ONCOLOGY ISSUES

The Journal of the Association of Community Cancer Centers
March | April 2015

A Model Symptom Management Clinic

Hits the target with improved patient satisfaction & reduced hospitalizations

GRANIX®
(TBO-FILGRASTIM)
Injection

Take a bite out of G-CSF acquisition costs

Based on wholesale acquisition cost (WAC) of all short-acting G-CSF products as of November 11, 2013. WAC represents published catalogue or list prices and may not represent actual transactional prices. Please contact your supplier for actual prices.

GRANIX® is an option in short-acting G-CSF therapy

- A 71% reduction in duration of severe neutropenia vs placebo (1.1 days vs 3.8 days, $p<0.0001$)[1]
  - Efficacy was evaluated in a multinational, multicenter, randomized, controlled, Phase III study of chemotherapy-naïve patients with high-risk breast cancer receiving doxorubicin (60 mg/m^2 IV bolus)/docetaxel (75 mg/m^2)[1]
- The safety of GRANIX was established in 3 Phase III trials, with 680 patients receiving chemotherapy for either breast cancer, lung cancer, or non-Hodgkin lymphoma (NHL)[1]
- Now offering a new presentation for self-administration

Indication

- GRANIX is a leukocyte growth factor indicated for reduction in the duration of severe neutropenia in patients with nonmyeloid malignancies receiving myelosuppressive anticancer drugs associated with a clinically significant incidence of febrile neutropenia.

Important Safety Information

- **Splenic rupture:** Splenic rupture, including fatal cases, can occur following the administration of human granulocyte colony-stimulating factors (hG-CSFs). Discontinue GRANIX and evaluate for an enlarged spleen or splenic rupture in patients who report upper abdominal or shoulder pain after receiving GRANIX.
- **Acute respiratory distress syndrome (ARDS):** ARDS can occur in patients receiving hG-CSFs. Evaluate patients who develop fever and lung infiltrates or respiratory distress after receiving GRANIX, for ARDS. Discontinue GRANIX in patients with ARDS.
- **Allergic reactions:** Serious allergic reactions, including anaphylaxis, can occur in patients receiving hG-CSFs. Reactions can occur on initial exposure. Permanently discontinue GRANIX in patients with serious allergic reactions. Do not administer GRANIX to patients with a history of serious allergic reactions to filgrastim or pegfilgrastim.
- **Use in patients with sickle cell disease:** Severe and sometimes fatal sickle cell crises can occur in patients with sickle cell disease receiving hG-CSFs. Consider the potential risks and benefits prior to the administration of GRANIX in patients with sickle cell disease. Discontinue GRANIX in patients undergoing a sickle cell crisis.
- **Capillary leak syndrome (CLS):** CLS can occur in patients receiving hG-CSFs and is characterized by hypotension, hypoalbuminemia, edema and hemoconcentration. Episodes vary in frequency, severity and may be life-threatening if treatment is delayed. Patients who develop symptoms of CLS should be closely monitored and receive standard symptomatic treatment, which may include a need for intensive care.
- **Potential for tumor growth stimulatory effects on malignant cells:** The granulocyte colony-stimulating factor (G-CSF) receptor, through which GRANIX acts, has been found on tumor cell lines. The possibility that GRANIX acts as a growth factor for any tumor type, including myeloid malignancies and myelodysplasia, diseases for which GRANIX is not approved, cannot be excluded.
- **Most common treatment-emergent adverse reaction:** The most common treatment-emergent adverse reaction that occurred in patients treated with GRANIX at the recommended dose with an incidence of at least 1% or greater and two times more frequent than in the placebo group was bone pain.

Please see brief summary of Full Prescribing Information on adjacent page.

For more information, visit GRANIXhcp.com.

Reference: 1. GRANIX® (tbo-filgrastim) Injection Prescribing Information. North Wales, PA: Teva Pharmaceuticals; 2014.

TEVA Oncology

GRANIX®
(TBO-FILGRASTIM)
Injection

BRIEF SUMMARY OF PRESCRIBING INFORMATION FOR
GRANIX® (tbo-filgrastim) injection, for subcutaneous use
SEE PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

GRANIX is indicated to reduce the duration of severe neutropenia in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Splenic Rupture

Splenic rupture, including fatal cases, can occur following administration of human granulocyte colony-stimulating factors. In patients who report upper abdominal or shoulder pain after receiving GRANIX, discontinue GRANIX and evaluate for an enlarged spleen or splenic rupture.

5.2 Acute Respiratory Distress Syndrome (ARDS)

Acute respiratory distress syndrome (ARDS) can occur in patients receiving human granulocyte colony-stimulating factors. Evaluate patients who develop fever and lung infiltrates or respiratory distress after receiving GRANIX, for ARDS. Discontinue GRANIX in patients with ARDS.

5.3 Allergic Reactions

Serious allergic reactions including anaphylaxis can occur in patients receiving human granulocyte colony-stimulating factors. Reactions can occur on initial exposure. The administration of antihistamines, steroids, bronchodilators, and/or epinephrine may reduce the severity of the reactions. Permanently discontinue GRANIX in patients with serious allergic reactions. Do not administer GRANIX to patients with a history of serious allergic reactions to filgrastim or pegfilgrastim.

5.4 Use in Patients with Sickle Cell Disease

Severe and sometimes fatal sickle cell crises can occur in patients with sickle cell disease receiving human granulocyte colony-stimulating factors. Consider the potential risks and benefits prior to the administration of human granulocyte colony-stimulating factors in patients with sickle cell disease. Discontinue GRANIX in patients undergoing a sickle cell crisis.

5.5 Capillary Leak Syndrome

Capillary leak syndrome (CLS) can occur in patients receiving human granulocyte colony-stimulating factors and is characterized by hypotension, hypoalbuminemia, edema and hemoconcentration. Episodes vary in frequency, severity and may be life-threatening if treatment is delayed. Patients who develop symptoms of capillary leak syndrome should be closely monitored and receive standard symptomatic treatment, which may include a need for intensive care.

