substantial information on barriers to care in a rural cancer program, with these five main barriers identified:

1. Lack of certified oncologists
2. Proximity to cancer care
3. Poverty
4. Lack of and reduced access to medical insurance
5. Disparities in health outcomes among minority populations.

After graduation, Ms. Alexander was hired as the oncology social worker in Providence St. Joseph Health Cancer Program's Medical Oncology department.

The St. Joseph Health Humboldt Cancer Program's 2014 community needs assessment identified four of these five areas as barriers to care (excluding lack of certified oncologists). Because of these barriers, the cancer program potentially faces challenges with inadequate disease prevention, delayed detection of illness, misdiagnosis and late diagnosis, and inadequate referral processes without adequate intervention. These barriers are continually being addressed by St. Joseph Health Humboldt Cancer Program's Cancer Committee through quality assurance and prevention initiatives, as well as close collaboration with local medical community agencies and organizations.

Humboldt County and its surrounding counties have one of the largest indigenous populations in California. The county is home to the Yurok, Karuk, Wiyot, Tolowa, and Hoopa tribes. Humboldt State University Social Work Department's BASW and MSW programs emphasize working with indigenous peoples, which became an integral part of April's master's project. The project explored barriers to healthcare and health disparities faced by these communities as a result of past colonialism and cultural genocide, which continue to negatively impact indigenous communities today. These barriers to care remain in the forefront of social justice issues that rural health communities should be examining and addressing within their patient populations. Eliminating barriers to care in these populations is paramount to improving social work practice in cancer care delivery.

Student Volunteers Improve Quality of Care

Quality of care is a constant priority for cancer programs—both rural and urban. The Providence St. Joseph Health Cancer Program has expanded in the past three years with another local oncology practice joining the cancer program, thus increasing the patient to staff ratio. The addition of volunteers would help provide higher quality of care for the patients and reduce tasks for the oncology nurses while also improving quality of care for patients. Ms. Alexander interned in the infusion clinic during her graduate year in the Humboldt State University social work program and saw the need to create a volunteer program for the clinic. Still attending the university, she had close connections with the social work professors and staff, so approaching them about student volunteers was a natural progression. One of the classes taught in the social work bachelor's program curriculum was a volunteer experience class. Ms. Alexander approached the class professor, who was happy to recommend five student volunteers in the social work bachelor's program. This collaboration would prove beneficial for both the university and the cancer program.

The Ins & Outs of Training Student Volunteers

Students are encouraged to begin the volunteer application process as early as possible in the semester because completion of required background checks and medical tests can take a substantial amount of time. After an initial interview by the MSW, students complete their hospital volunteer orientation, which includes a full background check, immunizations, a physical, and drug testing. Secondly, students complete a full day of hospital volunteer training led by hospital managers and directors. They then go through additional cancer program training, which includes the cancer program's history, active listening, and psychosocial and chairside training conducted by the cancer program's MSW. Lastly, students complete on-site training with the infusion clinic's medical assistant to learn hands-on clinic tasks and safety protocols. All training hours count toward the students' volunteer hours for their class.

In collaboration, the Cancer Support Services manager, infusion clinic charge nurse, volunteer director, and MSW identified the following infusion clinic volunteer tasks:

- Disinfecting chemo chairs.
- Bringing patients in from the waiting room.
- Accompanying patients out to their car.
- Obtaining drinks, blankets, and other items.
- Delivering lunches.
- Offering psychosocial support to patients and caregivers.
- Getting DVD players, coloring supplies, books, etc.
- Giving out basic resources, such as support group flyers.
- Reporting patient concerns to social workers and clinical staff.
- Helping medical assistants and nurses with deliveries to the lab.
- Stocking of non-clinical supplies.
- Copying and organizational office tasks.
- Assisting with community outreach and events.

In the initial volunteer days, the MSW introduces the students to patients and ensures that students are rounding in the clinic and meeting both the psychosocial and practical needs of patients while assisting the clinic staff. Students utilize AIDET (Acknowledge, Introduce, Duration, Explanation, and Thank You) with patients and learn to work with the infusion nurses and cancer program staff. Students are also encouraged to embody the four St. Joseph values of service, excellence, dignity, and justice while interacting with patients.

The MSW conducts a daily check-in with the students, schedules volunteer meetings as needed, and utilizes text messaging and email correspondence with students to improve communication. To obtain input on the volunteer program, regular communication with the cancer program staff and clinic charge nurse has been helpful. Per the hospital's volunteer policy, students are not permitted to perform clinical duties; per the program's dress policy, students wear "student volunteer" name tags while in the clinic. Students do not have access to the EHR (electronic health record) or any HIPAA-protected patient clinical information. If volunteers are sick or unable to volunteer, they are asked to find a replacement, if possible. The minimum volunteer commitment

is one year; students can take vacations and school breaks as needed. Students are also encouraged to assist with cancer program community events, such as health fairs, prevention activities, and education opportunities, and are invited to visit cancer program staff meetings and tumor boards. Tasks such as filing and copying are kept to a minimum to maximize the students' learning experience. Students are also encouraged to propose ideas for projects; one idea included utilizing a former dental hygienist's oral hygiene guide for patients undergoing chemotherapy.

Impact of the Student Volunteer Program


The program is currently in its third year, and is continuing to exceed the expectations of cancer program staff and leadership. It has proven to be a very positive collaboration between the university and cancer program. Students are given the opportunity to immerse themselves in a clinical environment with hands-on learning to increase their interest in the oncology field and hone their social work skills. One student described the volunteer experience as "life-changing," and most of the student volunteers' feedback has been very positive. The Humboldt State University Social Work Department Field Director Yvonne Doble, MSW, is now working with the cancer program and has added the program to the list of intern sites for the BSW and MSW programs. Every year the cancer program has the opportunity to come and speak to the junior year social work students about internship possibilities and familiarize them with the student volunteer program and what it has to offer.

The hospital and cancer program have both benefited substantially from the student volunteer program since its creation. For example, diversified staff allocation has been one benefit of adding volunteers to the program. The student volunteers have also had a positive effect on patient care; during the first-year



Providence St. Joseph Health Humboldt Eureka Hospital Campus.

Figure 1. Rural Chemotherapy Clinic Student Volunteer Support Program

<p>Purpose of Program</p>	<ul style="list-style-type: none"> • Increase psychosocial care services • Provide listening support for patients and caregivers • Allow patients and caregivers a “break” during treatment • Decrease staff duties 	<p>Impact on Cancer Program</p>
<ul style="list-style-type: none"> • Educating students about oncology clinical practice • Supporting oncology staff in the clinic • Increasing patient quality of and access to psychosocial care • Providing a hands-on learning environment 		<ul style="list-style-type: none"> • Increased patient satisfaction during program rollout • Diversified staff allocation • Strengthened a positive collaboration between university and cancer program • Increased student interest in oncology field
<p>Volunteer Duties</p>		<p>Model for Rural Cancer Programs</p> <ul style="list-style-type: none"> • Can be easily replicated in other rural university communities • “Program in a Box” component • Can be integrated into other university social science disciplines
<p>Supportive Services</p>		
<ul style="list-style-type: none"> • Providing psychosocial support • Providing family and caregiver support • Assisting staff with projects • Carrying out clinical support tasks 		
<ul style="list-style-type: none"> • Enhance patient care • Improve comprehensive services 		

pilot program the cancer program saw an improvement in patient satisfaction scores. To date, the tangible benefits of the student volunteer program have included:

- Improvement of patient care
- Expansion of comprehensive services
- Increase in psychosocial care offered
- Additional listening support for patients
- Assistance with staff duties.

The hospital’s volunteer department plans to use the cancer program’s student volunteer training manual binder as a prototype for the other departments so that each department will have its own specialized training manual and program. These volunteer opportunities will improve patient care across all hospital departments.

Patients have benefited from the student volunteer program in many ways. For example, patients have more support while they are in the clinic, allowing family members and caretakers to take needed breaks while their loved one is getting an infusion. Patients form supportive relationships with the student volunteers who have more time to sit and talk with them than the clinic staff generally do. Their needs are met more quickly due to the additional volunteers who are available to get a pillow, drink, or movie. Since the student volunteers are not clinical staff, some patients feel more comfortable opening up and discussing their cancer journey with them. Student volunteers have come up with creative activities for patients to pass the time while they’re getting an infusion, including a rolling coloring cart, which holds coloring and art supplies, books, and other creative outlets that are offered to patients during their infusion.

Lessons Learned

For cancer programs looking to implement a similar student volunteer program, Providence St. Joseph Health Cancer Program offers these lessons learned.

#1. The Importance of Program Monitoring. One of the biggest lessons gleaned from the student volunteer program has been the need for continuous program monitoring and readjustment to meet the changing needs of the rural oncology infusion clinic. An increase in patient visits, decrease in staff, or changes to hospital policy are to be expected, and programmatic changes must be made to best meet the needs of the current patient population. Something important to keep in mind is that volunteers are not a replacement for staff, but rather an extension to the services staff provides, and clinic staff should be made aware of this fact. Remember, students are volunteering for a learning experience and are not available all year round, while on semester breaks, etc. Cancer program management and staff should provide continual guidance and input into the student volunteer program process, thereby ensuring its continual success and sustainability. Additionally, university grants can often be used to help pay for student immunizations, physicals, screenings, and tests.

#2. Communication Is Key. Keeping tabs on the pulse of the student volunteer program includes regular communication with management and clinical staff and practitioners, students, and university professors and faculty. Working with the students on their learning agreements and incorporating their ideas into these agreements helps to promote buy-in. Providence St. Joseph Health

Cancer Program has found that assisting students in acclimating to a clinical environment and developing their people skills and sensitivity to oncology patients' needs quickly becomes paramount to providing good patient care. Additional training or "refresher courses" may be needed to ensure students are understanding their volunteer role and providing the best assistance possible. Reminding clinic staff of what students can and cannot do per hospital policy is also helpful in making sure that the policy is being followed appropriately. Regular appreciation of student volunteers is vital to maintaining the program, and meetings, daily check-ins, and expressions of gratitude go a long way toward ensuring confidence and trust in the student volunteers. It's also helpful to make student volunteers aware of their duties by giving them daily checklists to keep them focused on daily volunteer duties.

#3 Self-Care Focus Increases Program Sustainability. Focusing on self-care and being cognizant of personal transference are important aspects of the students' learning experience. Burnout and compassion fatigue are rampant in the medical and social work fields, so training students early on about how to minimize these conditions while they are volunteering at the cancer program is vital. Students need to be educated on how patient interactions can trigger internal emotions and feelings, which may be difficult or confusing to process. Student volunteers also need to learn how to work through these emotions in a healthy way. Students volunteers are encouraged to practice good self-care by taking breaks and communicating with supervisors or professors when concerns arise; they are generally very open to being mentored in the necessity of self-care. Self-care plans, workshops, journaling, support groups, and education are all healthy avenues for increasing adequate levels of self-care. Student volunteers also learn how to establish good boundaries with the patients and caregivers they serve while maintaining a professional relationship. The student volunteer experience may well be their first introduction to the medical social work field and oncology care; therefore, it's critical that those supervising the student volunteers create a solid foundation for them and communicate that caring for themselves is a vital part of sustainability in the healthcare field.

#4 The Sky is the Limit. A student volunteer program provides amazing multi-factorial support to the students, staff, and patients of a cancer program. It can also prove to be a positive collaboration among social work, psychology, and/or hospital cancer programs. In fact, cancer programs may want to consider establishing a similar partnership with a nursing program. Though a student volunteer program requires a time investment on the part of both the university and hospital, Providence St. Joseph Health Cancer Program found that the payback is deeply rewarding for the university, patients, and hospital staff. A student volunteer program can serve to increase the interest of students in the field of oncology and train up a new oncology work force. Additionally, other hospital departments that do not have specialized volunteer training programs can also benefit. For rural cancer programs especially, student volunteer programs are a great solution for meeting unique community needs. Simply put, the positive impact that properly

trained and supported student volunteers can have on oncology staff, cancer patients, and caregivers cannot be underestimated. **OI**

April Alexander, MSW, ASW, is an oncology social worker and supervisor of the student volunteer program at Providence St. Joseph Health Cancer Program, Eureka, Calif. She can be reached at april.alexander@stjoe.org.

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April Alexander, MSW, (back row, third from left) with infusion center nurses and clinic staff, showing appreciation for infusion clinic student volunteers.



Using a Collective Brain to Defeat the Deadliest Brain Tumor

Sometimes referred to as the “terminator,” glioblastoma (GBM) is one of the deadliest forms of brain cancer.¹ Drug developers and clinical trial sponsors in oncology have described the glioblastoma research and development (R&D) landscape as a “graveyard” because of the many failed trials.² The disease takes around 16,000 Americans from their families and friends each year.³ Glioblastoma is the most common—and lethal—form of brain cancer, yet virtually no effective treatment options exist, despite such high-profile passings as those of U.S. Senator Edward Kennedy and Delaware Attorney General Beau Biden, and the recent diagnosis of Senator John McCain.

The Defeat GBM Research Collaborative launched in 2013 with an eye toward transforming the clinical landscape for this complex, adaptable, and aggressive cancer.

The idea was simple: change the way we fund and conduct glioblastoma research and change the calculus behind years of heartbreaking disappointments and achingly slow progress against these tumors. The ultimate intervention designed, however, would need to be as sophisticated as the adversary, and would require the input and buy-in of many of the top minds in neuro-oncology—a “collective brain”—in the quest to overcome one of cancer’s most challenging puzzles.

Past is Prologue

The traditional R&D process for cancer drugs is lengthy and filled with challenges, risks, bottlenecks, and inefficiencies. For example, one-off treatments are discovered and then developed in a highly-sequential, time-consuming manner. While the typical drug development process in oncology is estimated to take about 10 years, glioblastoma patients continue to be diagnosed with life expectancies of less than two years.

After analyzing the state of the science in glioblastoma research, it was determined that the scope of the scientific endeavor needed to cover the entire spectrum of preclinical research—from basic science and target discovery to translational research to drug discovery and development.

In brain cancer, thousands of interventional clinical trials have been conducted over the past four decades, with only a handful of new drug approvals succeeding in extending life—and in each case only by a few months. Since 1994, the failure ratio in brain cancer clinical trials has been more than 25:1.⁴

Glioblastoma was first described in the medical literature in 1926.⁵ At that time, patients who were not operated on lived around three months beyond diagnosis. With the addition of surgery, patients’ lives would be extended by a few short months. That prognosis remained for nearly 50 years, until the mid-to-late 1970s when radiation became the standard treatment for gliomas, increasing life expectancy for patients to an average of nine months.⁶ Survival would persist at around nine months for 20 more years, until chemotherapy was first successfully added to the standard of care for

glioblastoma patients, improving survival to a median of around 12 months.⁶ From 1993, incremental advances in the type, delivery, and doses of chemotherapy (including nitrosoureas and temozolomide) and radiation, combined with improved imaging and surgical techniques, extended the overall survival to 12 to 15 months. Finally, from 2008 to 2016, the introduction of bevacizumab and Optune has pushed that range to between 12 and 18 months on average.

All told, there are four FDA-approved drugs (temozolomide, bevacizumab, carmustine wafer, and lomustine), and one FDA-approved device to treat glioblastoma, along with surgery and radiation. Ninety years of research have yielded only enough improvements to extend life by, at most, a year and a half. Meanwhile, certain forms of breast, prostate, blood, and skin cancers are now curable or at least manageable as chronic diseases.

Further, the glioblastoma research field is filled with some of the greatest scientific minds in the world, and has benefited from massive government-funded efforts like The Cancer Genome Atlas, which chose glioblastoma as its first tumor type for genomic sequencing.

When The Cancer Genome Atlas published its findings on glioblastoma in 2008, the research and patient advocacy field was certain that with this tumor's genome decoded, we were on the cusp of a massive breakthrough in treatment development. Yet nearly a decade later, very little has changed in the glioblastoma therapy landscape.

“The knowledge base is incredibly deep in many ways,” says Paul Mischel, MD, a principle investigator in the Defeat GBM Research Collaborative from the Ludwig Institute for Cancer Research, San Diego. “The map of the genes that make proteins and their alterations in this cancer has largely been identified, so one would expect or anticipate that this would actually make a difference in the lives of patients. But for a variety of reasons... that information has yet to really benefit patients.”

Despite great effort from many different funders as well as labs across the field of neuro-oncology, we were not making enough progress against this disease, motivating leaders in this field to begin conversations with the National Brain Tumor Society about the need for fresh approaches to this difficult disease.

In 2012, we took a step back and asked ourselves: “*Why isn't more progress being made? What is stopping great science from becoming great medicine?*”

“This is a devastating cancer and there hadn't really been any advances in the field,” says Dr. Mischel. “Now, in the past 20 years there's really been a sea-change where our understanding of the biology of the disease is really quite sophisticated. The challenge in front of us now is to be able to use those advances for the benefit of patients.”

Forging A New Path

We needed systemic change in the way that limited funds were being distributed and spent for glioblastoma research, as well as



Members of the Defeat GBM Research Collaborative and Cure GBM, LLC, at the National Brain Tumor Society's 2015 Scientific Summit.

the approaches and incentives for moving science through the lab and to the clinic.

The National Brain Tumor Society had been following the lead of our nation's biggest biomedical research funders, the National Institutes of Health, using R01-style grants as a gold standard for seeding research projects. This strategy alone was not working well enough to move the needle for glioblastoma patients. In many ways, it encouraged labs to compete against one another with single-investigator projects.

We could not fund transformative research solely through discreet grants, handed out each year to a cadre of different researchers working on different projects. This process would only perpetuate the traditional model of one-off research efforts by individual labs slogging through the clunky, step-by-step process to move the science forward toward new treatments.

It wasn't that past grant-funding hadn't been impactful—in fact, it had laid a great foundation of knowledge that underpins future research efforts—but rather, we wanted to create a model that would capitalize on advances in biomedical science and technology as we moved deeper into the second decade of the 21st century and the so-called “precision medicine” era. It was about speeding the pace with which discoveries were being made—and ensuring their ability to be moved further down the entire pipeline, from the lab to the clinic with minimal interruption.

With a team of visionaries in the field we created a new model: our “Defeat” model for research.⁷ Instead of funding more individual grants, we would establish and lead a large, directed, broad-based multidisciplinary collaborative capable of converting basic research into drug candidates in coordination with one another. Thus the idea for the Defeat GBM Research Collaborative was born.

Building a New Foundation

We knew that our concept would not easily align with the traditional research system. Researchers might want to work together, they might want to share data and materials, but if their institutions' legal departments wrapped them in red tape, our concept could not move forward.