5.6 Potential for Tumor Growth Stimulatory Effects on Malignant Cells

The granulocyte colony-stimulating factor (G-CSF) receptor through which GRANIX acts has been found on tumor cell lines. The possibility that GRANIX acts as a growth factor for any tumor type, including myeloid malignancies and myelodysplasia, diseases for which GRANIX is not approved, cannot be excluded.

6 ADVERSE REACTIONS

The following potential serious adverse reactions are discussed in greater detail in other sections of the labeling:

- Splenic Rupture [*see Warnings and Precautions (5.1)*]
- Acute Respiratory Distress Syndrome [*see Warnings and Precautions (5.2)*]
- Serious Allergic Reactions [*see Warnings and Precautions (5.3)*]
- Use in Patients with Sickle Cell Disease [*see Warnings and Precautions (5.4)*]
- Capillary Leak Syndrome *[see Warnings and Precautions (5.5)]*
- Potential for Tumor Growth Stimulatory Effects on Malignant Cells [*see Warnings and Precautions (5.6)*]

The most common treatment-emergent adverse reaction that occurred at an incidence of at least 1% or greater in patients treated with GRANIX at the recommended dose and was numerically two times more frequent than in the placebo group was bone pain.

6.1 Clinical Trials 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 clinical practice.

GRANIX clinical trials safety data are based upon the results of three randomized clinical trials in patients receiving myeloablative chemotherapy for breast cancer (N=348), lung cancer (N=240) and non-Hodgkin's lymphoma (N=92). In the breast cancer study, 99% of patients were female, the median age was 50 years, and 86% of patients were Caucasian. In the lung cancer study, 80% of patients were male, the median age was 58 years, and 95% of patients were Caucasian. In the non-Hodgkin's lymphoma study, 52% of patients were male, the median age was 55 years, and 88% of patients were Caucasian. In all three studies a placebo (Cycle 1 of the breast cancer study only) or a non-US-approved filgrastim product were used as controls. Both GRANIX and the non-US-approved filgrastim product were administered at 5 mcg/kg subcutaneously once daily beginning one day after chemotherapy for at least five days and continued to a maximum of 14 days or until an ANC of ≥10,000 x 10^6/L after nadir was reached.

Bone pain was the most frequent treatment-emergent adverse reaction that occurred in at least 1% or greater in patients treated with GRANIX at the recommended dose and was numerically two times more frequent than in the placebo group. The overall incidence of bone pain in Cycle 1 of treatment was 3.4% (3.4% GRANIX, 1.4% placebo, 7.5% non-US-approved filgrastim product).

Leukocytosis

In clinical studies, leukocytosis (WBC counts > 100,000 x 10^6/L) was observed in less than 1% patients with non-myeloid malignancies receiving GRANIX. No complications attributable to leukocytosis were reported in clinical studies.

Additional Adverse Reactions

Other adverse reactions known to occur following administration of human granulocyte colony-stimulating factors include myalgia, headache, vomiting, Sweet's syndrome (acute febrile neutrophilic dermatosis), cutaneous vasculitis and thrombocytopenia.

6.2 Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity. The incidence of antibody development in patients receiving GRANIX has not been adequately determined.

7 DRUG INTERACTIONS

No formal drug interaction studies between GRANIX and other drugs have been performed.

Drugs which may potentiate the release of neutrophils, such as lithium, should be used with caution.

Increased hematopoietic activity of the bone marrow in response to growth factor therapy has been associated with transient positive bone imaging changes. This should be considered when interpreting bone-imaging results.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C

Risk Summary

There are no adequate and well-controlled studies of GRANIX in pregnant women. In animal reproduction studies, treatment of pregnant rabbits with tbo-filgrastim resulted in increased spontaneous abortion and fetal malformations at systemic exposures substantially higher than the human exposure. GRANIX should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Animal Data

In an embryofetal developmental study, pregnant rabbits were administered subcutaneous doses of tbo-filgrastim during the period of organogenesis at 1, 10 and 100 mcg/kg/day. Increased abortions were evident in rabbits treated with tbo-filgrastim at 100 mcg/kg/day. This dose was maternally toxic as demonstrated by reduced body weight. Other embryofetal findings at this dose level consisted of post-implantation loss, decrease in mean live litter size and fetal weight, and fetal malformations such as malformed hindlimbs and cleft palate. The dose of 100 mcg/kg/day corresponds to a systemic exposure (AUC) of approximately 50-90 times the exposures observed in patients treated with the clinical tbo-filgrastim dose of 5 mcg/kg/day.

8.3 Nursing Mothers

It is not known whether tbo-filgrastim is secreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when GRANIX is administered to a nursing woman. Other recombinant G-CSF products are poorly secreted in breast milk and G-CSF is not orally absorbed by neonates.

8.4 Pediatric Use

The safety and effectiveness of GRANIX in pediatric patients have not been established.

8.5 Geriatric Use

Among 677 cancer patients enrolled in clinical trials of GRANIX, a total of 111 patients were 65 years of age and older. No overall differences in safety or effectiveness were observed between patients age 65 and older and younger patients.

8.6 Renal Impairment

The safety and efficacy of GRANIX have not been studied in patients with moderate or severe renal impairment. No dose adjustment is recommended for patients with mild renal impairment.

8.7 Hepatic Impairment

The safety and efficacy of GRANIX have not been studied in patients with hepatic impairment.

10 OVERDOSAGE

No case of overdose has been reported.

TEVA Oncology

Manufactured by:
Sicor Biotech UAB
Vilnius, Lithuania
U.S. License No. 1803

Distributed by:
Teva Pharmaceuticals USA, Inc.
North Wales, PA 19454

Product of Israel

GRX-40581 January 2015

This brief summary is based on TBO-004 GRANIX full Prescribing Information.

Oncology
MANAGEMENT
CONSULTING GROUP

- Financial and Market Analyses
- New Center Development
- Hospital/Physician Integration
- Strategic Planning
- Operational Assessments
- Revenue Cycle Reviews
- Implementation and Interim Leadership
- Performance and Financial Benchmarking

Relationships are built on many things…

Like having access to the best **oncology knowledge.**

Our clients value the credibility and insight offered by OMC Group specialists to help them succeed in a challenging environment.