We began by building a framework that would facilitate true collaboration. We needed a sophisticated business approach to managing scientific research that would bring institutes representing our key principle investigators on as “research partners” to a neutral, central organization. With that, the National Brain Tumor Society created a subsidiary: Cure GBM, LLC.

Cure GBM, LLC, is managed by a board of directors and president separate from that of the National Brain Tumor Society Board of Directors and executive leadership (though some overlap). The LLC manages, operates, and facilitates all activities between participants in the Defeat GBM Research Collaborative, such as:

- Managing the budget and finances
- Marketing, communications, and fundraising
- Providing data and infrastructure support
- Coordinating meetings and research reviews.



National
Brain Tumor
Society

Defeat GBM Research Collaborative

Driving research to new brain cancer therapies

Each partner institution representing researchers within the Collaborative would sign “collaborative agreements” with the LLC, allowing Cure GBM to act as a clearinghouse to help overcome legal barriers to data and material sharing and transfer. Once an institution had signed an agreement with Cure GBM, LLC, their researchers could share raw data and materials with other participants in the Collaborative in real-time without needing to wait for their institutions' legal department to execute a new Material Transfer Agreement or Memorandum of Understanding in each instance. Finally, the fact that an impartial corporation governed the Collaborative gave confidence to participating organizations and individuals that no singular entity would solely benefit from the work of the group.

After analyzing the state of the science in glioblastoma research, the Collaborative determined that the scope of the scientific endeavor needed to cover the entire spectrum of preclinical research—from basic science and target discovery to translational research to drug discovery and development. With the right individuals and structure, we believed we could take on all these areas at once in a coordinated and synergistic approach. To do so, we broke down the scientific plan into four integrated “Core” projects and teams: Discovery, Drug Development, Biomarkers, and “SMART”⁸ Clinical Trials led by experts in each particular discipline (target discovery/genomics/molecular biology; preclinical modeling; biomarker identification and validation; drug screening; and clinical trial operations), all in close collaboration to enable swift scientific translation.

Finally, the Collaborative needed to ensure that its efforts were accountable, milestone-based, and subject to rigorous and frequent review. To do so, the Collaborative decided that a scientific director would join the president and Managing Board to establish and



David Arons speaks at the National Brain Tumor Society's 2016 Scientific Summit.

lead a Strategic Scientific Advisory Council. The council would provide oversight to the scientific projects, manage the research portfolio (including development of a Scientific Research Plan), nominate individuals or entities to conduct research, and establish and evaluate annual research milestones.

Alfred Yung, MD, (at the time, chair of the Neuro-Oncology Department at MD Anderson Cancer Center) was named the scientific director. Several of the early advisors to the Defeat GBM Research Collaborative were named to the Strategic Scientific Advisory Council, including Webster Cavenee, PhD, of the Ludwig Institute for Cancer Research, and Anna Barker, PhD, formerly of the NCI, and now at Arizona State University and the National Biomarker Development Alliance.

Putting the Pieces Together

With a basic infrastructure and model in place, and a diverse and distinguished panel of cancer research experts from multiple fields comprising the Strategic Scientific Advisory Council, the task shifted toward identifying the right projects, institutions, and investigators needed to fill out the Defeat GBM Research Collaborative.

The Power of the “Defeat” Model

The Defeat model, on which the LLC and Collaborative are built, harnesses an infrastructure that facilitates collaboration and data and information sharing, putting scientists to work in areas where they can leverage their expertise while coordinating across a multidisciplinary team all working toward a singular goal. The Defeat model is defined by two major characteristics:

1. A “Cores” design (see below) that allows new findings in one area of the Collaborative to move quickly and efficiently on to the next stage of research without barriers or typical delays seen in single-investigator funding models. In short, much of

the traditional sequential process required in translating basic discovery from lab to clinical testing can be accelerated by enabling seamless integration across cores to execute on research priorities in synchrony.

2. A business and research management model that facilitates all the Collaborative’s operational and administrative needs so that researchers can spend more time in the lab and less time doing paperwork. Cure GBM, LLC, serves as a “command-and-control” structure, as well as an administrative hub to enable glioblastoma research at institutions across the country.

Further, the infrastructure is designed to move multiple findings continuously through the “Cores,” thus avoiding an “all the eggs in one basket” scenario. With top labs from around the United States working together, quality and well-researched data is produced at a level requisite for beginning first-in-human trials. In short, participating world-class researchers leverage their strengths and expertise, and the National Brain Tumor Society, via Cure GBM, LLC, provides the infrastructure to move the science forward.

In 2013, with Strategic Scientific Advisory Council guidance, Defeat GBM’s four “Cores” were established with scientists/physicians in each area of research selected to lead each of the four Core project teams.

- **Core 1. Target Discovery** was assigned to the Ludwig Institute for Cancer Research, San Diego, where Dr. Frank Furnari’s lab would work on identifying high-value treatment targets and associated treatment resistance mechanisms.
- **Core 2. Drug Development** would be led by Drs. John de Groot and Erik Sulman of MD Anderson Cancer Center, who would focus on drug testing across cellular and animal models representative of different classes of glioblastoma subtypes. They would be joined by genomics and computational biology expert Roel Verhaak, PhD, of the Jackson Laboratory and Ingo Mellinger, MD, a physician-scientist and expert in brain tumor molecular pathogenesis and clinical trial investigation from Memorial Sloan Kettering Cancer Center.
- **Core 3. Predictive Markers (Biomarkers)** would be led by Dr. Paul Mischel of Ludwig Institute for Cancer Research, University of San Diego, and Timothy Cloughesy, MD, of University of California, Los Angeles, as co-principal investigators (co-PIs) to investigate clinical biomarkers that predict response and resistance to treatment in glioblastoma patients.
- **Core 4. Innovative, Adaptive Clinical Trials** is intended to support biomarker-driven, early-phase clinical trials investigating promising agents identified from preclinical work in the other cores.

This research plan was designed to get the top minds in the field working together—yet within their own areas of expertise—to accelerate the translation of basic research into clinical candidates for human trials.

Making Progress: Moving toward the Clinic

In 2014, funding for the Collaborative raised through philanthropic contributions began flowing to the principal investigators and scientific experiments began. Now, nearing the halfway point

of Defeat GBM's five-year, \$10 million commitment, the Collaborative is bringing forth a host of both new therapeutic targets as well as drugs of interest to be evaluated in the clinic.

While the scientific research underlying the Collaborative is intense, sophisticated, and truly leading-edge, the theory behind it is quite simple: Advance our understanding of tumor biology and gain a deeper understanding of why treatments—that were expected to work—have failed to provide benefit for glioblastoma patients. To develop new, effective treatment strategies for these patients, the Collaborative seeks to:

- Discover how these tumors are protecting themselves from, or escaping, the effects of current treatments.
- Find vulnerabilities in these tumors (their Achilles' heel).
- Create better laboratory models to recreate these effects for use in studies.
- Test potential drugs against these mechanisms with the goal of identifying drugs that can stop them.

So far, Defeat GBM researchers have been able to identify new ways in which glioblastoma tumor cells evade drugs that try to stop them. Collectively, nearly 20 new discoveries have been made that present a multitude of potential new approaches for treating glioblastoma.

Further, Defeat GBM's Drug Development Core has successfully identified potential new drug candidates for further evaluation and testing as possible future glioblastoma treatments. Importantly, these tests have been conducted in newly-developed laboratory models that are better at mimicking how a glioblastoma will actually behave in human patients. In total, the Defeat GBM teams are working on further testing for 11 encouraging drug candidates—some in combinations with current and other therapies—in addition to 21 drugs identified from initial screens that researchers would like to analyze further, which they've identified and prioritized.

“We are poised to move into the clinic soon, and we're very excited about working with NBTS to translate our latest discoveries into the clinic,” says John de Groot, MD, a principle investigator and head of the Drug Development Core.

Next Steps

Operationally, the Defeat GBM Research Collaborative is still a relatively young initiative. Yet, the convergence of the findings made to date has the group already talking about the clinic. The design and makeup of the Collaborative have allowed a portfolio of novel and actionable precision medicine therapeutic targets and biomarkers, and potential clinical candidates, to be developed at a particularly rapid rate.

Several next steps involving close collaboration across different research Cores are now underway with the goal of advancing top scientific findings to go/no-go decisions for clinical trials in glioblastoma patients.

Organizationally, the Defeat GBM Research Collaborative is poised for continued and expanded collaboration with stakeholders who share a common purpose in accelerating brain tumor research in a dynamic team environment. The model is designed to be scalable with new Cores being added, as well as additional investment partners and scientific endeavors, as appropriate,

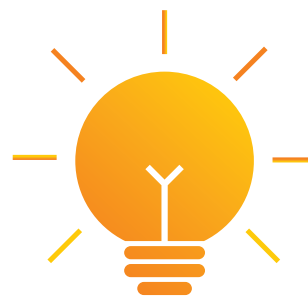
depending on how the research efforts progress and on guidance provided by the Strategic Scientific Advisory Council.

The ultimate goal is to improve survival for glioblastoma patients—a critical, unmet need. Yet, we also hope the Defeat GBM Research Collaborative can serve as a demonstration project that illustrates how to optimize research efforts through novel models for collaborative, multidisciplinary science. There is real opportunity to transform the landscape of one of the world's deadliest cancers, and the field owes it to glioblastoma patients past, present, and future to capitalize on it.

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The Role of the Oral Oncology Nurse Navigator



Oral Oncology Nurse Navigators Improve Patient Care & Satisfaction

According to the Pharmaceutical Research Manufacturers of America, 836 clinical compounds are currently in development for oncology and blood disorders,¹ and an estimated 25 to 30 percent of cancer therapeutic drugs in development pipelines are oral medications.^{2,3} Not only are an increasing number of oral therapies being approved, several commercially available, FDA approved oral therapies were recently granted additional indications. As such, oncology providers across all care settings need to recognize this market trend while understanding the challenges in successfully transitioning treatment options from predominantly IV regimens to a growing percentage of oral chemotherapy regimens. While oncology programs and practices must take into account numerous considerations when ramping up their oral chemotherapy services, this article focuses on one unique and very important role to facilitate this transition: the oral oncology nurse navigator.⁴

This a relatively new position gaining acceptance with oncology program and practice leadership. Importantly, the roles and responsibilities of the oral oncology nurse navigator are adaptive and responsive to meeting both the shift in the oncology marketplace and specific needs across practice settings.⁵ These healthcare professionals are essential to the continuity of care critical to oncology patients receiving oral chemotherapy. This article covers specific roles and responsibilities within two distinct oncology care settings: the community level and health system level.

In-Office Dispensing at Hematology-Oncology Associates of Central New York

In 2014 Hematology-Oncology Associates of Central New York identified the need to open an in-office dispensary and, with the

Patients prescribed oral chemotherapies must understand that while taking an oral medication may offer flexibility with regards to when and where patients take their medications, it does not exempt them from the toxicities normally associated with IV chemotherapy.

support of senior management, implemented this patient-centered service in the community oncology practice setting. The in-office dispensing team works with a common goal of delivering quality and value by offering specialty medications to oncology patients.

Adding in-office dispensing is complex, and the decision must be made with careful consideration, taking into account overhead costs and patient service metrics. Hematology-Oncology Associates of Central New York started by defining roles and responsibilities for the three positions in its in-office dispensing team: pharmacist, oral oncology nurse navigator, and pharmacy technician. Next, the practice identified tasks and delineated these into four domains, assigning internal stakeholders who were ultimately accountable, responsible, consulted, and informed to each task. Target completion dates for tasks were also assigned so that the in-office dispensing team could meet specific milestones, and remain on budget, on time, and in scope. This project management approach helped transition the in-office dispensing

service from concept to practice and continues today—as Hematology-Oncology Associates of Central New York continually evaluates systems to deliver the best value to all internal and external stakeholders.

The Role of the Oral Oncology Nurse Navigator

Many patient-specific considerations come into play with dispensing oral oncolytics, including:

- Financial constraints
- Impaired cognition
- Co-morbidities
- Adherence to treatment regimens.

At the same time, having the capability to prescribe, dispense, and manage oral oncolytics directly from the physician’s practice can help to address these considerations.

Patients prescribed oral anti-cancer agents must understand that while taking an oral medication may offer flexibility with regards to when and where patients take their medications, it does not exempt them from the toxicities normally associated with IV chemotherapy. Further, if patients are nonadherent to the prescribed treatment regimen, their disease may progress. For these reasons, the role of the oral oncology nurse navigator is vital to helping patients manage their toxicities and maintain adherence.

To manage adherence and reduce waste at time of refill, the oral oncology nurse navigator contacts the provider to confirm if the patient is to continue his or her medication based on laboratory values and clinical assessment.

At Hematology-Oncology Associates of Central New York, before a patient is dispensed an oral oncolytic, the oral oncology nurse navigator assesses the patient’s ability to read and follow directions. If health literacy concerns exist, steps are taken to ensure the patient has the appropriate assistance to be compliant and safe. This assessment and education is documented in the practice’s electronic health record (EHR). Patients then have a formal “chemo teach” appointment with an advanced practitioner. Once this appointment is completed and consent forms are signed, patients can fill their oral medication prescription(s) at the in-office dispensing service.

The ever-increasing cost of oral chemotherapy makes it crucial for the oral oncology nurse navigator to be vigilant in securing financial assistance for patients.⁶ Specifically, the nurse navigator works closely with patients and families to ensure adherence and that their oral therapy treatment regimen is not interrupted due

to high out-of-pocket costs. Co-payments are reviewed with patients at the time of the prescription fill. If there is any need for co-pay assistance as needed, the oral oncology nurse navigator gathers the necessary information to apply to one of the many patient assistance foundations or to the pharmaceutical company’s co-pay support program. Once the oral oncology nurse navigator applies for foundation assistance on behalf of a patient, she is diligent in following up with the application.

When patients pick up their prescription(s) at the in-office dispensing pharmacy, the oral oncology nurse navigator reviews the medication again with patients and/or their caregivers. This review includes:

- How and when to take the prescribed medication.
- What to do if a dose is missed.
- An explanation of side effects, as well as how to manage them.
- How to safely handle the medication.
- Proper disposal of any unused medication.

The oral oncology nurse navigator also reviews any supportive medications (if prescribed), such as antiemetics and steroids.

The in-office dispensing team at Hematology-Oncology Associates of Central New York created “teaching sheets” for each oral oncolytic. All information is organized onto one page in a reader-friendly format. (In late 2017 Hematology-Oncology Associates of Central New York expects to adopt new oral chemotherapy education sheets being developed jointly by the Association of Community Cancer Centers, the Oncology Nursing Society, the Hematology/Oncology Pharmacy Association, and the National Community Oncology Dispensing Association.) Patients receive contact information and are instructed to call the office immediately with any concerns. After all patient questions have been answered, the oral oncology nurse navigator tells patients that they will receive a follow-up phone call approximately one week from their start date on the oral oncolytic to address any questions or concerns.

During this one-week follow-up call, the nurse navigator reinforces the discussion held at the time of initial dispense. The call is documented in the EHR and a copy of the note is sent to the patient’s provider. If there are any concerns, the oral oncology nurse navigator immediately contacts the provider to discuss management plans and determine if the patient needs to come in on the same day for a “sick call.” If a patient reports an issue, the oral oncology nurse navigator schedules another reassessment call, usually within one to two days; the provider is always consulted, and an assessment note is written.

To manage adherence and reduce waste at time of refill, the oral oncology nurse navigator contacts the provider to confirm if the patient is to continue his or her medication based on laboratory values and clinical assessment. Patients may require a change in the medication dose for many reasons, including a change in therapy or even a medication holiday, and this step helps avoid unnecessary oral oncolytic refills. One of the practice’s goals is for patients not to have extra medication at their home. Eliminating unnecessary refills of expensive medications also reduces waste, which benefits employers, payers, and all healthcare stakeholders.

At each refill, the oral oncology nurse navigator asks patients and/or caregivers how many tablets or capsules they have left from the previous prescription. At this time, the nurse navigator will also ask if there were any missed doses and the reasons for non-compliance. If non-compliance concerns arise, the oral oncology nurse navigator helps patients (and caretakers if necessary) develop a process to improve compliance that will ultimately lead to better clinical outcomes.

Each oral chemotherapy prescription is filled for a maximum of 30 days. With this policy, the practice can maintain tighter control on patient adherence as the oral oncology nurse navigator is speaking to patients at least once a month about their oral anti-cancer regimen.

A cancer diagnosis is a life-altering event marked by uncertainty and challenges, which may be difficult for patients to overcome. Hematology-Oncology Associates of Central New York makes every effort to provide passionate financial support, guidance, and compassion. Creating a good relationship with the patient is as important as helping the patient obtain their oral oncolytic. Staff are in touch with patients throughout their oral oncolytic treatment, which allows them to establish trust and form a strong bond with the care team.

The Oral Oncolytic Program at Norton Cancer Institute

Norton Cancer Institute currently has eight outpatient oncology offices and three radiation oncology centers serving Louisville, Kentucky, and Southern Indiana, employing 34 physicians and 33 advanced practice providers. The institute provides comprehensive cancer care, including medical oncology, gynecological oncology, orthopedic oncology, and radiation therapy. As a regional leader in oncology care, Norton Cancer Institute is committed to providing quality care to the patients it serves, including supportive services such as lymphedema therapy, patient navigation, genetic counseling, prevention and early detection, behavioral oncology, palliative care, survivorship, and specialty pharmacy services. In addition, the institute has four cancer resource centers that offer nutritional counseling, yoga, massage, and art and music therapy, as well as oversight for numerous support groups.

Over the last several years, Norton Cancer Institute has seen a significant increase in the use of oral oncolytics. More and more patients are moving from traditional intravenous chemotherapy treatment plans to oral oncolytic regimens. As oral oncolytics usage grows, it is crucial that organizations develop a model of care that addresses the challenges this shift in therapy creates—challenges not only in how care is delivered, but also in how care is monitored.

As stated previously, patients on oral chemotherapy are equally at risk for experiencing unwanted side effects and potentially are at higher risk for complications due to providers' limited ability to control patient compliance behaviors. Patient education, side effect management, medication adherence, financial constraints, and a variety of other barriers are real issues facing providers and therefore require a change in practice. As such, Norton Cancer

Institute recognized the need to create a robust oral oncolytic program that promotes optimal patient outcomes and prioritizes patient safety.