With more than 13 years of experience assisting oncology organizations, Oncology Management Consulting Group is a leading provider of services to healthcare institutions of all types, from physician practices and small community hospitals to some of the most prominent health systems in the U.S.

OMC Group knows oncology… and our array of services will help you run your organization more efficiently.

To learn more about OMC Group and how we can assist you, please visit our website at www.oncologymgmt.com or call us at 215.766.1280

OMC Group
215-766-1280
www.oncologymgmt.com
solutions@oncologymgmt.com

Oncology
MANAGEMENT
CONSULTING GROUP

NHOBS

NATIONAL HOSPITAL ONCOLOGY BENCHMARK STUDY™
Comprehensive Oncology Knowledge for Hospitals and Health Systems

The 2nd Annual National Hospital Oncology Benchmark Study (NHOBS)™ is now available for purchase. Please visit **www.NHOBS.com.**

contents

Oncology Issues
March | April 2015
Vol. 30 | No. 2

DEPARTMENTS

ACCC
Association of Community Cancer Centers

ONCOLOGY ISSUES
The Journal of the
Association of Community Cancer Centers

Oncology Issues serves the multidisciplinary specialty of oncology care and cancer program management.

Archived editions of *Oncology Issues* are available to members at: www.accc-cancer.org

FROM THE EDITOR

ACCC—Your Innovation Station

BY CHRISTIAN DOWNS, JD, MHA

As I've written many times in my column, community oncology faces a number of delivery challenges. Our issues in medical oncology have been well documented, but we also face obstacles in surgical oncology, radiation oncology, pathology, imaging, diagnostics, and psychosocial support services.

And while reimbursement for services is an important issue for each of these areas—it is not the sole challenge. For example, prior to implementation of the Affordable Care Act, one of the greatest concerns facing the oncology community was the workforce shortage. The reimbursement environment aside, many were asking whether there would be enough providers to meet patient demand.

Another issue sometimes overlooked in favor of more immediate challenges is innovation. Cancer treatment and delivery is one of the fastest innovating (and evolving) areas of healthcare. At the same time, innovation is often expensive—due not only to high costs associated with researching and developing the innovation, but also with delivering that innovation to market or to a specific patient population.

In this edition of *Oncology Issues*, we look at a few "innovative" ways to deliver quality cancer care. Our goal: to support your adaptation of innovation in a manner that is meaningful and appropriate for your practice setting.

In our cover article, Anne Arundel Medical Center, Annapolis, Md., shares the care delivery challenges it faced after the purchase of a private oncology practice. Increased patient volume, introduction of a new EHR and chemotherapy ordering system, and a less than optimal workflow with infusion nurse triage functions in a separate location from the physician practice all combined to have a negative impact on quality care and patient satisfaction. This 2014 ACCC Innovator Award Winner took quick and decisive action, developing and implementing an evidence-based Symptom Management Clinic that improved patient satisfaction and reduced the number of ED visits and hospital admissions.

Next, *Oncology Issues*' editorial chair, Susan van der Sommen, MHA, CMPE, FACHE, shares how her program took innovation head-on in their effort to obtain Patient-Centered Specialty Practice (PCSP) recognition. Their hard work and effort paid off—practice efficiencies were achieved; cost-savings were realized in terms of reduced ER visits, hospital admissions, and hospital LOS; and new quality improvement (QI) initiatives were identified.

Another 2014 ACCC Innovator Award Winner, the Edward and Marie Matthews Center for Cancer Care, Plainsboro, N.J., took a novel (and cost-effective!) approach to implementing psychosocial distress screening (CoC Standard 3.2). Tasked with using existing resources and with help from another ACCC member program, a work-group developed a home-grown distress screening tool that was easily incorporated into daily routine—across an entire healthcare system.

In our last feature article, we take an even deeper dive into innovation. In his article "Patient-Specific Therapeutic Vaccines for Metastatic Melanoma," Robert Dillman, MD, discusses cutting-edge treatment options for patients with metastatic melanoma, including clinical trials using vaccines derived from autologous tumor cell lines. His article dovetails nicely with ACCC's newest education initiative, which is scheduled to launch this spring: ACCC's Institute for Clinical Immuno-oncology (ICLIO). Designed for community-based providers to better understand the innovation that is immuno-oncology and how this new treatment paradigm can be delivered in their practice settings, ICLIO will offer a number of exciting programs and tools, including a clinical scholars engagement program, monthly e-newsletters, a series of educational webinars, and a national education conference. So stay tuned! OI

PRESIDENT'S MESSAGE

Keep Moving Forward!

BY BECKY L. DEKAY, MBA

For Christmas, I was given a Fitbit Flex™ health and fitness tracker. I believe someone is sending me a message! But he's right—I need to get moving, eat better, and drink more water! This gift made me start thinking about how cancer care providers can use technology to help patients stay physically active (when possible) and, more importantly, keep track of their medications. So I did some research.

Most everyone has a cell phone these days; many of which are "smart phones." One way to put this technology to work for cancer patients is to ask them to take a picture of all of their medications and bring it with them to their next appointment. Our patients are doing this now and enjoy not having to lug around a paper or plastic bag filled with pills.

Then my thoughts turned to issues around oral chemotherapy. Since the introduction of oral agents, many providers have voiced concerns, such as: *How do we know how much of the drug was administered? Is the patient taking the correct dose? Is the patient taking the medication on time? Is the patient adhering to the treatment regimen? Is the patient taking "holidays" or breaks from the medication?*

My research turned up a number of apps, ranging from free to those with a one-time charge between $1 and $3, including Pill Alert, Pill Pro, Med Reminder, Med Helper, Pill Control, and Pill Manager. Many apps include alarms that can be used to "remind" patients when it is time to take their medication. There is also a start-up company that has developed a wireless pill bottle that alerts patients when they have to take their meds and keeps track of their usage and dosage; however, this technology is on the pricey side and distribution is in question. I'd love to hear if anyone is using this type of technology in their program as I'd like to implement something similar for our patients. And, of course, ACCC has just released its mobile resource, Oral Therapies—A Patient-Centered Approach, to help cancer care teams assess and support their patients with oral adherence, including identifying areas where additional education and support may be needed.

Next, I thought about fitness from the patient perspective. While hundreds of apps are available, I focused on free ones, such as Walk the Walk, Walk-Pedometer Step Counter, Walkspree Inspire, Bike and Walk, Bike Free, Bike Coach, etc. Other apps can help cancer patients track their weight or participate in yoga, meditation, or Pilates. Again, patients can use alarm features on these apps to remind them when it's time to exercise or meditate.

I am not promoting one specific application over another and only listed the ones above because they are free. Instead, I am suggesting that providers begin to investigate ways to use technology that is readily available to help our patients participate more fully in their care, including guiding our patients in the appropriate and safe use of technology.

In my short time using Fitbit, I've found myself more motivated and willing to try and reach my daily goals. Now, will these types of tools, apps, and programs encourage our patients? I don't know, but I think it's worth a try!

Before I close out my last "President's Message," I'd like to thank you all for giving me the opportunity to serve you as ACCC President. To me, there is nothing more inspiring than working and networking with others who share my passion for improving the care and quality for cancer patients. In 2003 Dr. Andrew von Eschenbach, then director of the National Cancer Institute, issued a challenge goal of eliminating death and suffering from cancer by 2015. Obviously, we did not meet that challenge—but not for lack of trying! New and improved treatments and cures are available and great strides have been made. But your passion continues to be critical in the War on Cancer. Persevere, and together we will triumph! OI

Coming in Your 2015 *ONCOLOGY ISSUES*

- The Journey to Cultural Competence
- Cancer Clinical Trials: Enhancing Infrastructure & Accrual
- Closing the Gap: An Outpatient Nutrition Clinic
- Capturing Quality Data to Improve Palliative Care
- An Innovative Patient Companion Program
- Closing the Loop with a Post-Biopsy Breast Clinic
- Implementing Oncology Inpatient Bedside Scheduling
- A Patient Tracking System Helps Transition Patients to a Multidisciplinary Nurse Care Model
- An Oncology Nurse Navigator-Led Psychosocial Program
- The Cancer Care Collaborative—Where Patients are An Active Member of the Cancer Care Team
- Developing & Implementing a Patient Advisory Council
- A Behavioral Oncology Program to Support Medically Complex Patients
- Cancer Prehabilitation: A Growing Field

more online @
www.accc-cancer.org

fast

TOOL

Oral Therapies—A Patient-Centered Approach

ACCC's new tool aims to help providers identify patients needing additional education and support resources before starting oral chemotherapy. Available at www.accc-oralchemo.org.

PROFILE

Put a Spotlight on Your Cancer Program

Each *Oncology Issues* features a two-page article "spotlighting" the services, achievements, and accomplishments of an ACCC member program or practice. These articles offer great exposure for your program, including the opportunity to let your referring providers and patients know about your services and staff. Has your cancer program been profiled? Contact: jkornak@accc-cancer.org to schedule an interview today.

VIDEO

Financial Advocacy Network

This "one-stop" destination for comprehensive financial advocacy information offers online training materials and videos, practical tools, peer-to-peer networking, and more. Plus, free Financial Advocacy Regional Meetings. Register at: www.accc-cancer.org/FinancialAdvocacy.

MEETING

ACCC's Oncology Reimbursement Meetings

Review the specifics of documentation, coding, and billing for infusion services and radiation oncology. Hear an update on how providers are working with new payment models. Learn important data points for your cancer program's financial health. Register for this free meeting at: www.accc-cancer.org/ReimbursementMeeting.

OIG Expects to Recover $4.9 Billion in Improper Payments in FY 2014

Source. OIG. Semi-Annual Report to Congress: April 1-Sept. 30, 2014. http://oig.hhs.gov/reports-and-publications/archives/semiannual/2014/sar-fall2014.pdf.

Collectively, Pioneer ACOs Saved the Medicare Trust Fund about $41 Million in 2013

Source. BNA Healthcare Daily Report, Oct. 9. 2014.

3 Trends to Impact the Healthcare Industry in 2015

1. The Next-Generation Sequencer hitting the clinical market. Sequencing is used to understand cancer generally, but in the future expect it to be part of cancer testing strategies for specific patients.

2. Interest in patient monitoring solutions and telemedicine. Aging Baby Boomers will require solutions outside the hospital, driving hospitals and physicians to treat patients at home.

3. Demand for biopharmaceutical production. The biopharmaceutical production market demonstrated 11% revenue growth and reached $41 billion in 2014.

Source. www.marketresearch.com. "Projected 2015 Trends in Healthcare." Read more at: http://hubs.ly/yorrslo.

Oncology Issues is published bimonthly at the Association of Community Cancer Centers, 11600 Nebel St., Suite 201, Rockville, MD 20852. Editorial correspondence, changes of address, manuscripts, and letters to the editor should be addressed to: Managing Editor, Oncology Issues, 11600 Nebel St., Suite 201, Rockville, MD 20852-2557. Author's instructions available at www.accc-cancer.org.

Articles, editorials, letters to the editor, and other contributed materials represent the opinions of the authors and do not represent the opinions of the Association of Community Cancer Centers or the institution with which the author is affiliated unless the contrary is specified.

Basic rate: $55 per year for healthcare providers, plus $4.99 for shipping. ACCC membership dues pay for general, delegate, and chapter member subscriptions. Back issues available for $12.50 per copy, prepaid. Bulk rates available upon request.

Send correspondence, display advertising, insertion orders, printing materials to Mal Milburn, Oncology Issues, 11600 Nebel St., Suite 201, Rockville, MD 20852. Questions for general information may be directed to 301-984-5704.

Please send address changes to Association of Community Cancer Centers, 11600 Nebel St., Suite 201, Rockville, MD 20852.

facts

Help Put "Personal" Back into Personalized Cancer Care

Choosing a cancer treatment team is personal. The top three criteria for patients and caregivers when choosing a treatment facility are timely information (**91%**), a care team willing to answer questions (**90%**), and involving patients and caregivers fully in treatment decisions (**87%**).