The Role of the Oral Oncology Nurse Navigator

In 2013 Norton Cancer Institute filled the role of oral oncology nurse navigator with an oncology nurse with 25 years' experience at Norton Healthcare. Since that time, the growing trend of utilizing oral therapies to treat cancer has become evident. Currently at Norton Cancer Institute, an approximate average of 60 patients begin a new oral oncolytic regimen every month.

As the number of patients taking an oral agent for cancer continued to grow, the institute began to identify common pitfalls and challenges when caring for these patients. The goal was to overcome these barriers by developing an oral chemotherapy process that was consistent across all eight clinics and multiple providers.

At the Norton Cancer Institute, the oral oncology nurse navigator assists both the multidisciplinary team and patients, overcoming barriers with prescribing, addressing adherence challenges, and more. While the nurse navigator functions under the direction of nursing leadership for the institute, she also collaborates with the in-house dispensing specialty pharmacy. Coordination of care and communication between the pharmacy and the interdisciplinary team are essential to patient safety, as well as patient and provider satisfaction. The oral oncology nurse navigator also functions as a resource to the nursing staff, providing education on and assisting with the oral chemotherapy process. And finally, the nurse navigator is a resource to patients, providing ongoing education and emotional support, assessing for adherence concerns and toxicities, and recommending strategies to improve adherence and self-care.

Once an oral oncolytic is prescribed, providers face the uncertainty of how and when the patient will obtain the medication and when treatment will be initiated. All too frequently, the burden of communicating this information to the clinic falls on the patient. Norton Cancer Institute developed documentation tools in the EHR to remove this burden from the patient. All members of the multidisciplinary team, including the dispensing pharmacists, financial counselors, and social workers, document updates regarding the patient's acquisition of the oral anti-cancer medication. Development of an oral chemotherapy flow sheet built into the nursing encounters has resulted in consistent documentation. Included in this flow sheet is information regarding the dispensing pharmacy, start date, financial concerns, adherence assessment, toxicity assessment, reinforcement of self-care techniques and when to call the office, patient understanding, and confirmation of appointments for monitoring and provider visits. Now, when the patient returns to the clinic for follow-up, the provider has access to the patient's start date, and follow-up appointments for adherence and monitoring are appropriately scheduled.

Utilizing the 2013 ASCO/ONS Chemotherapy Administration Safety Standards⁷ as a framework, and with the support and input of nursing directors and oncologists, Norton Cancer Institute


developed and implemented a nursing process that ensures that patients receive the education, support, and monitoring required to navigate the complex world of oral oncolytics. Prior to putting this process into practice, the oral oncology nurse navigator conducted educational in-services at each clinic site. This process, which is primarily nurse-driven, includes:

- A comprehensive education session conducted by an oncology-certified nurse or clinical pharmacist.
- Scheduled outreach calls to confirm acquisition of the oral anti-cancer medication.
- Documentation of the start date.
- Confirmation that the patient correctly understands how to take the medication.
- After the oral oncolytic is initiated, a one-week follow-up call to patients for adherence and side effect assessment.

This oral chemotherapy process was added as a yearly nursing competency. The oral oncology nurse navigator serves as a resource to the validators, assisting with this annual competency validation. The nurse navigator also collects patient-specific data categorized within each clinic, which is reported monthly to the Norton Cancer Institute's director of quality.

Because the oral oncology nurse navigator has direct and frequent communication with the in-house dispensing pharmacy, she can communicate essential information to the clinics regarding the patients' acquisition of their medication. Such communication includes alerting nurse clinicians or managers of a new prescription for which patient education and consent still need to take place. When the patient's insurance dictates the medication to be filled by another specialty pharmacy, the navigator contacts the pharmacy to ensure the prescription has been received and is processed in a timely manner. The oral oncology nurse navigator also confirms that the monitoring tests and follow-up appointments are scheduled appropriately in conjunction with the date the patient started taking the therapy. Upon FDA approval of a new oral anti-cancer agent, using supportive documentation, the oral oncology nurse navigator develops the medication side effect/self-care handout that is provided during the education sessions.

Ongoing support and education are crucial for oncology patients to remain adherent to their oral anti-cancer medication. When patients can effectively identify, manage, and report side effects, their ability to continue the medication for a longer duration improves. As this persistence increases, so does the potential for maximized patient outcomes. For those individuals prescribed an oral anti-cancer agent as a first-line treatment, the oral oncology nurse navigator calls every one to two weeks between office visits. The nurse navigator also takes referrals to follow up with any individuals who may be experiencing adherence or toxicity concerns. Any toxicities interfering with ADLs (activities of daily living) or concerns are reported to the clinic for physician review and additional interventions. Referrals are also frequently made to other members of the multidisciplinary team as necessary, such as to nutrition counseling or the behavioral oncology program.

The shift from treating patients with standard infusion therapies to oral or combination regimens is an exciting time in cancer care, requiring flexibility from all members of the cancer care team. As the oral chemotherapy process at Norton Cancer Institute continues to evolve, so does the multifaceted role of the oral oncology nurse navigator. Through these changes, ongoing self-assessment, and process development, the end goal remains the same: to provide a safe nurturing environment for patients taking chemotherapy—regardless if it is in the clinic or home setting. 

Mary K. Anderson, BSN, RN, OCN, is an oral oncology nurse navigator and Rebecca S. McMahan, MHA, BSN, RN, OCN, is director of Patient Care Services at Norton Cancer Institute, Louisville, Ky. Michael J. Reff, RPh, MBA, is founder and executive director of the National Community Oncology Dispensing Association, Inc., a 501(c)3 grassroots organization focused on the continuity of care for patients receiving oral chemotherapy, www.NCODA.org. Reff is also pharmacist and Deborah R. Walters, RN, OCN, is dispensing nurse navigator at Hematology-Oncology Associates of Central New York, Syracuse, N.Y.

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Beginning
January
2018



Oncology Issues Will Be Peer-Reviewed!

AS OF JANUARY 2018, *Oncology Issues*, the official journal of the Association of Community Cancer Centers (ACCC), will be published as a peer-reviewed journal in partnership with Taylor & Francis, an academic and professional publisher of scholarly journals, books, eBooks, text books, and reference works. With this partnership, we look forward to increasing the visibility and reach of our content within the oncology community.

WE INVITE YOU TO SERVE AS A PEER REVIEWER

ACCC seeks individuals from its multidisciplinary membership to serve as peer reviewers. If you are interested in helping to ensure the quality of feature articles in our award-winning journal, fill out our short form at acc-cancer.org/peer-review.



Painting a Brighter World in Cancer Care



*“If you have been recently diagnosed with cancer,
it’s a significant moment in your life. Art gives
you an opportunity to step away from that moment.
Art allows you to express what you’re going through
in a beneficial and impactful way.”*

SCOTT FEIGHT, EXECUTIVE DIRECTOR, FOUNDATION FOR HOSPITAL ART

A New Idea for Support and Healing

The Foundation for Hospital Art (FFHA) is a unique, captivating organization, yet many do not know about the foundation’s geographic footprint and the uplifting impact it has made in the lives of so many cancer patients across the world. Over the last 30+ years and with the help of more than 1 million volunteers and patients, the Foundation for Hospital Art has created more than 44,000 paintings for more than 4,000 hospitals in 195 countries. It is the foundation’s mission to extend compassion through art. Founder John Feight conceptualized the idea of conducting PaintFest in 1975 when he volunteered to paint a mural at Northside Hospital in Atlanta, Ga. The idea developed over the many years Feight spent painting in hospitals and seeing the comfort art provided to patients, medical staff, and visitors. The end result: the 1984 establishment of the Foundation for Hospital Art.

John witnessed firsthand traditional hospital settings, typically exemplified by white, sterile walls and ceilings. Exam rooms, waiting rooms, and corridors—areas where healthcare professionals and other caregivers work long days, and where families and patients spend many hours waiting—are too often colorless,

lifeless, and certainly not inviting. As Feight painted murals across the country, experience after experience proved to him that nothing a hospital could provide in the way of technological and scientific advances was as supportive as an atmosphere of compassion—both human and aesthetic—in institutions where patients, caregivers, and staff spend time to be healed or, for some, to die.

From concept to execution, the Foundation for Hospital Art is officially dedicated to involving patients and volunteers worldwide to create colorful, soothing artwork donated to hospitals to help soften the often-stressful hospital experience.

Each PaintFest is a unique and special event, but all are filled with smiles, joy, and the common goal of caring about people. The amazing thing about PaintFest is that no artistic experience is needed! The Foundation for Hospital Art leverages a paint-by-color block methodology design and technique that allows everyone to participate—regardless of their skill with a brush. Through the years, volunteers as young as three and as old as 103 have participated in PaintFest events, culminating in beautiful, colorful, and healing environments in communities across the world.



Top: 2016 PaintFest America participants. Bottom: “Stars of Hope” mural.

Engaging Cancer Programs Across the U.S.

One of the most unique projects ever undertaken by the Foundation for Hospital Art was the 2016 PaintFest America endeavor. The idea for PaintFest America came from Scott Feight, the foundation’s executive director. The initial concept was simple: unite cancer patients across the country with a common goal of care and comfort. The execution, on the other hand, was quite complex and relied on the dedication of cancer programs from around the nation. In just 50 days, the Foundation for Hospital Art painted and donated more than 200 murals across 51 cancer programs in all 50 states, plus the District of Columbia. The mission became one state per day for 50 days. FFHA staff and volunteers crossed the country kicking off the project on July 5 in Washington, D.C., at the MedStar Washington Hospital Center, Washington Cancer Institute. The team then traveled from East Coast to West Coast, from north to south and everywhere in between, until the PaintFest America finale on August 23 in New York City at the Mount Sinai Beth Israel Cancer Center. Each participating cancer program painted between 3 and 10 murals with images depicting living organisms, such as plants and animals, to bring life and vibrant color to sterile hospital walls. A special Foundation for Hospital Art mural designed for the PaintFest America event, titled “America the Beautiful,”

was inspired by Katharine Lee Bates’ historic lyrics and was a favorite of patients at every stop.

Creating a Living Mural


Perhaps the most special mural of all was created by cancer patients and survivors who painted part of a national mural titled “Stars of Hope.” For this piece, each state’s panel depicts the state bird and flower superimposed upon stars and a map of the United States. A ribbon signifying hope flows throughout the entire design. On the final day of the tour, all 50 panels were assembled in New York for all to see. More than art, the mural represented the beautiful stories of cancer patients in every state across this wonderful country. The power to overcome adversity was on full, colorful display.

The intent of PaintFest America was certainly to bring people, who had been touched by cancer, together through art, but the project achieved so much more. PaintFest America brought hope, healing, and brief reprieve to hundreds of patients, family members, physicians, and hospital staff members, creating beauty in the midst of hardship for the few hours they spent painting. The time and dedication of these volunteers transformed into more than 400 warm, vibrant murals that will continue to spread comfort to patients for years to come.

Hosting a PaintFest for Your Community

PaintFest events are the perfect complement to a long day of meetings. Easily organized in a social setting, PaintFest enhances networking, relationship-building, and a company's corporate citizenship profile. PaintFest is scalable and can be held during patient, community, and team-building events; or at conferences and meetings for hospitals and health systems. Remember: Artistic talent is not required; everyone can successfully participate. Designs are drawn in advance, and volunteers simply follow the dots and their hearts. If you are interested in hosting a PaintFest event for your cancer program, hospital, or health system, the Foundation for Hospital Art can help develop the perfect PaintFest event for your community, provide a budget, and describe how the funding works. The Foundation for Hospital Art provides customized budgets for each PaintFest. Factors such as the number of painters, the number of paintings and paint stations, and the location of the event impact program costs.

PaintFest America brought hope, healing, and brief reprieve to hundreds of patients, family members, physicians, and hospital staff members, creating beauty in the midst of hardship for the few hours they spent painting.

Once everything is finalized, foundation artists prepare the color-coded artwork and supplies in our studio and ship them directly to the PaintFest location. Foundation for Hospital Art staff can attend and help orchestrate the event or, if you choose, provide instruction so that you can conduct smaller events on your own. During a PaintFest event, volunteers team up to complete the paintings by following the "color code." The artwork is touched up by our staff and then donated to your organization or to a requesting hospital on behalf of the sponsor. The sponsor is acknowledged in the signature on the painting. Publicity is optional, but we have found that media coverage can be significant and positive. Interested cancer programs can visit hospitalart.org or call 678.324.1705 for more information. 

Scott Feight is the executive director of the Foundation for Hospital Art (FFHA), Marietta, Ga. Kelley D. Simpson, MBA, is an FFHA Board Member and senior partner of Oncology Solutions, LLC, Atlanta, Ga. Visit hospitalart.org or call 678.324.1705 for more information.

A Survivor & Patient Perspective

The Foundation for Hospital Art received so much from each local event held during PaintFest 2016. The stories are innumerable—and uplifting—but one story in particular touched us very closely. Two sisters, one with cancer and one who provided support, attended a PaintFest event held in the northeast. The supportive, caring sister wrote:

"One week after that fun experience, my sister went into the hospital on an emergency basis. She was in ICU for a long, long time and then back to the hospital, into rehab, back into the hospital, and is now, as of today, in what seems to be her final rehab visit. She had all kinds of things medically go awry at once. It was like a perfect storm of maladies, and it knocked her for a loop. And I was so upset because we just shared a great time painting.

I have spent all fall and this winter flying to visit her in the many medical facilities she's been treated in. The reason I am telling you this is that this year—for the first time ever—my sister decided she wanted to put a photo of herself in her Christmas cards to be mailed to our family and friends. She chose the photo of herself holding up part of the orange mural she painted at 2016 PaintFest America. I decided to follow in her footsteps and put a photo of myself and a photo of the two of us from 2016 PaintFest America in my Christmas cards.

I wanted to let you know that PaintFest America was inspiring for me as a cancer survivor, but this year it took on new meaning as the artistic spirit of the event spread beyond the local hospital murals. The spirit of the PaintFest photographs became artistic memories for my sisters and our family and friends as the art spread forward from us to those on our mailing lists. The movie Pay It Forward came alive this year for my family as PaintFest gave us the opportunity to do just that.

My sister is doing so well now at her final rehab place. She has been walking, eating, breathing, and talking on her own now, and she will be back home by late winter/early spring or maybe sooner. I stayed with her last summer for one solid month. On the last day, when I asked her to name her top three favorite activities we did, her first one was PaintFest America. Thank you for organizing the event. You will never know how much it meant to our family and my sister's healing."



2016 PaintFest America participants.

2016 PaintFest Stories at ACCC Member Programs Across the Country

- “PaintFest America Visits Winship” at Winship Cancer Institute of Emory University, Atlanta, Ga. (winshipcancer.emory.edu/roundup/issues/2016/july-18.html)
- “The Healing Power of Art” at Lahey Hospital and Medical Center, Burlington, Mass. (lahey.org/News/The_Healing_Power_of_Art.aspx)
- “ECCC Selected to Represent West Virginia in National PaintFest America” at Cabell Huntington Hospital, Edwards Comprehensive Cancer Center, Huntington, W. Va. (cabellhuntington.org/news/wns/eccc-selected-to-represent-west-virginia-in-national-paintfest-america)
- “PaintFest: A Creative Force at PCAM” at Abramson Cancer Center, Philadelphia, Pa. (pennmedicine.org/news/internal-newsletters/hupdate/2016/august/paintfest-a-creative-force-at-pcam)
- “National Painting Event for Cancer Awareness Stops by Florida Hospital” at Florida Hospital Cancer Institute, Orlando, Fla. (orlandosentinel.com/health/vital-signs/os-paintfest-america-florida-hospital-20160713-story.html)
- “PaintFest America: UAB Mural Painting Event Helps Cancer Patients through Art” at University of Alabama at Birmingham Comprehensive Cancer Center, Birmingham, Ala. (al.com/news/birmingham/index.ssf/2016/07/paintfest_america_uab_mural_pa.html)
- “PaintFest America Makes a Colorful Stop for Davenport Cancer Patients” and “Cancer Patients to Participate in PaintFest America” at Genesis Cancer Care Institute, Davenport, Iowa (wqad.com/2016/07/26/paintfest-america-makes-a-colorful-stop-for-davenport-cancer-patients) and (wvik.org/post/cancer-patients-participate-paintfest-america#stream/0)
- “Cancer Patients and Survivors Give Each Other Essential Support, through Painting” at Olathe Medical Center, Olathe, Kansas (fox4kc.com/2016/07/25/painting-brings-together-cancer-fighters)
- “PaintFest America Aims to Brighten Walls, and Patients’ Days” at Mount Sinai Medical Center, The Derald H. Rutenberg Treatment Center, New York, N.Y. (inside.mountsinai.org/blog/paintfest-america-aims-to-brighten-walls-and-patients-days)
- “PaintFest America is Coming to Sussex County!” at Beebe Healthcare, Robert & Eolyne Tunnell Cancer Center, Lewes, Del. (beebehealthcare.org/news/tunnell-cancer-center/paintfest-america-coming-sussex-county)





ACCC 44TH ANNUAL MEETING & CANCER CENTER BUSINESS SUMMIT

March 14–16, 2018

Renaissance Washington, DC Downtown Hotel

HEALTHCARE REFORM IS UNDERGOING A WAVE OF RADICAL CHANGE AND DISRUPTIVE INNOVATION, with stakeholders transitioning to value-based care delivery models to reduce costs and improve quality of care. At the same time, leveraging advanced technologies, experimenting with various business models, and developing new relationships are changing the way that medicine is practiced.

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Hear cutting-edge approaches for navigating these inevitable business and policy-related changes in oncology, including:

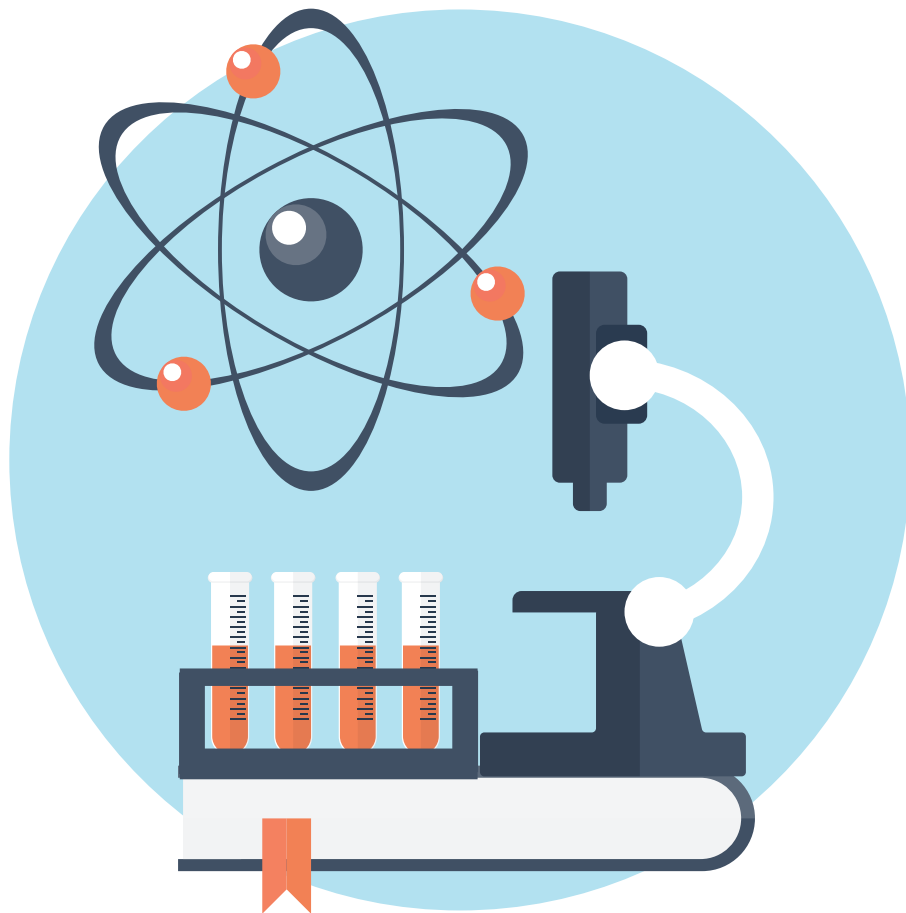
- Alternative Payment Models & the Impact on Oncology
- Integrated Cancer Care Teams: Opportunities & Challenges
- Identifying High Cost Cancer Patients & Developing Successful Interventions
- Technology's Role in the Redesign of Oncology
- Patient Engagement & Expectations—What's Realistic & Where Do We Need to Go?
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CO-HOSTS





Best of ASCO 2017

ASCO 2017 was filled with new information and long lines as 39,000 oncologists worldwide came together to hear the latest advances in cancer care. The quality of research and originality of studies, however, made any inconvenience worthwhile. Here are my thoughts about the best of ASCO 2017.

Practice Management Issues

At the pre-ASCO session on Economics of Cancer Care, presentations focused on the OCM, MIPS, and drug pricing. Every oncology practice is now impacted by either MACRA, MIPS, or alternative payment models, which started in January 2017. Because of the compliance-related frustration of reporting in the

OCM, networking with other participants is necessary, and attending meetings at ASCO, ACCC, and other venues is strongly recommended. The best tip was to stress coordination among physicians, nurses, and advanced practitioners, as well as specialists and supportive care services.

Another issue of importance is value. There is not agreement on the elements of value, and this is evident in the comparisons of ASCO (version 1 and version 2), ESMO, NCCN, ICER, and others. S. Cheng and coauthors (Abstract 6509) described the very poor correlation coefficient values for each of the frameworks (ASCO1, ASCO2, and ESMO) and the poor agreement between the frameworks and ultimate decisions by the payers NICE and pCODR.

ACRONYM LEGEND

ACA: Affordable Care Act

ADT: Androgen deprivation therapy

ALL: Acute lymphocytic leukemia

AML: Acute myelocytic leukemia

CBR: Clinical benefit rate (CR+PR+SD)

CNS: Central nervous system

CR: Complete response

DFS: Disease-free survival

EGFR: Epidermal growth factor

ESMO: European Society of Medical Oncology

HR: Hazard Ratio

ICER: Institute for Clinical and Economic Review

IMiD: Immunomodulatory drug

LBA: Late breaking abstract

MACRA: Medicare Access and Chip Reauthorization Act

MIPS: Merit-based Incentive Payment System

Mo: Months

NCCN: National Comprehensive Cancer Network

NHL: Non-Hodgkin's lymphoma

NICE: National Institute for Health Care Excellence

NSCLC: Non-small cell lung cancer

OCM: Oncology Care Model

OS: Overall survival

pCODR: Pan Canadian Oncology Drug Review

PFS: Progression free survival

PR: Partial response

PSA: Prostate-specific antigen

QOL: Quality of life

R-CHOP: Rituximab, cyclophosphamide, doxorubicin, vincristine plus prednisone

R-CVP: Rituximab, cyclophosphamide, vincristine plus prednisone

RR: Response rate (CR+PR)

SD: Stable disease

Vs: Versus

Breast Cancer

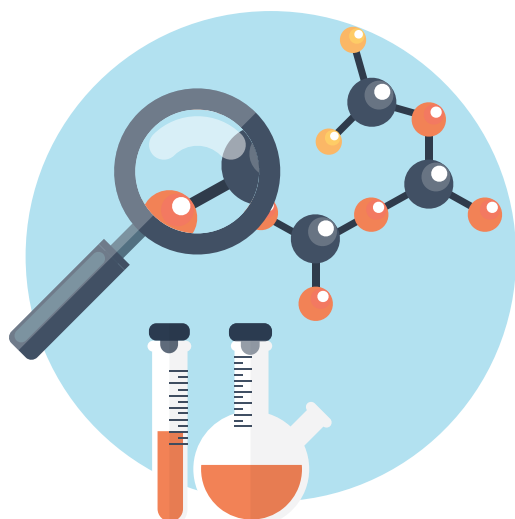
- In a plenary session, M. Robson and colleagues (**Abstract LBA4**) presented a Phase III trial of olaparib monotherapy vs treating physician choice of chemotherapy (TPC with capecitabine, eribulin, or vinorelbine) in patients with a germline BRCA mutation with up to 2 lines of prior chemotherapy. PFS was improved in olaparib patients 7.0 mo vs 4.2 mo, HR 0.58 ($p=0.0009$).
- **Abstract LBA500**, G. Von Minckwitz and colleagues presented results of the APHINITY trial. Addition of pertuzumab to chemotherapy plus trastuzumab increased invasive DFS from 90.6% to 92.3% at 4 years, HR 0.81 ($p=0.045$). The improvement: 3.2% in node-positive patients and 2.3% in hormone receptor-negative patients.
- **Abstract LBA10066**, M. Lambertini et al. showed that in patients with breast cancer, pregnancy did not adversely affect DFS, HR 0.85 ($p=0.15$). In patients with estrogen receptor negative cancer, pregnancy appeared to improve survival, HR 0.57 ($p=0.02$). Pregnancy appears safe in all breast cancer patients.
- In the ALTO trial, A. Moreno-Aspitia et al. (**Abstract 502**) showed that addition of lapatinib to trastuzumab adjuvant therapy increased the DFS slightly from 82% to 85% at 6 years, HR 0.86.
- R. Nanda et al. (**Abstract 506**) showed in the I-SPY 2 trial that pembrolizumab improved the pathological CR rate with paclitaxel in triple negative breast cancer patients from 19% to 71%, and in hormone receptor-positive patients from 14% to 28%.
- In patients with isolated locoregional recurrence, I. Wapnir et al. (**Abstract 513**) showed that for hormone receptor-positive

patients, the addition of chemotherapy to surgery, radiation, and hormonal therapy did not change DFS or OS. However, for hormone receptor-negative patients, 10-year OS with chemotherapy was 73% vs only 53% without, HR 0.48.

- G. Sledge et al. (**Abstract 1000**) presented the MONARCH 2 trial in endocrine-resistant patients. Abemaciclib plus fulvestrant increased the PFS to 16.4 mo vs fulvestrant alone 9.3 mo, HR 0.55, ($p<0.00001$). RR was increased to 48% from 2%.
- R. Finn and colleagues (**Abstract 1001**), however, reported that in the PALOMA-1 trial the OS of letrozole was 34.5 mo and only increased to 37.5 mo with addition of palbociclib ($p=0.28$ not significant).
- **Abstract 1002**, L. Malorni et al. showed that in patients with progression on prior endocrine therapy, addition of palbociclib presented an increase in PFS to 11.5 mo compared to only 6.5 mo with palbociclib alone, HR 0.53 ($p=0.02$). Palbociclib can reverse resistance.
- E. Perez and colleagues (**Abstract 1003**) described the MARIANNE trial. The less expensive trastuzumab plus docetaxel had the same effect on OS compared to T-DM1 or T-DM1 plus pertuzumab. Duration of response seemed longer on T-DM1, however.
- W. Gradishar et al. (**Abstract 1004**) showed superiority of a non-chemotherapy treatment with lapatinib plus trastuzumab plus aromatase inhibitor, PFS 11 mo vs 5.7 mo without lapatinib ($p=0.006$) or without trastuzumab 8.3 mo ($p=0.04$). Patients had prior chemotherapy with trastuzumab.
- In 31 HER2+ breast cancer patients with brain metastases treated with neratinib and capecitabine, R. Freedman and colleagues (**Abstract 1005**) showed a RR of 49% and SD at 6 cycles of 32%, with a median duration of response of 5.5 mo and OS 13.5 mo.
- **Abstract 1011**, C. Anders and coauthors reported on the treatment of HER2+ breast cancer patients with brain metastases treated with everolimus, trastuzumab, and vinorelbine. There was a CBR at 6 mo of 27% and OS was 12.2 mo.

Colorectal Cancer

- In a plenary session presentation, Q. Shi and colleagues (**Abstract LBA1**) studied a meta-analysis of 3 national adjuvant studies of Stage III and II colon cancer patients. Although overall FOLFOX or XELOX for 3 mo was noninferior to 6 mo of therapy, in patients with stage T4 or N2 disease, 3 mo was inferior to 6 mo of therapy, DFS HR 1.12. Consensus of the discussion suggested that in T1-3 N1 disease, 3 mo of therapy was sufficient and less toxic (17% grade 2 or higher neurotoxicity vs 48% with 6 mo); however, for T4 or N2 patients, 6 mo would be preferable but with consideration of the neurotoxicity.





- F. Innocenti et al. (**Abstract 3504**) showed the molecular correlates of patients on metastatic disease study CALGB/SWOG 80405 (Alliance) comparing bevacizumab with cetuximab. Patients with MSI-high showed superiority of bevacizumab vs cetuximab OS 30 mo vs 11 mo, HR 0.13 ($p=0.0002$). In patients with BRAF mutation, bevacizumab was superior to cetuximab, OS 17 mo vs 10 mo, HR 0.49.
- In protocol S1406, S. Kopetz and colleagues (**Abstract 3505**) showed that in the 7% of colon cancer patients with mutated BRAF in second- or third-line chemotherapy, addition of vemurafenib to irinotecan plus cetuximab increased PFS from 2.0 mo to 4.3 mo, HR 0.48 ($p=0.001$). OS increased from 5.9 mo to 9.6 mo, HR 0.7 ($p=0.19$).
- In an interesting study, K. Ng and colleagues (**Abstract 3506**) showed that in previously untreated metastatic colon cancer patients who were receiving FOLFOX chemotherapy with bevacizumab (the SUNSHINE study), addition of high doses of vitamin D 8000 iu/day for 2 weeks then 4000 iu/day, had superior results compared to low-dose vitamin D 400 iu/day. PFS was longer 13.1 mo vs 11.2 mo, HR 0.69 ($p=0.04$), and there was less diarrhea ($p=0.02$).
- **Abstract 10006**, E. Van Blarigan et al. showed that among localized colorectal cancer patients treated with adjuvant chemotherapy on CALGB protocol 89803 (Alliance), patients who complied with American Cancer Society guidelines for diet, obesity, alcohol intake, and exercise had a longer OS, HR 0.58 ($p=0.01$), and a longer DFS, HR 0.69 ($p=0.03$).

Gastrointestinal and Pancreatic Cancer

- **Abstract 4004**, S. Al-Batran et al. revealed that in patients with gastric or GE-junction cancer, neoadjuvant plus adjuvant chemotherapy with FLOT (5-FU, leucovorin, oxaliplatin, plus docetaxel) was superior to ECF/ECX (epirubicin, cisplatin, and 5-FU or capecitabine) with PFS 30 mo vs 18 mo; HR 0.75 ($p=0.004$), and OS 50 mo vs 35 mo ($p=0.001$). FLOT may be the new standard of care for resectable gastric or GE-junction cancer.
- In a practice-changing abstract, J. Primrose et al. (**Abstract 4006**) showed results of the BILCAP study with an OS of 53 mo with adjuvant capecitabine vs 36 mo with observation, HR 0.75 ($p=0.03$). This regimen is now the standard of care.
- S. Hingorani and colleagues (**Abstract 4008**) demonstrated that addition of PEGPH20 (degrades hyaluronan) to nab-paclitaxel plus gemcitabine as first-line treatment of metastatic pancreatic adenocarcinoma patients (HALO202 study) increased the PFS to 9.2 mo vs 5.2 mo, HR 0.57 ($p=0.048$), in patients with a high hyaluronan level.

Genitourinary Cancer Non-Prostate

- **Abstract 4501**, D. Bajorin et al. presented long-term follow-up of the KEYNOTE-045 trial comparing pembrolizumab with chemotherapy (paclitaxel, docetaxel, or vinflunine) in urothelial cancer patients. 18 mo OS was 36% with pembrolizumab and only 20% with chemotherapy, HR 0.7 ($p=0.001$).
- D. Smith and colleagues (**Abstract 4503**) showed initial results with epacadostat plus pembrolizumab with a RR of 35%. This appears to be an exciting combination.

Genitourinary Cancer Prostate

- In a plenary session presentation, K. Fizazi et al. (**Abstract LBA3**) studied patients with high-risk metastatic hormone-naïve prostate cancer (LATITUDE study). Patients received ADT or ADT plus abiraterone. Addition of abiraterone increased OS to 60% at 42 mo vs 34.7 mo without, HR 0.62 ($p=0.001$).
- In a practice-changing abstract, (**Abstract LBA5003**) N. James et al. compared the treatment of high-risk prostate cancer patients undergoing radiation, with abiraterone or without it (the STAMPEDE trial). Abiraterone improved OS by 37%, HR 0.63 ($p=0.00001$).
- In localized prostate cancer, A. Nabid and colleagues (**Abstract 5008**) showed that radiation therapy with either 36 mo or 18 mo of ADT gave equal OS. QOL and sexual satisfaction were better in the 18-mo group.
- In patients with recurrent prostate cancer, K. Chi and colleagues (**Abstract 5002**) showed that enzalutamide produced a 50% decrease of PSA in 73% of patients vs only 53% with abiraterone plus prednisone ($p=0.004$), but with similar time to PSA progression 8.0 mo vs 7.4 mo.
- **Abstract 5001**, M. Hussain et al. studied relapsed or recurrent prostate cancer patients with a BRCA2 mutation or other DNA repair deficiency (25% of prostate cancer patients), and showed that the addition of veliparib to abiraterone plus prednisone increased PFS to 13.8 mo vs 8.0 mo without veliparib ($p=0.02$).



Gynecologic Cancer

- In ovarian cancer patients at primary surgery, P. Harter et al. (**Abstract 5500**) showed from the LION study that omitting lymphadenectomy resulted in equivalent OS 69 mo compared to patients with complete surgery plus lymphadenectomy 65 mo. Morbidity and mortality were reduced by omitting the lymphadenectomy.
- In an important study, A. Du Bois et al. (**Abstract 5501**) demonstrated that following recurrence and chemotherapy of ovarian cancer, addition of cytoreductive surgery resulted in a longer PFS 19.6 mo compared to 14.0 mo without surgery.
- D. Matei and colleagues (**Abstract 5505**) showed that following endometrial carcinoma surgery with a high-risk of recurrence, adding radiation to chemotherapy did not increase PFS or OS. Completion of chemotherapy was more difficult after radiation.

Head/Neck Cancer

- In **Abstract 6010**, O. Hamid et al. reported a 34% RR to epacadostat (an IDO inhibitor) and pembrolizumab in third-line head and neck squamous cell cancer. Epacadostat also produced a 35% RR in urothelial tumors according to D. Smith et al. (**Abstract 4503**), a 50% RR in renal cell cancer in **Abstract 4515** (P. Lara and colleagues), and is being studied with nivolumab in multiple tumors according to R. Perez and colleagues (**Abstract 3003**). This is an exciting new combination of immunotherapy.
- **Abstract 101**, E. Cobain and colleagues reported on 500 patients with head and neck squamous cell cancer, showing 12.2% germline mutations and tumor somatic changes in 78%, but with only 19% actually using a targeted drug. OS was 12 mo in mutation-guided therapy.
- M. Gillison and colleagues (**Abstract 6019**) compared nivolumab to physician-chosen chemotherapy (methotrexate, docetaxel, or cetuximab) in patients with platinum-resistant head and neck squamous cell cancer. Nivolumab produced longer OS 7.7 mo vs 3.3 mo, HR 0.56.

Health Sciences Research

- In an important plenary session paper, E. Basch and colleagues (**Abstract LBA2**) studied patients with metastatic solid tumors being treated with chemotherapy. Patients who were emailed a symptom evaluation form to self-report 12 symptom complexes (patient-reported outcome patients) with physician/nurse follow-up were compared to usual care. Patient-reported outcome patients produced longer OS, 31.2 mo vs 26 mo, HR 0.83 (p=0.03), with increased QOL and 7% fewer ER visits. Physicians can implement this kind of program immediately.

- **Abstract 10009**, H. Singh et al. of the FDA reported on the 10-year (2005-2015) review of numbers of older adults in clinical trials. Older adults, particularly patients over 75, were under-represented in clinical trials, only 12% of patients compared to 29% of patients <75 who were diagnosed with cancer in 2013.
- **Abstract 6521**, X. Han and colleagues showed that after the ACA, Stage I diagnosis increased (breast cancer 48.9% after ACA vs 47.8% before, colon 23.7% vs 22.8%, and lung cancer 17.7% vs 16.6%).

Immunotherapy

- CAR-T cell therapy was one of the most exciting areas of new therapeutic approaches. Carl June, MD, of the University of Pennsylvania, received the David A. Karnofsky Memorial Award for his pioneering work on engineering T cells in targeted cancer therapy and discussed his work during the June 3 Karnofsky Lecture.
- **Abstract 3008**, J. Wargo et al. presented interesting data on metastatic melanoma patients being treated with anti-PD-1 immunotherapy. The gut microbiome differed in responders vs non-responders. More Clostridiales were seen in responders vs more Bacteroidales in non-responders.
- L. Derosa et al. (**Abstract 3015**) showed that in patients with renal cell carcinoma receiving anti-PD-1 therapy, receiving antibiotic from 2 mo prior up to 1 mo after therapy was associated with decreased response. PFS was 3.4 mo with antibiotic vs 5.2 mo without (p=0.01). More importantly, OS was only 12.2 mo with antibiotic vs 20.8 mo without (p=0.001).