While men and women face similar cancer journeys, they are driven by different needs. Women are more motivated by the support of family and friends to get well (**56%** women vs. **46%** men), while men are more motivated by their desire to live a healthy life and resume daily activities (**43%** men vs. **36%** women).

Building cultural connections will help improve the cancer patient experience. **79%** of African-American patients say they are driven by their faith and spirituality; **84%** of Hispanic patients say they are driven by family responsibilities and support; **74%** of Caucasian patients say they are driven by their desire to live a healthy life and perform daily activities.

Cancer patients may get lost trying to translate common healthcare terminology. More than **1/3** of cancer patients state they don't understand or have never heard of terms like genomic testing, integrative cancer care, precision cancer care, and survivorship.

Source. The Cancer Experience: A National Study of Patients and Caregivers. www.cancercenter.com/press-center/press-releases/2013/03/one-in-four-dissatisfied-with-cancer-care/~/media/FA8070C-77DA84401BB9950023D4BDD76.ashx.

The ABCs of Diffusing Angry Patients

Acknowledge the anger

Be benevolent

Curtail confrontation

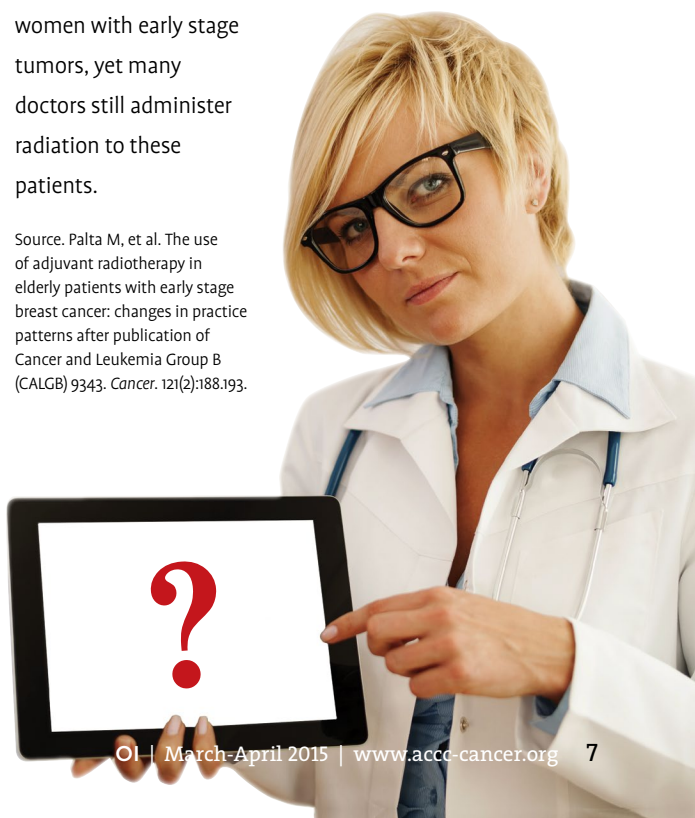
Don't forget to document

Source. Weber S. Diffusing Angry Patients: It's as Simple as ABCD. www.physicianspractice.com.

Are Elderly Women with Early Stage Breast Cancer Being Over-Treated?

While clinical trial data support omitting radiation treatments in elderly women with early stage breast cancer, nearly **2/3** of these women continue to receive it. A 2004 clinical trial showed that adding radiation therapy to surgery plus tamoxifen does not reduce 5-year recurrence rates or prolong survival in elderly women with early stage tumors, yet many doctors still administer radiation to these patients.

Source. Palta M, et al. The use of adjuvant radiotherapy in elderly patients with early stage breast cancer: changes in practice patterns after publication of Cancer and Leukemia Group B (CALGB) 9343. *Cancer*. 121(2):188.193.



From Volume to Value

BY LEAH RALPH

Shifting our healthcare system from payment based on "volume" to one based on "value" has become a familiar and frequent adage among policymakers in recent years. In an effort to rein in costs, there's been a renewed focus on moving our current reimbursement system from one that incentivizes quantity of services to one that encourages better coordinated, quality care. We've seen this trend crop up in every major healthcare law in recent years—from the Medicare Modernization Act (MMA) in 2003 to the Affordable Care Act (ACA) in 2010. The ACA created the $10 billion Center for Medicare and Medicaid Innovation (CMMI), whose sole purpose is to develop and test innovative ways to pay providers. Even last year's bipartisan, bicameral sustainable growth rate (SGR) legislation—our biggest hope for a long-term SGR fix—ultimately tied payment updates to participation in some form of alternative payment arrangement.

In January, the U.S. Department of Health and Human Services (HHS) effectively upped the ante. For the first time in Medicare's history, the agency announced explicit goals for tying Medicare payments to alternative payment models and value-based payments. According to HHS, by 2016, 30 percent of all fee-for-service (FFS) Medicare payments will be tied to alternative payment models—including, but not limited to, Accountable Care Organizations (ACOs), medical homes, and bundled payments for episodes of care. By 2018, 50 percent of payments will be tied to these models. The agency also set a goal of tying 85 percent of traditional Medicare payments to quality or value by 2016 and 90 percent by 2018 through such programs as the Hospital Value-Based Purchasing or Hospital Readmissions Reduction programs.

Notably, the first benchmark is next year—a laudable, but ambitious, goal. Certainly the announcement signals the Obama Administration is making this issue a priority, and we can expect to see an accelerated push to transition Medicare payments and, in turn, private payers.