Leukemia, Myelodysplastic Syndrome, Lymphoma

- **Abstract 7500**, I. Flinn et al. reported on patients with indolent non-Hodgkin's lymphoma or mantle cell lymphoma treated in the BRIGHT study. Bendamustine plus rituximab was slightly superior to standard R-CHOP or R-CVP in 5-year PFS (indolent non-Hodgkin's lymphoma HR 0.7 p=0.06 and mantle cell lymphoma HR 0.4 p=0.004).

- M. Rummel and coauthors (**Abstract 7501**) presented the StiL NHL1 study in indolent non-Hodgkin's lymphoma patients treated with bendamustine plus rituximab or CHOP-R. OS at 10 years was statistically equal (71% with bendamustine plus rituximab vs 66% for CHOP-R), but time to next treatment was better in bendamustine plus rituximab-treated patients, HR 0.52 ($p < 0.001$). Bendamustine plus rituximab appears to be a preferable initial treatment.
- **Abstract 7003**, J. Altman et al. showed CR rate of 55% in FLT3 mutation-positive relapsed or refractory AML treated with gilteritinib. 20/60 patients had a deep molecular response, with OS improved to 417 days vs 199 days in patients without a deep molecular response ($p < 0.001$).
- E. Stein and colleagues (**Abstract 7004**) reported a CR rate of 19% in relapsed AML patients with an IDH2 mutation (8-15% of AML patients) treated with enasidenib.

Lung Cancer

- In patients with small cell lung cancer, T. Owonikoko and coauthors (**Abstract 8505**) reported the results of ECOG-ACRIN 2511 study treating patients with cisplatin and etoposide with or without veliparib. PFS increased to 6.1 mo with veliparib vs 5.5 mo without veliparib, HR 0.63 ($p = 0.01$), OS was 10.3 mo vs 8.9 mo.
- In patients with mesothelioma, A. Scherpereel and colleagues (**Abstract LBA8507**) showed RR 19% to nivolumab and 26% after nivolumab plus ipilimumab. OS was 10.4 mo on nivolumab, and was still 65% at 12 mo on nivolumab plus ipilimumab.
- Also in patients with mesothelioma, A. Nowak et al. (**Abstract 8506**) showed that treatment with pemetrexed plus cisplatin with or without nintedanib, produced OS favoring nintedanib,

HR 0.77 but $p = 0.3$ only. PFS was better in nintedanib-treated patients, HR 0.54 ($p = 0.01$).

- In patients with NSCLC, J. Chaft and colleagues (**Abstract 8508**) showed following nivolumab as neoadjuvant therapy 2 doses, 20/21 patients were resected, PR was only 10% but with major pathological response ($< 10\%$ viable tumor cells) in 9/21 (43%) of patients. PD-L1 did not correlate with pathology response. RECIST response did not correlate with pathology response either.
- In patients with Stage II or IIIA NSCLC, Y. Wu et al. (**Abstract 8500**) compared gefitinib with cisplatin plus vinorelbine adjuvant therapy in patients with an EGFR mutation. DFS was superior with gefitinib 28.7 mo vs with cisplatin plus vinorelbine 18.0 mo, HR 0.6 ($p = 0.005$).
- **Abstract LBA9007**, T. Mok and coauthors showed that in the ARCHER 1050 study in NSCLC patients with an EGFR mutation, dacomitinib was superior to gefitinib PFS 14.7 vs 9.2 mo, HR 0.59 ($p = 0.001$), and OS 14.8 mo vs 8.3 mo, HR 0.4 ($p = 0.001$).
- **Abstract LBA9008**, A. Shaw and colleagues showed that alectinib was superior to crizotinib in patients with ALK-positive NSCLC, with PFS not yet reached vs 11.1 mo, HR 0.47 ($p < 0.0001$).
- T. Mok and colleagues (**Abstract 9005**) showed in the AURA3 trial that patients with T790M-positive NSCLC and brain metastases had good CNS responses to osimertinib; RR 70% vs only 31% with chemotherapy ($p = 0.015$). CNS PFS was longer with osimertinib 11.7 mo vs 5.6 mo with chemotherapy, HR 0.32 ($p = 0.004$).
- **Abstract 10017**, J. Malhotra et al. reported on the surveillance of over 10,000 patients with Stage I or II NSCLC. Compliance with annual imaging for recurrence or for second cancers was only 56% at 30 mo and 44% at 60 mo. OS of patients who were compliant with imaging vs non-compliant was improved, HR 0.86 at 18 mo and HR 0.68 at 60 mo of compliance.



Melanoma

- C. Robert et al. (**Abstract 9504**) reported long-term follow-up on KEYNOTE-006. In ipilimumab-naïve patients with metastatic melanoma randomized to either of 2 doses of pembrolizumab or ipilimumab, 33 mo OS favored pembrolizumab patients at 50% vs 39% on ipilimumab. RR was 42% on pembrolizumab vs 16% on ipilimumab. After stopping pembrolizumab at 24 mo, 23% were in CR and 23/24 continued in CR; 64/68 in PR continued in PR; and 10/12 in SD remained in SD. 91% were progression free at 12 mo after stopping.
- G. Long and colleagues (**Abstract 9505**) reported on long-term follow-up of dabrafenib plus trametinib. 5-year OS was 28% and even higher (51%) in patients with normal lactate dehydrogenase and < 3 organs involved by melanoma.

- **(Abstract 9507)** H. Tawbi and colleagues presented the results of melanoma patients with brain metastases treated with nivolumab 1 mg/kg plus ipilimumab 3 mg/kg, followed by nivolumab maintenance in the CheckMate 204 study. Brain CR was 21%, PR 33%, and stable 5%. Median time to response was 2.8 mo. Confirming the activity of immunotherapy, G. Long and coauthors **(Abstract 9508)** reported brain RR to nivolumab plus ipilimumab of 50% with a 6 mo PFS of 50%.

Multiple Myeloma

- J. Berdeja et al. **(Abstract 3010)** reported 6/6 responses in myeloma patients to CAR-T in study bb2121. F. Fan and coauthors **(Abstract LBA3001)** reported a RR of 100% with B38M CAR-T cell therapy. Additionally, in the JCAR017 trial, J. Abramson et al. **(Abstract 7513)** showed a 60% CR rate in relapsed NHL, and B. Shah and colleagues **(Abstract 3024)** reported 6/8 CR in relapsed/refractory ALL in the Zuma-3 trial.
- A. Jakubowiak and coauthors **(Abstract 8000)** described the results of a Phase Ib study of daratumumab plus KRd (carfilzomib, lenalidomide, and dexamethasone). RR was 100%, CR 43%, and 6 mo PFS was 100%.
- **Abstract 8005**, N. Rajee et al. compared zoledronic acid with denosumab in 1,700 patients with myeloma. Denosumab was noninferior and PFS was 46 mo with renal toxicity only 10% on denosumab, but PFS was only 35 mo and renal toxicity 17% on zoledronic acid. PFS HR was 0.82 (p=0.036) favoring denosumab. There were no QOL studies done.
- **Abstract 6522**, A. Olszewski and colleagues showed that closure of the Medicare Part D coverage gap by the ACA resulted in reduced out-of-pocket costs for 1 year of “IMiD” therapy from \$6,502 to \$4,925 without low-income subsidies, and down to \$7 with the subsidies.



Patient and Survivor Care

- In SCORAD III, P. Hoskin et al. **(Abstract LBA10004)** showed that in patients with epidural cord compression, radiation with one fraction (one day) was equal to radiation with 5 daily fractions, resulting in ambulation at 8 weeks; 70% vs 73%.
- G. Rodin et al. **(Abstract LBA10001)** found that psychosocial interventions were successful in relieving distress and depression with the CALM protocol, and relieving fear as shown by J. Beith and colleagues **(Abstract LBA10000)**.

Precision Medicine

- In the ProfILER study, O. Tredan and colleagues **(Abstract LBA100)** tested a 69-gene panel in 2,676 patients, with 1,944 successful profiles. 52% had an active genomic alteration, but 1/3 of those had poor performance status and were not treated. Ultimately, 7% were treated with a matched drug with an impressive OS of 3.3 years and 34.8% survival at 5 years. This is excellent data—showing value in selected patient groups.

Sarcoma

- **Abstract LBA2501**, D. Hyman and colleagues showed an RR of 76% in patients with tropomyosin receptor kinase-mutated soft tissue sarcomas treated with larotrectinib, resulting in 75% of all patients being able to undergo surgical resection. 12% of patients had a CR.

Tumor Biology

- **Abstract LBA100**, O. Tredan and coauthors presented the results of molecular analysis with targeted exon sequencing and comparative genomic hybridization of 2,590 patients in the ProfILER study. 51.5% had at least 1 actionable mutation. A molecular tumor board recommended mutation targeted therapy in 644 patients and 101 started the recommended therapy. PFS was 2.8 mo in those patients, RR was 2.3% CR, and 15.1% PR. At 6 mo 24% are alive and progression free.
- N. Ammakkanavar et al. **(Abstract 102)** showed a 9% change in therapy with next generation sequencing in 250 patients, with a PFS of 5 mo and an average cost of \$10,000.

Closing Thoughts

ASCO 2017 was an interesting meeting, giving attendees valuable information that will help them manage their practices and change the way they treat their patients. Be sure to review the abstracts on the ASCO website and the subsequently published manuscripts to be confident of the results, side effects, and clinical interpretations. 📺

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Kicking Off the Education Project

The ACCC education project, “Virtual Molecular Tumor Boards,” examines how innovative formats can help ensure that communication and quality patient care standards are maintained across cancer programs. ACCC introduced this project at the 2016 ACCC National Oncology Conference by hosting a panel discussion with representatives from Seattle Cancer Care Alliance, Washington University in St. Louis, and Frederick Regional Health System. Panelists spoke about leveraging videoconferencing technology to communicate and collaborate on ways to improve molecular testing and patient care in the community (see “Using Virtual Molecular Tumor Boards to Access the Experts,” Table 1, page 52).

A virtual molecular tumor board format is especially appealing because it allows participation by a variety of providers across a wide geographic area. Members of multidisciplinary teams from different sites can be invited to join in virtual patient discussions and contribute to treatment plans.³ Virtual molecular tumor board discussions often lead to recommendations based on targetable genetic alterations.⁴

For this education project, ACCC conducted site visits and group interviews, developing a series of 12 webinars with cancer providers at the following ACCC member programs:

- Seattle Cancer Care Alliance (SCCA)
- University of California Davis (UC Davis)
- Sanford Health
- The Center for Cancer Prevention and Treatment at St. Joseph Hospital (SJO)

ACCC would like to thank the project advisory committee and the members of the cancer teams at these organizations for their guidance, valuable input, and active participation in the Virtual Molecular Tumor Boards project.

Evolving Role of Virtual Molecular Tumor Boards

While the purpose of virtual molecular tumor boards continues to evolve, cancer providers now practice in an era where multiple mutations may be targetable in patients with lung and/or breast cancer; now is a prime time for cancer programs to assess how these tumor boards may enhance care and provide additional support and resources for their providers and patients. Virtual molecular tumor boards can serve several key purposes, including:

- **Clinical research:** to identify potential patients who may be eligible for clinical trials.
- **Continuing education:** to disseminate education about molecular testing, report interpretations, and actionable results that may impact treatment plans for patients.

- **Collaboration:** to bring a team of multidisciplinary providers together to discuss evolving topics, controversial issues, or treatment approaches that are dependent on coordinated care from different members of the team.
- **Engagement and alignment:** to ensure that providers across multiple locations are testing and treating patients in a uniform, consistent manner that is based on clinical practice guidelines and the best available evidence.

Virtual molecular tumor boards can be held between a major academic center and a community cancer program. To illustrate this concept, ACCC held a webinar with Seattle Cancer Care Alliance (SCCA) and Summit Cancer Centers on Oct. 26, 2016. During the webinar, Arvind Chaudhry, MD, PhD, (Summit) and V.K. Gadi, MD, PhD, (SCCA) demonstrated how a virtual molecular tumor board could facilitate collaborative discussions on the care of complex patients with breast cancer. They covered a myriad of topics, including molecular testing, assessing for treatment responses, and identifying patients who may be eligible for clinical trials (see “Virtual Molecular Tumor Board Breast Cancer Case Studies,” Table 1, page 52).

As the topic of molecular testing and genomic profiling often refers to complex terms and concepts, ACCC provided an overview of genomic profiling in a Dec. 14, 2016, webinar with Jeffrey Gregg, MD, from UC Davis. Dr. Gregg reviewed genomic alterations found in cancer and explained how mutations, insertions/deletions, fusions, and copy number changes may be targets for drug therapy (see “Overview of Genomic Profiling,” Table 1, page 52).

Ongoing Molecular Testing Issues in Lung Cancer

The landscape of molecular testing in NSCLC has rapidly expanded with the recent approvals of multiple therapies targeting EGFR, ALK, ROS1, and BRAF. Immunotherapy has further advanced the treatment of NSCLC. In 2013, only one targeted agent was approved for ALK+ NSCLC. Today, there are five targeted agents approved for ALK+ NSCLC. There are also three targeted agents approved for EGFR+ NSCLC and a fourth agent approved for patients with EGFR+ NSCLC who have the T790M mutation. In an April 28, 2017, webinar, Melissa Johnson, MD, from Sarah Cannon Research Institute Tennessee Oncology reviewed the evolving landscape of targeted agents for NSCLC. She discussed the latest evidence around agents that target EGFR, ALK, ROS1, and other potentially actionable mutations. Her presentation illustrated how a virtual molecular tumor board could help clinicians in the community learn about ongoing

(continued on page 49)

Figure 1. SJO Lung Cancer Trials

Non-Small Cell Lung Cancer						Small Cell Lung Cancer	Rare Diseases or any Lung Patient Failing Treatment
THERAPY	Adjuvant (neoadjuvant genetic testing)	2nd line + squamous	2nd line +	1st line for brain metastasis	Liquid biopsy	Prophylactic cranial irradiation	Targeted therapies (genomic panel testing)
STAGE	Clinical IB-IIIa No neoadjuvant chemotherapy/radiation therapy Surgical candidate	Stage IV or any stage recurrent (pure squamous) EGFR/ALK negative or not tested	Stage IIIB-IV Failed ≥ 1 lines of systemic therapy, including doublet regimen	Stage IV with central nervous system metastasis	Stage IIIB-IV	Limited or extensive; No central nervous system metastasis; Responding to chemotherapy (English speaking only)	All Stages
TRIAL	ALCHEMIST	LUNG-MAP	SERANO (screening trial, refer to UCI)	NOVOCURE METIS EF-25	BIOCEPT LIQUID BIOPSY	NRG-CC003	NCI-MATCH
AGENT	For completely resected adeno: order ALK/EGFR (Central Lab) If ALK+ ALK inhibitor/ Placebo If EGFR+ EGFR inhibitor/ Placebo If adeno ALK/EGFR- or squamous, test for PDL1. For PDL1+ PD-1 blocking antibody vs. observation after surgery and chemotherapy	Research Order Foundation One 1 Arm Trial Non Match: PD-1 blocking antibody + CTLA-4 blocking antibody vs. PD-1 blocking antibody Match Targets: upcoming	Coming Soon Test for METex 14 Skipping Alteration (archived or fresh) @ Central Lab If positive, refer for treatment with C-MET targeting agent	IT Fields for SRS for 1-10 brain metastases vs. supportive care Excel resected or WBRT Must be receiving therapy for extracranial disease May continue on systemic therapy KPS ≥ 70	Liquid biopsy + tumor tissue to determine molecular marker status for EGFR, ALK, and ROS1	Prophylactic cranial irradiation (PCI) +/- hippocampal avoidance +/- NMDA receptor antagonist use	24 treatment arms for actionable mutations

Source. sjo.org/our-services/the-center-for-cancer-prevention-and-treatment/cancer-programs/thoracic-oncology-program-lung/clinical-trials.



(continued from page 47)

advances and updates in lung cancer molecular testing and the potential clinical role of emerging agents on the horizon (see “The New Age of Molecular Testing and Targeted Therapies for Lung Cancer,” Table 1, page 52).

As additional targeted therapies are approved, the complexity of treating patients with NSCLC is fundamentally revolving around the role of repeat biopsy and repeat molecular testing after patients are started on targeted treatment. Retesting may be necessary to identify potential resistance patterns. The use of liquid biopsy tests (circulating tumor DNA or ctDNA) is one of the latest technologies that has generated a significant level of interest among cancer providers. Cancer programs may need to revisit their own molecular testing policies and procedures to customize them based on the current landscape of available tests, therapies, and the latest clinical evidence. Broad next-generation sequencing (NGS), which is also called comprehensive genomic profiling, is gaining popularity in community settings. As part of the ACCC virtual molecular tumor board webinar series, on Jan. 25, 2017, Jeffrey Gregg, MD, discussed the role of next-generation sequencing for NSCLC. He explained how comprehensive genomic profiling may identify potentially actionable targets in patients with advanced NSCLC who may otherwise have no other treatment options on the horizon (see “Precision Medicine and Personalized Cancer Therapy in Lung Cancer,” Table 1, page 52).

The Mar. 13, 2017, ACCC webinar featured the team at St. Joseph Hospital of Orange County (SJO) describing how they have been advancing their molecular testing policies to deliver precision care in their own communities. The team also regularly disseminates information to other clinicians about ongoing clinical trials such as NCI-MATCH, TAPUR, ALCHEMIST, Lung-MAP, and others. As they continue to refine their molecular testing policies, they also align their processes with their clinical research efforts. An example of the SJO Lung Cancer Trials can be seen in Figure 1, left.

Ongoing Molecular Testing Issues in Breast Cancer

Although providers routinely test patients with breast cancer for ER, PR, and HER2, the method of HER2 testing has evolved over the years. This evolution has recently led to some debates regarding optimal testing and interpretation for accurate results. The American Society of Clinical Oncology (ASCO)/College of American Pathologists (CAP) guideline for HER2 testing in breast cancer was originally released in 2007.⁵ In 2013, ASCO and CAP updated their guideline to improve the accuracy of HER2 testing to ensure that every eligible patient is identified and treated with HER2 targeted therapies.⁶ Sometimes, HER2 results are reported as “equivocal,” which means that the test is neither positive nor negative. In such cases, oncologists confer with the pathologist regarding the need for additional HER2 testing on the same or

a different tumor sample. While some cancer programs have clear policies and procedures on how to handle equivocal HER2 test results, others leverage tumor boards to discuss some of the latest testing methods and to review guideline recommendations. During a May 4, 2017, ACCC webinar, Michele Carpenter, MD, and David Margileth, MD, from SJO shared their experiences of leveraging their multidisciplinary team to discuss the optimal approach for handling equivocal HER2 test results (see “Challenging Issues in Breast Cancer Management,” Table 1, page 52).

Since certain types of breast cancers are linked with hereditary factors, patients often receive genetic testing and counseling. However, hereditary mutations such as BRCA1 and BRCA2 are different from molecular targets such as HER2. Germline (also called hereditary) testing is not the same as somatic mutation testing. To review these issues, Olufunmilayo Olopade, MD, FACP, from the University of Chicago presented a webinar on March 24, 2017, to help clarify the differences between clinical genetics vs. tumor genomic profiling. Clinicians need to clearly understand these differences so that patients are referred for the right types of mutation testing and genetic counseling that may impact their care (see “Clinical Genetics vs. Tumor Genomic Profiling: Relevance in Cancer Care,” Table 1, page 52).

Developing a Virtual Molecular Tumor Board Program

ACCC spent time with several member programs to learn how they developed, implemented, and sustained their virtual molecular tumor boards. The ideal program would effectively engage clinicians, maximize meaningful participation, and lead to improved patient care. As ACCC spoke with its members, several key trends and themes emerged, based on different goals and priorities, that led to tailored models for each cancer program.

Trend 1. Clinical Champions

A common theme was the importance of identifying at least one provider who will champion the virtual molecular tumor board effort, influence peers, and demonstrate value in how the tumor board may lead to improved patient care. The champion may be a medical oncologist, pathologist, or surgeon who recognizes the importance of finding potentially targetable mutations in patients with cancer. Other members of the cancer care team, such as advanced practice providers or nurse navigators, may also play a key role in championing virtual molecular tumor boards. Administrative support can enable these champions to overcome institutional barriers around scheduling, time allocation, and resource utilization. Education and outreach tactics must reach providers who work in different locations or specialize in treating specific malignancies.

At UC Davis, pathologist Jeffrey Gregg, MD, plays a key role in developing, organizing, and coordinating its virtual molecular



tumor boards. At Sanford, medical oncologist Steven Powell, MD, serves as a willing clinical champion who effectively engages other members of his team to discuss patient cases and make collaborative treatment decisions that improve patient outcomes. For more see “Engaging Multidisciplinary Clinicians in Genomic Tumor Boards,” Table 1, page 52).

Trend 2. Identifying and Preparing Patient Cases

Preparing cases for each virtual molecular tumor board can be time-consuming work, especially if the molecular test results are complex to interpret. Clinical research nurses or nurse navigators can be key to summarizing the patient case, extracting molecular test results, and coordinating the presentation of pathology and radiology findings. Some institutions discuss every patient who undergoes comprehensive genomic profiling at their weekly virtual molecular tumor boards; other cancer programs have rotating schedules that allow different providers to identify and select patients for presentation. Some cancer programs have added a process into their EHRs so that providers can submit a consultative virtual molecular tumor board request for a selected cancer patient.⁷ Using a case submission form (Figure 2, right) can help to ensure that the right pathology, radiology, and test results are prepared for the case presentation.

Trend 3. Scheduling Considerations

Cancer programs that are starting a virtual molecular tumor board program may begin with a single monthly meeting. High-volume cancer programs may need to hold weekly virtual molecular tumor boards to allow members of their team to contribute to the care of patients undergoing molecular testing. During a one-hour meeting, it may be possible to hold in-depth discussions around four to six patient cases. Sanford, which began with a single virtual molecular tumor board meeting each week, expanded its schedule to include two weekly meetings that occur at the conclusion of regular tumor boards. When scheduling virtual molecular tumor boards, consider the time zones of the remote participants. When SCCA engaged in a virtual molecular tumor board project, the schedule had to take into account network sites across three different time zones.

Trend 4. Access to Genomic Experts

Many cancer programs employ genetic counselors to speak with patients about hereditary genetic risks. However, the interpretation of comprehensive genomic profiling reports requires the skill of bioinformatics specialists, molecular pathologists, and other genomic experts. Community cancer programs may consider developing collaborations and partnerships with academic organizations or other institutions that provide this level of consultative expertise. Some lab testing companies allow their molecular pathologists and bioinformatics specialists to participate in virtual

molecular tumor board discussions. These individuals provide test interpretation services, but do not provide clinical treatment advice. UC Davis conducts its virtual molecular tumor board in partnership with Foundation Medicine to gain access to genomic experts who have seen a wide variety of unusual mutations in cancer patients. Virtual molecular tumor board discussions can be an effective way to identify patients who may be candidates for clinical trials. Some molecular testing companies include clinical trial matching information in the test results. Commercial companies like N-of-One offer clinical interpretation and trial matching services. The American College of Medical Genetics and Genomics (ACMG) and the Association for Molecular Pathology (AMP) are national organizations that train and equip genomic experts in cancer. For more see “The Role of Genetics Professionals in a Community Cancer Program,” Table 1, page 52.

Trend 5. Role of Technology

The use of secure video conferencing technology platforms lets remote participants engage in rich clinical discussions about treatment plans. These platforms allow providers and researchers to participate in discussions while they are off-site. The use of multiple screens and monitors in the tumor board conference room also allows pathology, radiology, and other disciplines to seamlessly present their findings. Technology platforms can enable remote participants to toggle screens and follow the discussions. At Sanford, the team has developed a progress note template to summarize the discussions from their virtual molecular tumor boards. This template allows providers to easily review the information as they are developing treatment plans and coordinating follow-up care. Be sure to obtain legal and regulatory review around potential issues that may impact patient privacy and liability.

Trend 6. Participation and Engagement

The effective use of virtual molecular tumor boards ultimately provides more patient-centered care. Clinicians, particularly medical oncologists and nurses, are most likely to directly experience this value with their own patients. As a result, they may be naturally inclined to actively participate in virtual molecular tumor boards and even emerge as potential champions. Other clinicians, such as surgeons, radiologists, pathologists, and pulmonologists, may need additional motivation to keep them engaged. These essential members of the cancer care team play a critical and active role in virtual molecular tumor board discussions that impact treatment plans for patients. At Sanford, the cancer center provides free lunch and CME credits at every virtual molecular tumor board. Cancer programs that employ physicians may choose to track participation at virtual molecular tumor boards and link a portion of physician compensation to their attendance. For more, see



“Real-World Considerations When Implementing a Genomic Tumor Board Program,” Table 1, page 52.

Looking to the Future

As the term “precision medicine” becomes more ubiquitous in cancer care delivery, the role of molecular testing is increasingly an integral part of shaping personalized treatment decisions and care plans. Cancer therapy that is driven by genomic testing can lead to more personalized treatment approaches that improve clinical outcomes.⁸ The growing complexity of molecular testing and interpretation presents both a challenge and an opportunity for community cancer programs to develop collaborative


approaches that effectively engage teams of clinicians to care for patients. Furthermore, implementing newer cancer treatments, such as immunotherapy, may require testing for PD1/PD-L1 and other biomarkers. Before starting a virtual molecular tumor board, cancer programs must clearly define the metrics for success and perform a baseline assessment prior to launch. In the rapidly evolving era of precision medicine, clear communication between members of the multidisciplinary team is essential in providing optimal patient care. An effective virtual molecular tumor board can be a valuable care collaboration tool that improves knowledge, elevates care delivery, and ultimately improves outcomes in cancer patients. 

Figure 2. An Example of a Case Submission Form

Tumor Board _____	
Date Submitted _____	
Patient Name _____	E# _____
Presenting Physician _____	
Data to Review	Dates
<input type="checkbox"/> Pathology	_____
<input type="checkbox"/> Imaging	_____
<input type="checkbox"/> Nuclear medicine	_____
<input type="checkbox"/> Other _____	_____
Clinical Focus	
New patient/new presentation (full review)	_____
Specific clinical focus area	_____
Surveillance/interval evaluation	_____
** Case brief submitted by 12:00 noon on the day prior to the conference.	
Source: Sanford Health	



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Table 1. Virtual Molecular Tumor Boards: An ACCC Educational Series

ACCC partnered with the Association for Molecular Pathology to host 12 educational webinars that utilize case-based lessons surrounding molecular testing for breast and lung cancer. Featuring experts from these leading cancer programs: Seattle Cancer Care Alliance, University of California Davis, Sanford Health, and St. Joseph Hospital of Orange, The Center for Cancer Prevention and Treatment, the webinars listed below can be accessed online at: acc-cancer.org/resources/virtual-tumor-boards.asp.

1.	Using Virtual Molecular Tumor Boards to Access the Experts
2.	Virtual Molecular Tumor Board: Breast Cancer Case Studies
3.	Overview of Genomic Profiling
4.	Precision Medicine and Personalized Cancer Therapy in Lung Cancer
5.	An Ongoing Journey to Advance Molecular Testing in Lung Cancer
6.	The Role of Genetics Professionals in a Community Cancer Program
7.	Clinical Genetics vs. Tumor Genomic Profiling: Relevance in Cancer Care
8.	The New Age of Molecular Testing and Targeted Therapies for Lung Cancer
9.	Challenging Issues in Breast Cancer Management
10.	Engaging Multidisciplinary Clinicians in Genomic Tumor Boards
11.	Real-World Considerations When Implementing a Genomic Tumor Board Program
12.	Key Concepts and Future Directions in Molecular Testing and Care Delivery

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ACCC Institute Envisions Next Gen Multidisciplinary Cancer Care

BY MARK SOBERMAN, MD, MBA, FACS

On June 22, 2017, ACCC invited stakeholders from a variety of disciplines to step away from the pressures and demands of daily business and come together in Washington, D.C., to envision next gen multidisciplinary cancer care. Facilitating this ACCC Institute for the Future of Oncology forum was Kavita Patel, MD, MS, FACP, a nonresident fellow at the Brookings Institution and practicing primary care internist at Johns Hopkins Medicine.

In my inaugural column in *Oncology Issues*, I described why I believe it's critical for those of us in oncology to pause and consider what our future multidisciplinary cancer care will look like. Each day, the imperative grows stronger as we continue the trek toward value-based care.

As we imagine, anticipate, and prepare for future cancer care delivery, we must also assess what is required to move from today's provider-focused, siloed care models to a future in which care is organized around the patient and the disease. Exciting advances in our understanding of cancer are revealing more subtypes and subtleties of the diseases known as cancer; as a result, anti-cancer therapies are becoming increasingly complex. New technologies and new therapies are already shaping next gen multidisciplinary cancer care, requiring that oncology expand to include new specialties and new collaborations to effectively diagnosis and deliver precision, patient-centered therapies.

For participants in this year's Insti-

tute—and for all of us involved in oncology—the shape of multidisciplinary cancer care is evolving as cancer therapies becomes more complex. At the same time, our health system is struggling through a metamorphosis, moving incrementally toward new payment models focused on value for all stakeholders (patients, payers, providers, and ultimately our society).

We challenged Institute participants to imagine what next gen multidisciplinary care will look like—no small task. We also asked that they frame their vision through the multifaceted lens of new payment models and patient-centered care delivery.

Shaking Up the Crystal Ball

In keeping with these tumultuous times in healthcare, we shook up the format for this year's forum. For the day's discussion, participants were divided into three multidisciplinary groups. These breakout discussion groups allowed more opportunities to hear the broadest range of perspectives. Participants were asked to envision next gen multidisciplinary cancer care in terms of three of today's critical challenges:

- The need to improve care coordination.
- The tension between personalized medicine and value-based care.
- The anticipated workforce shortages that projected to occur at the same time as increasing patient volumes.

Each topic was the focus of a breakout session. At the conclusion of each small

group conversation, all participants reconvened and each group reported its key takeaways. This was followed by a brief follow-up discussion by the full group.

Participants in this year's Institute forum truly reflected the many disciplines involved in quality cancer care delivery today: physicians, administrators, nurses, quality officers, pharmacists, palliative care providers, registry/data professionals, social workers, and representatives from patient advocacy organizations. The diverse group also represented community and academic programs and practices. Participants reflected the diversity found in today's oncology workforce generationally, culturally, and in terms of gender.

Engaged participants sharing diverse perspectives—all from the frontlines of community cancer care delivery—created a powerful synergy. From this year's Institute forum discussion, five top-level takeaways reflect the practical forces shaping next gen multidisciplinary cancer care.

- 1. Change saturation.** Cancer care delivery (operations, processes, new treatment advances, new accreditation and reporting requirements)—along with the U.S. healthcare system—is in a state of disruption. “Everything is changing. Nothing you knew yesterday, including our treatments, is the same,” said one participant.
- 2. Greater Connectivity.** On many different levels, increased connectivity is needed for cancer care (and healthcare) delivery.

About the ACCC Institute for the Future

This year marked the fifth ACCC Institute for the Future of Oncology annual forum. The Institute convenes leaders in community oncology for an annual one-day forum to discuss significant issues they are facing today and those that are on the horizon. Each year Institute participants come together to share their knowledge, experience, and wisdom on these issues and to discuss potential solutions that could be deployed across the continuum of community oncology.

The 2013 Institute forum examined two issues:

- The trend of hospital consolidation and increased physician integration and impacts on communities and providers.

- The potential of electronic health information exchange to improve patient care.

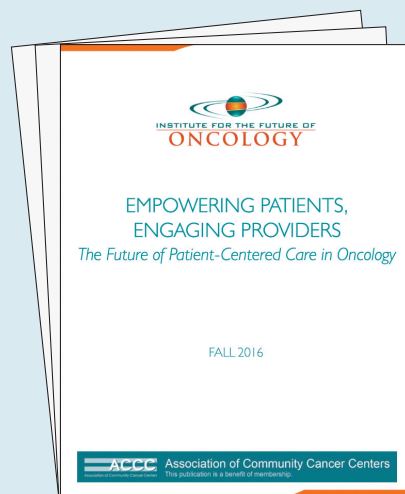
The 2014 Institute explored two key issues for the future of oncology care:

- Organizational leadership
- Communicating quality

The 2015 Institute discussed essential steps for achieving a positive impact on patient care within the next decade.

The 2016 Institute forum focused on:

- Identifying the concept of patient-centered care in oncology
- Exploring current models and existing barriers
- Recommending options to move from theory to practice.



Learn more and access Institute white papers on the ACCC website at acc-cancer.org/institute.

In the tech realm: greater connectivity needs include: EHR interoperability, more effective use of technology to support efficient care delivery (e.g., “paperwork” completed online in advance of appointments), “virtual” appointments, telehealth, etc.

In the high-touch realm: greater connectivity includes upfront distress screening and eliciting patient preferences and goals of care.

In the societal realm: greater connectivity includes care that integrates cultural competency and takes into consideration generational communication styles.

3. Culture Change in Healthcare.

For patients: increasing engagement; enabling and integrating shared-

decision making into the care process.


For staff recruitment and retention: Recognizing generational differences in workplace expectations and career drivers.

For care delivery: Integrating new non-traditional team members to the cancer care team, including primary care physicians, onco-generalists, home health providers, community health workers, specialty pharmacies, and others.

4. Technology Innovations. Rapid, continual advances in technology are driving constant change that impacts every aspect of cancer care delivery. Participants agreed that the delivery of next gen multidisciplinary cancer care requires greater use of technology on

the front-end of care. The team will include trained IT staff who can continually assess and improve workflow, keeping current with technology innovations and putting that information to work to support the care team.

5. Prevention. Next Gen Multidisciplinary Cancer Care will need to play an increased role in educating our population in disease prevention.

In the coming months through our national and regional meetings, ACCCExchange peer-to-peer dialogue, and ACCC education initiatives, we will be continuing this conversation so that ACCC can offer its members the tools and resources needed to be future ready. 

ACCC Institute Participant Takeaways

“Communication between providers, communication between EHR systems, communication between patients and providers—communication is where many of the breakdowns happen.”

“...the biggest takeaway for me is that large or small, metropolitan or rural... most oncology programs are facing similar hurdles.”

“The workforce needs to change. New skills are needed. New processes to ensure access to new therapies.”

“Everyone has some area of excellence to offer and some area of challenge in their daily practice—to learn from others.”

“The need for connectivity across all parts of the healthcare team (with team, patients, family, other groups). Care coordination must be patient-directed as well as patient-centered. Our technology must catch up with the speed of innovations. Care must be holistic—depth vs. breadth—and evidence-based. We need to harness big data to guide us.”

“Personalized medicine means different things to different people, we need to define it from the patient’s perspective.”

“The future has both certainty and uncertainty. Collaboration will be key to survival.”

“Expertise and knowledge sharing of participants was priceless. All these helped me gauge my organization and leverage perspective on current issues we are working on.”



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A REMINDER FROM ACCC'S BYLAWS COMMITTEE

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Dec. 1, 2017, is the deadline for submission of any proposed amendments to the ACCC Bylaws. Proposed recommendations should be sent to Betsy Spruill at bspruill@accc-cancer.org. ACCC's Bylaws are available online at: accc-cancer.org/about/pdf/Bylaws-2016.pdf.



ACCC 2017 Oncology Reimbursement Meetings

A comprehensive look at oncology reimbursement issues, tools to strengthen your program, and information to help you weather market changes. All members of the cancer care team who deal with oncology business and reimbursement will benefit from these meetings. Gain a full-spectrum perspective in just one day of sessions:


- Hear the latest trends in oncology coding and billing, navigate new regulations in 2017, and gain strategies to overcome reimbursement obstacles.
- Learn how to smoothly transition to new quality data reporting requirements

under the Merit-Based Incentive Program System (MIPS).

- Gain practical management how-to's for increasing efficiencies through the proper management of financial data.
- Hear strategies for the practical application of radiation oncology CPT codes in physician office and hospital settings.
- Gain insight to optimize insurance coverage by expanding access and eliminating barriers — helping to save money for your patients and program.

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Free to ACCC members; non-members are invited to join us at the low registration rate of \$69. Register today at accc-cancer.org/reimbursementmeeting. 

ACCC Welcomes its Newest Members

Grand Valley Oncology

Grand Junction, Colo.
Delegate Rep: Thomas Bui
Website: grandvalleyoncology.com

Hamilton Medical Center

Hamilton Cancer Institute
Dalton, Ga.
Delegate Rep: Jeff Heffelfinger,
D-MIN, FACHE
Website: hamiltonhealth.com

Memorial Hospital at Gulfport

Memorial Cancer Center
Gulfport, Miss.
Delegate Rep: Shelley Pringle, MS
Website: www.gulfportmemorial.com

University Hospitals Seidman Cancer Center

Cleveland, Ohio
Delegate Rep: Christine Kish
Website: uhhospitals.org

University of Toledo Medical Center

Eleanor N. Dana Cancer Center
Toledo, Ohio
Delegate Rep: Allen Seifert
Website: uthealth.utoledo.edu/centers/cancer

Are You Dense?