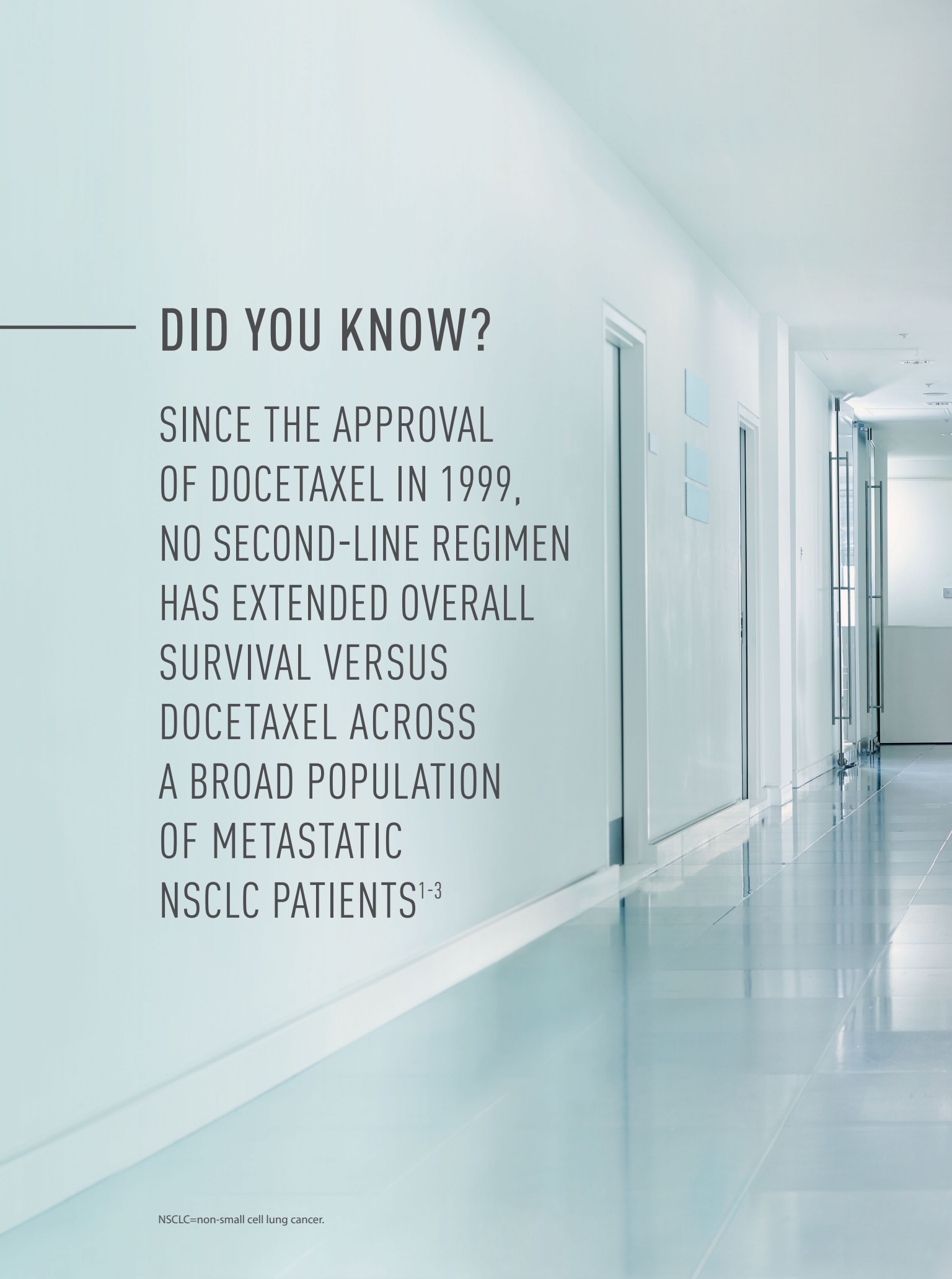
But this shift is a huge undertaking that will not only affect payments, but also fundamentally change incentives for how providers deliver care. Implementation will take time, and requires the right balance of forward momentum and important safeguards to ensure that patients continue to receive the most appropriate, quality care. As HHS moves full steam ahead, the provider community should urge policymakers to continue to work to find consensus on appropriate quality measures; establish a sound, fair methodology for calculating financial benchmarks and risk adjustment; and allow providers the time, resources, and flexibility they need to implement these new payment models.

Unlike primary care, specialists will face unique challenges in how to fit into these new models. The Centers for Medicare & Medicaid Services (CMS) has placed a particular focus on oncology, funding a major community oncology medical home initiative, the COME HOME project in 2012, and the recently released Oncology Care Model (OCM) that will test the bundling of payments for chemotherapy administration. But with other models, such as the Medicare Shared Savings Program (Medicare ACOs) that are primary care focused, it's still unclear how oncologists will be included or even participate. Caring for cancer patients is complex and often expensive, leaving inherent challenges in how to account for cancer care in alternative models. How will high-cost drugs and innovative therapies be treated in the construct of an ACO? Would high-cost cancer patients be included in the financial benchmark? What is oncology's role in shared risk and savings? ACCC and other organizations continue to work with CMS to answer these questions.

While it's still unclear how successful some of these new payment models will be, it is almost certain that components of these models will be reflected in any future, more permanent payment reform. We urge the provider community to remain active participants in the dialogue to ensure that we do, in fact, achieve meaningful, realistic payment reform in Medicare and beyond.

One way to actively engage is by becoming more involved with ACCC. If you are interested in serving on a committee, attending one of our Oncology Reimbursement Meetings, or becoming more involved in advocacy, please contact me at: lralph@accc-cancer.org. OI

Leah Ralph is ACCC's manager of provider economics & public policy.



DID YOU KNOW?

SINCE THE APPROVAL OF DOCETAXEL IN 1999, NO SECOND-LINE REGIMEN HAS EXTENDED OVERALL SURVIVAL VERSUS DOCETAXEL ACROSS A BROAD POPULATION OF METASTATIC NSCLC PATIENTS[1-3]

NSCLC=non-small cell lung cancer.

NEW FDA APPROVAL

CYRAMZA® (ramucirumab), in combination with docetaxel, is indicated for the treatment of patients with metastatic NSCLC with disease progression on or after platinum-based chemotherapy. Patients with epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving CYRAMZA.