My journey to patient breast health advocacy

BY NANCY M. CAPPELLO, PHD



Nearly 13 years ago, I slipped through a significant and potentially fatal crack in our healthcare system when I was diagnosed with advanced stage breast cancer. Following in the footsteps of my mother's yearly regimen, I never missed my annual mammography exam; however, within weeks of my eleventh normal mammogram, during a routine clinical breast exam, my gynecologist felt a ridge in my right breast. A diagnostic ultrasound illuminated a large lesion, undetectable by mammography, and later determined to be an advanced Stage IIIC breast cancer with metastases to 13 lymph nodes.

A Matter of Density

My new-found team of physicians informed me—after I had to practically arm-wrestle them into explaining why years of mammograms had missed the cancer—that the culprit was my extremely dense breast tissue. This was the first time in a dozen years that I had heard those words. Worse, I learned that the medical community knew about the limitations of mammography for women with dense breasts.

Blindsided and frightened about my late-stage disease, I was outraged that this critical information was unknown to most women. I was also compelled to educate the

public about dense breast tissue—both its significant masking and independent cancer risk. My goal: to help reduce preventable advanced disease and, in turn, reduce mortality from breast cancer.

What the Research Revealed

Knowledge is power. To gain as much information as possible, I went to the literature. I was astonished to discover a decade of scientific studies prior to my diagnosis concluding that 40 percent of women have dense breast tissue and that there are other tests, such as ultrasound and MRI, when added to mammography, that can significantly detect early-stage and node-negative cancers invisible by mammography. Starting in the mid-70s research also concluded that having dense breast tissue is an independent risk factor for breast cancer. I also was confronted with the brutal fact that my advanced-stage breast cancer leaves me at greater risk of dying prematurely from breast cancer despite never missing an annual mammography exam.

After requesting copies of my health records, I discovered 11 mammography reports from the radiologist to my referring physician, that were different from the 11 letters I received. Reading through my records, I was first astonished and later incensed as, year after year, each of the reports contained a sentence that stated, *"Patient has extremely dense breast tissue, which could lower the sensitivity of the mammogram."* Since from the time of my first baseline mammogram at 35 years of age up until

weeks before my shocking diagnosis, the information about my dense breast tissue and its impact was known to my doctors, but not revealed to me—the patient with the dense breasts.

Advocating for Change

In 2008 I founded Are You Dense, Inc. (areyoudense.org) and later, in 2011, Are You Dense Advocacy, Inc. (areyoudenseadvocacy.org) with a mission to educate the public about the risks and screening challenges of dense breast tissue to prevent missed, delayed, and advanced-stage cancer, thus reducing mortality. Working tirelessly with advocates in my home state of Connecticut, I began to pursue equal access to an early breast cancer diagnosis for women with dense breast tissue through the state's legislative process. Faced with strong opposition from the Connecticut Society of Radiologists, it took five years for the first-in-the-nation density reporting law to pass in 2009. It was a great victory. Leveraging the accumulating science, our tireless grassroots movement helped make the state of Connecticut a pioneer and subsequent leader in density reporting and breast health.

Since that watershed moment, 31 states have enacted density reporting legislation to give women the same information their healthcare providers have about their dense breast tissue. We continue to work on a national standard, through federal legislation. A bi-partisan proposed federal bill was introduced in the last Congress in both the senate and house, and we are currently advocating for a reintroduction in this current



Congress. Across the globe, patient advocates, inspired by Connecticut's revolutionary legislative efforts, are exposing the impact of dense breast tissue in their respective countries, including Australia, Canada, Ireland, France, and the United Kingdom.

From Policy to Practice

Immediately upon enactment of the 2009 Connecticut density reporting law, breast radiologist Jean Weigert, MD, who had testified in opposition to the bill, began gathering data to investigate whether screening breast ultrasound improves breast cancer detection in women with dense breast tissue and a recent normal mammogram result. In 2017 she published her third research paper, "The Connecticut Experiment; The Third Installment: 4 Years of Screening Women with Dense Breasts with Bilateral Ultrasound" and shared these findings in a recent OnLive interview.

"I pulled data from my five offices for years one through four [of the study]. I tallied it up, compared it, and found—much to my surprise—we continued to find 3.2 additional cancers per thousand in this cohort of patients with breast tissue density greater than 50 percent."

Additionally, Dr. Weigert's study demonstrated significant progress in reducing the false positive rate of biopsy, often cited as a harm of routine ultrasound screening, where ultrasound now equals the acceptable biopsy rate for mammography.

One of Dr. Weigert's year-four patients with a recent normal mammogram is 48 years old and at average risk of breast cancer. Having dense breasts, the patient underwent a recommended adjunct ultrasound that uncovered a 1.5 cm, triple negative, grade 3, invasive ductal carcinoma with one macro metastasis. If this patient's cancer continued to be missed by mammography and detection was thus delayed, her aggressive cancer most likely would have progressed to a more advanced stage, with fewer treatment options and worse survival outcomes.

The promise of early detection for me and innumerable women with dense breast tissue is vital to surviving the disease. As we look towards potentially changing breast

cancer screening guidelines for women of average risk who have dense breast tissue, Dr. Weigert's Connecticut Experiment reveals that we can significantly improve breast cancer detection by reducing interval cancer and advanced disease.

Randomized controlled trials of mammography conclude that the magnitude of the reduction of advanced stage breast cancer is associated with the magnitude of the reduction of mortality. Dr. Weigert's retrospective study establishes a powerful role for ultrasound in filling in the cracks in breast cancer screening, creating an

opportunity for a reduction in advanced disease and an improvement in survival outcomes—the ultimate goal of any breast cancer screening program. **OI**

Nancy M. Cappello, PhD, is a cancer survivor, and founder and director of Are You Dense, Inc. and Are You Dense Advocacy, Inc.



Nancy M. Cappello, PhD, was honored by UNICO, the largest Italian-American service organization in the United States, with its Americanism-Civis Illustris Award for her outstanding work in communities in the U.S. and around the world. Pictured (L to R) UNICO National President Tom Vaughn, Nancy and Joe Cappello, Francine Nido, UNICO Secretary.

Governor Rell signing the Breast Density Bill into law on May 20, 2010. Pictured (L to R) Cheryl Cepelak and Anne Morris from the Susan G. Komen for the Cure, Connecticut Representative Steve Fontana, Governor M. Jodi Rell, Nancy Cappello, and Connecticut Senator Joseph Crisco.

Resources for Further Reading

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Xtandi[®] (enzalutamide) 40 mg capsules

XTANDI[®] (enzalutamide) capsules for oral use
Initial U.S. Approval: 2012

BRIEF SUMMARY OF PRESCRIBING INFORMATION

The following is a brief summary. Please see the package insert for full prescribing information.

INDICATIONS AND USAGE

XTANDI is indicated for the treatment of patients with metastatic castration-resistant prostate cancer (CRPC).

CONTRAINDICATIONS

Pregnancy

XTANDI can cause fetal harm and potential loss of pregnancy.

WARNINGS AND PRECAUTIONS

Seizure

Seizure occurred in 0.5% of patients receiving XTANDI in clinical studies. In these trials patients with predisposing factors for seizure were generally excluded. Seizure occurred from 31 to 603 days after initiation of XTANDI. Patients experiencing seizures were permanently discontinued from therapy and all seizure events resolved. In a single-arm trial designed to assess the risk of seizure in patients with pre-disposing factors for seizure, 8 of 366 (2.2%) XTANDI-treated patients experienced a seizure. Three of the 8 patients experienced a second seizure during continued treatment with XTANDI after their first seizure resolved. It is unknown whether anti-epileptic medications will prevent seizures with XTANDI. Patients in the study had one or more of the following pre-disposing factors: the use of medications that may lower the seizure threshold (~ 54%), history of traumatic brain or head injury (~ 28%), history of cerebrovascular accident or transient ischemic attack (~ 24%), and Alzheimer's disease, meningioma, or leptomeningeal disease from prostate cancer, unexplained loss of consciousness within the last 12 months, past history of seizure, presence of a space occupying lesion of the brain, history of arteriovenous malformation, or history of brain infection (all < 5%). Approximately 17% of patients had more than one risk factor.

Advise patients of the risk of developing a seizure while receiving XTANDI and of engaging in any activity where sudden loss of consciousness could cause serious harm to themselves or others.

Permanently discontinue XTANDI in patients who develop a seizure during treatment.

Posterior Reversible Encephalopathy Syndrome (PRES)

There have been reports of posterior reversible encephalopathy syndrome (PRES) in patients receiving XTANDI. PRES is a neurological disorder which can present with rapidly evolving symptoms including seizure, headache, lethargy, confusion, blindness, and other visual and neurological disturbances, with or without associated hypertension. A diagnosis of PRES requires confirmation by brain imaging, preferably magnetic resonance imaging (MRI). Discontinue XTANDI in patients who develop PRES.

ADVERSE REACTIONS

Clinical Trial Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Three randomized clinical trials enrolled patients with metastatic prostate cancer that has progressed on androgen deprivation therapy (GnRH therapy or bilateral orchiectomy), a disease setting that is also defined as metastatic CRPC. Two trials were placebo-controlled (Studies 1 and 2), and one trial was bicalutamide-controlled (Study 3). In Studies 1 and 2, patients received XTANDI 160 mg or placebo orally once daily. In Study 3, patients received XTANDI 160 mg or bicalutamide 50 mg orally once daily. All patients continued androgen deprivation therapy. Patients were allowed, but not required, to take glucocorticoids.

The most common adverse reactions (≥ 10%) that occurred more commonly (≥ 2% over placebo) in the XTANDI-treated patients from the two randomized placebo-controlled clinical trials were asthenia/fatigue, back pain, decreased appetite, constipation, arthralgia, diarrhea, hot flush, upper respiratory tract infection, peripheral edema, dyspnea, musculoskeletal pain, weight decreased, headache, hypertension, and dizziness/vertigo.

Study 1: XTANDI versus Placebo in Metastatic CRPC Following Chemotherapy

Study 1 enrolled 1199 patients with metastatic CRPC who had previously received docetaxel. The median duration of treatment was 8.3 months with XTANDI and 3.0 months with placebo. During the trial, 48% of patients on the XTANDI arm and 46% of patients on the placebo arm received glucocorticoids.

Grade 3 and higher adverse reactions were reported among 47% of XTANDI-treated patients and 53% of placebo-treated patients. Discontinuations due to adverse events were reported for 16% of XTANDI-treated patients and 18% of placebo-treated patients. The most common adverse reaction leading to treatment discontinuation was seizure, which occurred in 0.9% of the XTANDI-treated patients compared to none (0%) of the placebo-treated patients. Table 1 shows adverse reactions reported in Study 1 that occurred at a ≥ 2% higher frequency in the XTANDI arm compared to the placebo arm.

Table 1. Adverse Reactions in Study 1

	XTANDI N = 800		Placebo N = 399	
	Grade 1-4 ^a (%)	Grade 3-4 (%)	Grade 1-4 (%)	Grade 3-4 (%)
General Disorders				
Asthenic Conditions ^b	50.6	9.0	44.4	9.3
Peripheral Edema	15.4	1.0	13.3	0.8
Musculoskeletal And Connective Tissue Disorders				
Back Pain	26.4	5.3	24.3	4.0
Arthralgia	20.5	2.5	17.3	1.8
Musculoskeletal Pain	15.0	1.3	11.5	0.3
Muscular Weakness	9.8	1.5	6.8	1.8
Musculoskeletal Stiffness	2.6	0.3	0.3	0.0
Gastrointestinal Disorders				
Diarrhea	21.8	1.1	17.5	0.3
Vascular Disorders				
Hot Flush	20.3	0.0	10.3	0.0
Hypertension	6.4	2.1	2.8	1.3
Nervous System Disorders				
Headache	12.1	0.9	5.5	0.0
Dizziness ^c	9.5	0.5	7.5	0.5
Spinal Cord Compression and Cauda Equina Syndrome	7.4	6.6	4.5	3.8
Paresthesia	6.6	0.0	4.5	0.0
Mental Impairment Disorders ^d	4.3	0.3	1.8	0.0
Hypoesthesia	4.0	0.3	1.8	0.0
Infections And Infestations				
Upper Respiratory Tract Infection ^e	10.9	0.0	6.5	0.3
Lower Respiratory Tract And Lung Infection ^f	8.5	2.4	4.8	1.3
Psychiatric Disorders				
Insomnia	8.8	0.0	6.0	0.5
Anxiety	6.5	0.3	4.0	0.0
Renal And Urinary Disorders				
Hematuria	6.9	1.8	4.5	1.0
Pollakiuria	4.8	0.0	2.5	0.0
Injury, Poisoning And Procedural Complications				
Fall	4.6	0.3	1.3	0.0
Non-pathologic Fractures	4.0	1.4	0.8	0.3
Skin And Subcutaneous Tissue Disorders				
Pruritus	3.8	0.0	1.3	0.0
Dry Skin	3.5	0.0	1.3	0.0
Respiratory Disorders				
Epistaxis	3.3	0.1	1.3	0.3

a CTCAE v4.

b Includes asthenia and fatigue.

c Includes dizziness and vertigo.

d Includes amnesia, memory impairment, cognitive disorder, and disturbance in attention.

e Includes nasopharyngitis, upper respiratory tract infection, sinusitis, rhinitis, pharyngitis, and laryngitis.

f Includes pneumonia, lower respiratory tract infection, bronchitis, and lung infection.

Study 2: XTANDI versus Placebo in Chemotherapy-naïve Metastatic CRPC

Study 2 enrolled 1717 patients with metastatic CRPC who had not received prior cytotoxic chemotherapy, of whom 1715 received at least one dose of study drug. The median duration of treatment was 17.5 months with XTANDI and 4.6 months with placebo. Grade 3-4 adverse reactions were reported in 44% of XTANDI-treated patients and 37% of placebo-treated patients. Discontinuations due to adverse events were reported for 6% of XTANDI-treated patients and 6% of placebo-treated patients. The most common adverse reaction leading to treatment discontinuation was fatigue/asthenia, which occurred in 1% of patients on each treatment arm. Table 2 includes adverse reactions reported in Study 2 that occurred at a ≥ 2% higher frequency in the XTANDI arm compared to the placebo arm.

Table 2. Adverse Reactions in Study 2

	XTANDI N = 871		Placebo N = 844	
	Grade 1-4 ^a (%)	Grade 3-4 (%)	Grade 1-4 (%)	Grade 3-4 (%)
General Disorders				
Asthenic Conditions ^b	46.9	3.4	33.0	2.8
Peripheral Edema	11.5	0.2	8.2	0.4
Musculoskeletal And Connective Tissue Disorders				
Back Pain	28.6	2.5	22.4	3.0
Arthralgia	21.4	1.6	16.1	1.1
Gastrointestinal Disorders				
Constipation	23.2	0.7	17.3	0.4
Diarrhea	16.8	0.3	14.3	0.4
Vascular Disorders				
Hot Flush	18.0	0.1	7.8	0.0
Hypertension	14.2	7.2	4.1	2.3
Nervous System Disorders				
Dizziness ^c	11.3	0.3	7.1	0.0
Headache	11.0	0.2	7.0	0.4
Dysgeusia	7.6	0.1	3.7	0.0
Mental Impairment Disorders ^d	5.7	0.0	1.3	0.1
Restless Legs Syndrome	2.1	0.1	0.4	0.0
Respiratory Disorders				
Dyspnea ^e	11.0	0.6	8.5	0.6
Infections And Infestations				
Upper Respiratory Tract Infection ^f	16.4	0.0	10.5	0.0
Lower Respiratory Tract And Lung Infection ^g	7.9	1.5	4.7	1.1
Psychiatric Disorders				
Insomnia	8.2	0.1	5.7	0.0
Renal And Urinary Disorders				
Hematuria	8.8	1.3	5.8	1.3
Injury, Poisoning And Procedural Complications				
Fall	12.7	1.6	5.3	0.7
Non-Pathological Fracture	8.8	2.1	3.0	1.1
Metabolism and Nutrition Disorders				
Decreased Appetite	18.9	0.3	16.4	0.7
Investigations				
Weight Decreased	12.4	0.8	8.5	0.2
Reproductive System and Breast Disorders				
Gynecomastia	3.4	0.0	1.4	0.0

a CTCAE v4.

b Includes asthenia and fatigue.

c Includes dizziness and vertigo.

d Includes amnesia, memory impairment, cognitive disorder, and disturbance in attention.

e Includes dyspnea, exertional dyspnea, and dyspnea at rest.

f Includes nasopharyngitis, upper respiratory tract infection, sinusitis, rhinitis, pharyngitis, and laryngitis.

g Includes pneumonia, lower respiratory tract infection, bronchitis, and lung infection.

Study 3: XTANDI versus Bicalutamide in Chemotherapy-naïve Metastatic CRPC

Study 3 enrolled 375 patients with metastatic CRPC who had not received prior cytotoxic chemotherapy, of whom 372 received at least one dose of study drug. The median duration of treatment was 11.6 months with XTANDI

and 5.8 months with bicalutamide. Discontinuations with an adverse event as the primary reason were reported for 7.6% of XTANDI-treated patients and 6.3% of bicalutamide-treated patients. The most common adverse reactions leading to treatment discontinuation were back pain and pathological fracture, which occurred in 3.8% of XTANDI-treated patients for each event and in 2.1% and 1.6% of bicalutamide-treated patients, respectively. Table 3 shows overall and common adverse reactions ($\geq 10\%$) in XTANDI-treated patients.

Table 3. Adverse Reactions in Study 3

	XTANDI N = 183		Bicalutamide N = 189	
	Grade 1-4 ^a (%)	Grade 3-4 (%)	Grade 1-4 ^a (%)	Grade 3-4 (%)
Overall	94.0	38.8	94.2	37.6
General Disorders				
Asthenic Conditions ^b	31.7	1.6	22.8	1.1
Musculoskeletal And Connective Tissue Disorders				
Back Pain	19.1	2.7	18.0	1.6
Musculoskeletal Pain ^c	16.4	1.1	14.3	0.5
Vascular Disorders				
Hot Flush	14.8	0.0	11.1	0.0
Hypertension	14.2	7.1	7.4	4.2
Gastrointestinal Disorders				
Nausea	14.2	0.0	17.5	0.0
Constipation	12.6	1.1	13.2	0.5
Diarrhea	11.5	0.0	9.0	1.1
Infections And Infestations				
Upper Respiratory Tract Infection ^d	12.0	0.0	6.3	0.5
Investigational				
Weight Loss	10.9	0.5	7.9	0.5

a. CTCAE v 4.
b. Including asthenia and fatigue.
c. Including musculoskeletal pain and pain in extremity.
d. Including nasopharyngitis, upper respiratory tract infection, sinusitis, rhinitis, pharyngitis, and laryngitis.

Laboratory Abnormalities

In the two randomized placebo-controlled clinical trials, Grade 1-4 neutropenia occurred in 15% of patients treated with XTANDI (1% Grade 3-4) and in 6% of patients treated with placebo (0.5% Grade 3-4). The incidence of Grade 1-4 thrombocytopenia was 6% of patients treated with XTANDI (0.3% Grade 3-4) and 5% of patients treated with placebo (0.5% Grade 3-4). Grade 1-4 elevations in ALT occurred in 10% of patients treated with XTANDI (0.2% Grade 3-4) and 16% of patients treated with placebo (0.2% Grade 3-4). Grade 1-4 elevations in bilirubin occurred in 3% of patients treated with XTANDI (0.1% Grade 3-4) and 2% of patients treated with placebo (no Grade 3-4).

Infections

In Study 1, 1% of patients treated with XTANDI compared to 0.3% of patients treated with placebo died from infections or sepsis. In Study 2, 1 patient in each treatment group (0.1%) had an infection resulting in death.

Falls and Fall-related Injuries

In the two randomized placebo-controlled clinical trials, falls including fall-related injuries, occurred in 9% of patients treated with XTANDI compared to 4% of patients treated with placebo. Falls were not associated with loss of consciousness or seizure. Fall-related injuries were more severe in patients treated with XTANDI and included non-pathologic fractures, joint injuries, and hematomas.

Hypertension

In the two randomized placebo-controlled trials, hypertension was reported in 11% of patients receiving XTANDI and 4% of patients receiving placebo. No patients experienced hypertensive crisis. Medical history of hypertension was balanced between arms. Hypertension led to study discontinuation in < 1% of patients in each arm.

Post-Marketing Experience

The following additional adverse reactions have been identified during post approval use of XTANDI. Because these reactions were reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate the frequency or establish a causal relationship to drug exposure.

Body as a Whole: hypersensitivity (tongue edema, lip edema, and pharyngeal edema)

Gastrointestinal Disorders: vomiting

Neurological Disorders: posterior reversible encephalopathy syndrome (PRES)

Skin and Subcutaneous Tissue Disorders: rash

DRUG INTERACTIONS

Drugs that Inhibit CYP2C8

Co-administration of a strong CYP2C8 inhibitor (gemfibrozil) increased the composite area under the plasma concentration-time curve (AUC) of enzalutamide plus N-desmethyl enzalutamide by 2.2-fold. Co-administration of XTANDI with strong CYP2C8 inhibitors should be avoided if possible. If co-administration of XTANDI with a strong CYP2C8 inhibitor cannot be avoided, reduce the dose of XTANDI.

Drugs that Induce CYP3A4

Co-administration of rifampin (strong CYP3A4 inducer and moderate CYP2C8 inducer) decreased the composite AUC of enzalutamide plus N-desmethyl enzalutamide by 37%. Co-administration of strong CYP3A4 inducers (e.g., carbamazepine, phenobarbital, phenytoin, rifabutin, rifampin, rifapentine) with XTANDI should be avoided if possible. St John's wort may decrease enzalutamide exposure and should be avoided. If co-administration of a strong CYP3A4 inducer with XTANDI cannot be avoided, increase the dose of XTANDI.

Effect of XTANDI on Drug Metabolizing Enzymes

Enzalutamide is a strong CYP3A4 inducer and a moderate CYP2C9 and CYP2C19 inducer in humans. At steady state, XTANDI reduced the plasma exposure to midazolam (CYP3A4 substrate), warfarin (CYP2C9 substrate), and omeprazole (CYP2C19 substrate). Concomitant use of XTANDI with narrow therapeutic index drugs that are metabolized by CYP3A4 (e.g., alfentanil, cyclosporine, dihydroergotamine, ergotamine, fentanyl, pimozone, quinidine, sirolimus and tacrolimus), CYP2C9 (e.g., phenytoin, warfarin) and CYP2C19 (e.g., S-mephenytoin) should be avoided, as enzalutamide may decrease their exposure. If co-administration with warfarin cannot be avoided, conduct additional INR monitoring.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

XTANDI is contraindicated for use in pregnant women because the drug can cause fetal harm and potential loss of pregnancy. XTANDI is not indicated for use in females. There are no human data on the use of XTANDI in pregnant women. In animal reproduction studies, oral administration of enzalutamide in pregnant mice during organogenesis caused adverse developmental effects at doses lower than the maximum recommended human dose.

Animal Data

In an embryo-fetal developmental toxicity study in mice, enzalutamide caused developmental toxicity when administered at oral doses of 10 or 30 mg/kg/day throughout the period of organogenesis (gestational days 6-15). Findings included embryo-fetal lethality (increased post-implantation loss and resorptions) and decreased anogenital distance at ≥ 10 mg/kg/day, and cleft palate and absent palatine bone at 30 mg/kg/day. Doses of 30 mg/kg/day caused maternal toxicity. The doses tested in mice (1, 10 and 30 mg/kg/day) resulted in systemic exposures (AUC) approximately 0.04, 0.4 and 1.1 times, respectively, the exposures in patients. Enzalutamide did not cause developmental toxicity in rabbits when administered throughout the period of organogenesis (gestational days 6-18) at dose levels up to 10 mg/kg/day (approximately 0.4 times the exposures in patients based on AUC).

Lactation

Risk Summary

XTANDI is not indicated for use in females. There is no information available on the presence of XTANDI in human milk, the effects of the drug on the breastfed infant, or the effects of the drug on milk production. Enzalutamide and/or its metabolites were present in milk of lactating rats.

Females and Males of Reproductive Potential

Contraception

Males

Based on findings in animal reproduction studies, advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the final dose of XTANDI.

Infertility

Based on animal studies, XTANDI may impair fertility in males of reproductive potential.

Pediatric Use

Safety and effectiveness of XTANDI in pediatric patients have not been established.

Geriatric Use

Of 1671 patients who received XTANDI in the two randomized placebo-controlled clinical trials, 75% were 65 and over, while 31% were 75 and over. No overall differences in safety or effectiveness were observed between these patients and younger patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Patients with Renal Impairment

A dedicated renal impairment trial for XTANDI has not been conducted. Based on the population pharmacokinetic analysis using data from clinical trials in patients with metastatic CRPC and healthy volunteers, no significant difference in enzalutamide clearance was observed in patients with pre-existing mild to moderate renal impairment (30 mL/min \leq creatinine clearance [CrCl] \leq 89 mL/min) compared to patients and volunteers with baseline normal renal function (CrCl \geq 90 mL/min). No initial dosage adjustment is necessary for patients with mild to moderate renal impairment. Severe renal impairment (CrCl < 30 mL/min) and end-stage renal disease have not been assessed.

Patients with Hepatic Impairment

Dedicated hepatic impairment trials compared the composite systemic exposure of enzalutamide plus N-desmethyl enzalutamide in volunteers with baseline mild, moderate, or severe hepatic impairment (Child-Pugh Class A, B, or C, respectively) versus healthy controls with normal hepatic function. The composite AUC of enzalutamide plus N-desmethyl enzalutamide was similar in volunteers with mild, moderate, or severe baseline hepatic impairment compared to volunteers with normal hepatic function. No initial dosage adjustment is necessary for patients with baseline mild, moderate, or severe hepatic impairment.

OVERDOSAGE

In the event of an overdose, stop treatment with XTANDI and initiate general supportive measures taking into consideration the half-life of 5.8 days. In a dose escalation study, no seizures were reported at ≤ 240 mg daily, whereas 3 seizures were reported, 1 each at 360 mg, 480 mg, and 600 mg daily. Patients may be at increased risk of seizure following an overdose.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal studies have not been conducted to evaluate the carcinogenic potential of enzalutamide.

Enzalutamide did not induce mutations in the bacterial reverse mutation (Ames) assay and was not genotoxic in either the *in vitro* mouse lymphoma thymidine kinase (Tk) gene mutation assay or the *in vivo* mouse micronucleus assay.

Based on nonclinical findings in repeat-dose toxicology studies, which were consistent with the pharmacological activity of enzalutamide, male fertility may be impaired by treatment with XTANDI. In a 26-week study in rats, atrophy of the prostate and seminal vesicles was observed at ≥ 30 mg/kg/day (equal to the human exposure based on AUC). In 4-, 13-, and 39-week studies in dogs, hypospermatogenesis and atrophy of the prostate and epididymides were observed at ≥ 4 mg/kg/day (0.3 times the human exposure based on AUC).

Manufactured for and Distributed by: Astellas Pharma US, Inc., Northbrook, IL 60062

Marketed by:

Astellas Pharma US, Inc., Northbrook, IL 60062
Pfizer Inc., New York, NY 10017

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Rx Only

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076-2626-PM

Indication and Important Safety Information

Indication

XTANDI (enzalutamide) capsules is indicated for the treatment of patients with metastatic castration-resistant prostate cancer (CRPC).

Important Safety Information

Contraindications

XTANDI is not indicated for women. XTANDI can cause fetal harm and potential loss of pregnancy.

Warnings and Precautions

Seizure occurred in 0.5% of patients receiving XTANDI in clinical studies. In a study of patients with predisposing factors, seizures were reported in 2.2% of patients. See section 5.1 of the Prescribing Information for the list of predisposing factors. It is unknown whether anti-epileptic medications will prevent seizures with XTANDI. Permanently discontinue XTANDI in patients who develop a seizure during treatment.

Posterior Reversible Encephalopathy Syndrome (PRES)

In post approval use, there have been reports of PRES in patients receiving XTANDI. PRES is a neurological disorder which can present with rapidly evolving symptoms including seizure, headache, lethargy, confusion, blindness, and other visual and neurological disturbances, with or without associated hypertension. A diagnosis of PRES requires confirmation by brain imaging, preferably MRI. Discontinue XTANDI in patients who develop PRES.

Adverse Reactions

The most common adverse reactions ($\geq 10\%$) that occurred more commonly ($\geq 2\%$ over placebo) in the XTANDI patients from the two placebo-controlled clinical trials were asthenia/fatigue, back pain, decreased appetite, constipation, arthralgia, diarrhea, hot flush, upper respiratory tract infection, peripheral edema, dyspnea, musculoskeletal pain, weight decreased, headache, hypertension, and dizziness/vertigo. In the bicalutamide-controlled study of chemotherapy-naïve patients, the most common adverse reactions ($\geq 10\%$) reported in XTANDI patients were asthenia/fatigue, back pain, musculoskeletal pain, hot flush, hypertension, nausea, constipation, upper respiratory tract infection, diarrhea, and weight loss.

In the placebo-controlled study of patients taking XTANDI who previously received docetaxel, Grade 3 and higher adverse reactions were reported among 47% of XTANDI patients and 53% of placebo patients. Discontinuations due to adverse events were reported for 16% of XTANDI patients and 18% of placebo patients. In the placebo-controlled study of chemotherapy-naïve patients, Grade 3-4 adverse reactions were reported in 44% of XTANDI patients and 37% of placebo patients. Discontinuations due to adverse events were reported for 6% of both study groups. In the bicalutamide-controlled study of chemotherapy-naïve patients, Grade 3-4 adverse reactions were reported in 38.8% of XTANDI patients and 37.6% of bicalutamide patients. Discontinuations due to

adverse events were reported for 7.6% of XTANDI patients and 6.3% of bicalutamide patients.

Lab Abnormalities: In the two placebo-controlled trials, Grade 1-4 neutropenia occurred in 15% of XTANDI patients (1% Grade 3-4) and 6% of placebo patients (0.5% Grade 3-4). Grade 1-4 thrombocytopenia occurred in 6% of XTANDI patients (0.3% Grade 3-4) and 5% of placebo patients (0.5% Grade 3-4). Grade 1-4 elevations in ALT occurred in 10% of XTANDI patients (0.2% Grade 3-4) and 16% of placebo patients (0.2% Grade 3-4). Grade 1-4 elevations in bilirubin occurred in 3% of XTANDI patients (0.1% Grade 3-4) and 2% of placebo patients (no Grade 3-4).

Infections: In the study of patients taking XTANDI who previously received docetaxel, 1% of XTANDI patients compared to 0.3% of placebo patients died from infections or sepsis. In the study of chemotherapy-naïve patients, 1 patient in each treatment group (0.1%) had an infection resulting in death.

Falls (including fall-related injuries) occurred in 9% of XTANDI patients and 4% of placebo patients in the two placebo-controlled trials. Falls were not associated with loss of consciousness or seizure. Fall-related injuries were more severe in XTANDI patients, and included non-pathologic fractures, joint injuries, and hematomas.

Hypertension occurred in 11% of XTANDI patients and 4% of placebo patients in the two placebo-controlled trials. No patients experienced hypertensive crisis. Medical history of hypertension was balanced between arms. Hypertension led to study discontinuation in $< 1\%$ of patients in each arm.

Drug Interactions

Effect of Other Drugs on XTANDI Avoid strong CYP2C8 inhibitors, as they can increase the plasma exposure to XTANDI. If co-administration is necessary, reduce the dose of XTANDI.

Avoid strong CYP3A4 inducers as they can decrease the plasma exposure to XTANDI. If co-administration is necessary, increase the dose of XTANDI.

Effect of XTANDI on Other Drugs Avoid CYP3A4, CYP2C9, and CYP2C19 substrates with a narrow therapeutic index, as XTANDI may decrease the plasma exposures of these drugs. If XTANDI is co-administered with warfarin (CYP2C9 substrate), conduct additional INR monitoring.

Please see adjacent pages for Brief Summary of Full Prescribing Information.

References: 1. XTANDI [package insert]. Northbrook, IL: Astellas, Inc.

2. Shore ND, Chowdhury S, Villers A, et al. Efficacy and safety of enzalutamide versus bicalutamide for patients with metastatic prostate cancer (TERRAIN): a randomised, double-blind, phase 2 study. *Lancet Oncol* 2016;17(2):153-63. 3. Beer TM, Armstrong AJ, Rathkopf DE, et al., for the PREVAIL Investigators. Enzalutamide in metastatic prostate cancer before chemotherapy. *N Engl J Med* 2014;371(5):424-33.



Data vs bicalutamide

Median rPFS* was 19.5 months (95% CI, 11.8-NR) for patients receiving XTANDI + GnRH therapy† vs 13.4 months (95% CI, 8.2-16.4) for patients receiving bicalutamide + GnRH therapy† (HR = 0.60 [95% CI, 0.43-0.83])^{‡§1}

Upon progression on GnRH therapy† in mCRPC¹

START
Xtandi®

TO EXTEND SURVIVAL¹

23% reduction in risk of death with XTANDI + GnRH therapy vs placebo + GnRH therapy in PREVAIL^{1†1}

- Co-primary endpoint, OS: (HR = 0.77 [95% CI, 0.67-0.88])¹
- Median OS was 35.3 months (95% CI, 32.2-NR) with XTANDI vs 31.3 months (95% CI, 28.8-34.2) with placebo¹

Co-primary endpoint, rPFS*¹: (HR = 0.17 [95% CI, 0.14-0.21]; P < 0.0001)¹

CONVENIENT DOSING¹

Administer XTANDI as 160 mg (four 40 mg capsules) orally, once daily

Each capsule should be swallowed whole and should not be chewed, dissolved, or opened. If a patient experiences a ≥ Grade 3 toxicity or an intolerable side effect, withhold dosing for one week or until symptoms improve to ≤ Grade 2, then resume at the same or a reduced dose (120 mg or 80 mg), if warranted. For additional dosing information, see Drug Interactions and Full Prescribing Information.

Learn more about XTANDI at StartXtandi.com

Indication

XTANDI (enzalutamide) capsules is indicated for the treatment of patients with metastatic castration-resistant prostate cancer (CRPC).

Select Safety Information

XTANDI is not indicated for use in women. XTANDI can cause fetal harm and potential loss of pregnancy.

Seizure occurred in 0.5% of patients receiving XTANDI in clinical studies. In a study of patients with predisposing factors, seizures were reported in 2.2% of patients. See section 5.1 of the Prescribing Information for the list of predisposing factors. It is unknown whether anti-epileptic medications will prevent seizures with XTANDI. Permanently discontinue XTANDI in patients who develop a seizure during treatment.

There have been post approval reports of **posterior reversible encephalopathy syndrome (PRES)**, a neurological disorder which can present with rapidly evolving symptoms and requires confirmation by brain imaging. Discontinue XTANDI in patients who develop PRES.

CI, confidence interval; HR, hazard ratio; mCRPC, metastatic castration-resistant prostate cancer; NR, not reached; OS, overall survival; rPFS, radiographic progression-free survival. *Radiographic progression-free survival was defined as the time from randomization until first objective evidence of radiographic disease progression based on the assessments by Independent Central Review (ICR) or death, whichever occurred first.¹

[†]Or after bilateral orchiectomy.¹

[‡]As seen in the TERRAIN trial (Study 3): an additional trial in metastatic CRPC. TERRAIN was a multinational, double-blind, randomized trial that enrolled 375 patients and compared XTANDI + GnRH therapy, or after bilateral orchiectomy with bicalutamide + GnRH therapy, or after bilateral orchiectomy in patients who were asymptomatic or mildly symptomatic.^{1,2}

[§]Radiographic disease progression was assessed by ICR using the Prostate Cancer Clinical Trials Working Group 2 (PCWG2) criteria and/or Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 criteria for progression of soft tissue lesions.¹

^{||}As seen in the PREVAIL trial (Study 2): a multinational, double-blind, randomized, phase 3 trial that enrolled 1717 patients with metastatic CRPC who progressed on GnRH therapy, or after bilateral orchiectomy, and who had not received prior cytotoxic chemotherapy. All patients continued on GnRH therapy.^{1,3}

¹An updated survival analysis was conducted when 784 deaths were observed. The median follow-up time was 31 months. Results from this analysis were consistent with those from the prespecified interim analysis.¹

Please see reverse for Important Safety Information and for Brief Summary of Full Prescribing Information.

 **Xtandi**[®]
(enzalutamide)
40 mg capsules