ADVANCING THE SECOND-LINE TREATMENT OF METASTATIC NSCLC[4]

CYRAMZA is the first antiangiogenic agent FDA approved in combination with docetaxel for the second-line treatment of metastatic NSCLC, including nonsquamous and squamous histologies.[4]

CYRAMZA™
ramucirumab injection
10 mg/mL solution

TAKE ACTION

IMPORTANT SAFETY INFORMATION FOR CYRAMZA

WARNING: HEMORRHAGE
CYRAMZA increased the risk of hemorrhage, including severe and sometimes fatal hemorrhagic events. Permanently discontinue CYRAMZA in patients who experience severe bleeding.

Warnings and Precautions

Hemorrhage
- CYRAMZA increased the risk of hemorrhage and gastrointestinal hemorrhage, including severe and sometimes fatal hemorrhagic events. In Study 3, which evaluated CYRAMZA plus docetaxel in metastatic non-small cell lung cancer (NSCLC), the incidence of severe bleeding was 2.4% for CYRAMZA plus docetaxel and 2.3% for placebo plus docetaxel. Patients with NSCLC receiving therapeutic anticoagulation or chronic therapy with NSAIDs or other antiplatelet therapy other than once-daily aspirin or with radiographic evidence of major airway or blood vessel invasion or intratumor cavitation were excluded from Study 3; therefore, the risk of pulmonary hemorrhage in these groups of patients is unknown. Permanently discontinue CYRAMZA in patients who experience severe bleeding.

Arterial Thromboembolic Events
- Serious, sometimes fatal, arterial thromboembolic events (ATEs) including myocardial infarction, cardiac arrest, cerebrovascular accident, and cerebral ischemia occurred in clinical trials including 1.7% of 236 patients who received CYRAMZA as a single agent for gastric cancer in Study 1. Permanently discontinue CYRAMZA in patients who experience a severe ATE.

Hypertension
- An increased incidence of severe hypertension occurred in patients receiving CYRAMZA plus docetaxel (6%) as compared to placebo plus docetaxel (2%). Control hypertension prior to initiating treatment with CYRAMZA. Monitor blood pressure every 2 weeks or more frequently as indicated during treatment. Temporarily suspend CYRAMZA for severe hypertension until medically controlled. Permanently discontinue CYRAMZA if medically significant hypertension cannot be controlled with antihypertensive therapy or in patients with hypertensive crisis or hypertensive encephalopathy.

Infusion-Related Reactions
- Prior to the institution of premedication recommendations across clinical trials of CYRAMZA, infusion-related reactions (IRRs) occurred in 6 out of 37 patients (16%), including 2 severe events. The majority of IRRs across trials occurred during or following a first or second CYRAMZA infusion. Symptoms of IRRs included rigors/tremors, back pain/spasms, chest pain and/or tightness, chills, flushing, dyspnea, wheezing, hypoxia, and paresthesia. In severe cases, symptoms included bronchospasm, supraventricular tachycardia, and hypotension. Monitor patients during the infusion for signs and symptoms of IRRs in a setting with available resuscitation equipment. Immediately and permanently discontinue CYRAMZA for Grade 3 or 4 IRRs.

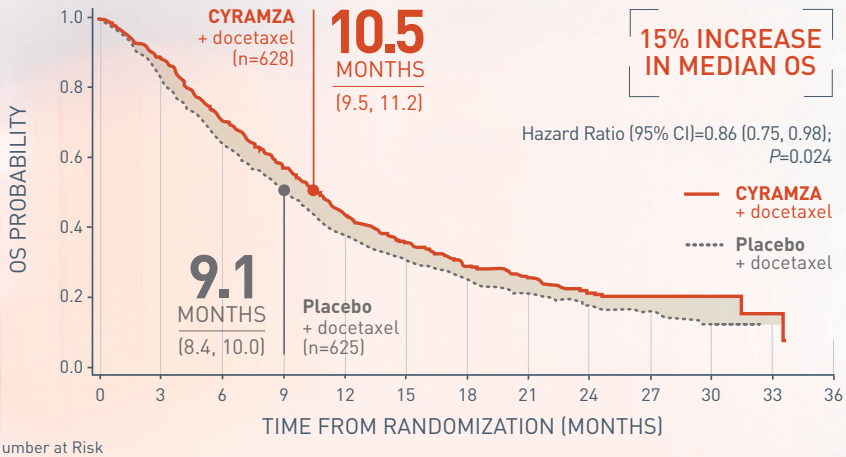
Gastrointestinal Perforations
- CYRAMZA is an antiangiogenic therapy that can increase the risk of gastrointestinal perforation, a potentially fatal event. In Study 3, the incidence of gastrointestinal perforation was 1% for CYRAMZA plus docetaxel versus 0.3% for placebo plus docetaxel. Permanently discontinue CYRAMZA in patients who experience a gastrointestinal perforation.

Impaired Wound Healing
- CYRAMZA has not been studied in patients with serious or nonhealing wounds. CYRAMZA is an antiangiogenic therapy with the potential to adversely affect wound healing. Withhold CYRAMZA prior to surgery. Resume CYRAMZA following the surgical intervention based on clinical judgment of adequate wound healing. If a patient develops wound healing complications during therapy, discontinue CYRAMZA until the wound is fully healed.

Clinical Deterioration in Child-Pugh B or C Cirrhosis
- Clinical deterioration, manifested by new onset or worsening encephalopathy, ascites, or hepatorenal syndrome, was reported in patients with Child-Pugh B or C cirrhosis who received single-agent CYRAMZA. Use CYRAMZA in patients with Child-Pugh B or C cirrhosis only if the potential benefits of treatment are judged to outweigh the risks of clinical deterioration.

CYRAMZA PLUS DOCETAXEL DEMONSTRATED A STATISTICALLY SIGNIFICANT IMPROVEMENT IN OVERALL SURVIVAL VS DOCETAXEL[4]

OVERALL SURVIVAL: MEDIAN - MONTHS (95% CI)



MAJOR OUTCOME MEASURE

15% INCREASE IN MEDIAN OS

Hazard Ratio (95% CI)=0.86 (0.75, 0.98); *P*=0.024

CYRAMZA + docetaxel

Placebo + docetaxel

Number at Risk

CYRAMZA + docetaxel	628	527	415	329	231	156	103	70	45	23	11	2	0
Placebo + docetaxel	625	501	386	306	197	129	86	56	36	23	9	0	0

- The percentage of deaths at the time of analysis was 68% (428 patients) and 73% (456 patients) in the CYRAMZA plus docetaxel and placebo plus docetaxel arms, respectively[4]

Demonstrated improvements across all three efficacy outcomes (OS, PFS, ORR)[4]

- **Median PFS** with CYRAMZA plus docetaxel was 4.5 months (95% CI: 4.2, 5.4) vs 3.0 months (95% CI: 2.8, 3.9) with placebo plus docetaxel (hazard ratio 0.76 [95% CI: 0.68, 0.86]; *P*<0.001)
  - The percentage of events at the time of analysis was 89% (558 patients) and 93% (583 patients) in the CYRAMZA plus docetaxel and placebo plus docetaxel arms, respectively
- **ORR** with CYRAMZA plus docetaxel was 23% (95% CI: 20, 26) vs 14% (95% CI: 11, 17) with placebo plus docetaxel (*P*<0.001)*

CI=confidence interval; OS=overall survival; PFS=progression-free survival; ORR=objective response rate.

*ITT population. Disease progression and tumor response were assessed by investigators in accordance with Response Evaluation Criteria in Solid Tumors (RECIST) 1.1.[5] ORR is defined as complete plus partial response.

REVEL TRIAL DESIGN (N=1253)

The phase III REVEL trial evaluated the efficacy and safety of CYRAMZA plus docetaxel vs placebo plus docetaxel in patients with metastatic NSCLC with disease progression on or after platinum-based chemotherapy. Major efficacy outcome measure was OS. Supportive efficacy outcome measures were PFS and ORR. All patients were required to have Eastern Cooperative Oncology Group performance status 0 or 1. Patients were randomized 1:1 (N=1253) to receive either CYRAMZA 10 mg/kg or placebo, in combination with docetaxel at 75 mg/m^2 every 21 days.[4]

VISIT www.CYRAMZAHCP.com

Reversible Posterior Leukoencephalopathy Syndrome (RPLS)

- RPLS has been reported at a rate of <0.1% in clinical studies with CYRAMZA. Confirm the diagnosis of RPLS with MRI and discontinue CYRAMZA in patients who develop RPLS. Symptoms may resolve or improve within days, although some patients with RPLS can experience ongoing neurologic sequelae or death.

Most Common Adverse Reactions

- The most commonly reported adverse reactions (all grades; Grade 3/4) occurring in ≥5% of patients receiving CYRAMZA plus docetaxel and ≥2% higher than placebo plus docetaxel in Study 3 were neutropenia (55% vs 46%; 49% vs 40%), fatigue/asthenia (55% vs 50%; 14% vs 11%), stomatitis/mucosal inflammation (37% vs 19%; 7% vs 2%), epistaxis (19% vs 7%; <1% vs <1%), febrile neutropenia (16% vs 10%; 16% vs 10%), peripheral edema (16% vs 9%; 0% vs <1%), thrombocytopenia (13% vs 5%; 3% vs <1%), lacrimation increased (13% vs 5%; <1% vs 0%), and hypertension (11% vs 5%; 6% vs 2%).
- The most common serious adverse events with CYRAMZA plus docetaxel in Study 3 were febrile neutropenia (14%), pneumonia (6%), and neutropenia (5%). The use of granulocyte colony-stimulating factors was 42% in CYRAMZA plus docetaxel-treated patients versus 37% in patients who received placebo plus docetaxel.
- Treatment discontinuation due to adverse reactions occurred more frequently in CYRAMZA plus docetaxel-treated patients (9%) than in placebo plus docetaxel-treated patients (5%). The most common adverse events leading to treatment discontinuation of CYRAMZA were infusion-related reaction (0.5%) and epistaxis (0.3%).
- Clinically relevant adverse reactions reported in ≥1% and <5% of CYRAMZA plus docetaxel-treated patients in Study 3 were hyponatremia (4.8% CYRAMZA plus docetaxel versus 2.4% for placebo plus docetaxel) and proteinuria (3.3% CYRAMZA plus docetaxel versus 0.8% placebo plus docetaxel).

Drug Interactions

- No pharmacokinetic interactions were observed between ramucirumab and docetaxel.

Use in Specific Populations

- Pregnancy Category C: Based on its mechanism of action, CYRAMZA may cause fetal harm. Advise females of reproductive potential to avoid getting pregnant, including use of adequate contraception, while receiving CYRAMZA and for at least 3 months after the last dose of CYRAMZA. Animal models link angiogenesis, VEGF and VEGF Receptor 2 to critical aspects of female reproduction, embryofetal development, and postnatal development. There are no adequate or well-controlled studies of ramucirumab in pregnant women. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, apprise the patient of the potential hazard to a fetus.
- Nursing Mothers: It is recommended to discontinue nursing or discontinue CYRAMZA due to the potential risks to the nursing infant.
- Females of Reproductive Potential: Advise females of reproductive potential that CYRAMZA may impair fertility.

Please see Brief Summary of Prescribing Information for CYRAMZA, including Boxed Warning for hemorrhage, on the next page.

RB-L HCP ISI 17DEC2014

References: 1. Reck M, Kaiser R, Mellemgaard A, et al. Docetaxel plus nintedanib versus docetaxel plus placebo in patients with previously treated non-small-cell lung cancer (LUME-Lung 1): a phase 3, double-blind, randomized controlled trial. *Lancet Oncol*. 2014;15:143-155. **2.** Supplement to: Reck M, Kaiser R, Mellemgaard A, et al. Docetaxel plus nintedanib versus docetaxel plus placebo in patients with previously treated non-small-cell lung cancer (LUME-Lung 1): a phase 3, double-blind, randomized controlled trial. *Lancet Oncol*. 2014;15:143-155. **3.** National Cancer Institute. Cancer drug information. FDA approval for docetaxel. http://www.cancer.gov/cancertopics/druginfo/fda-docetaxel/print. Accessed August 26, 2014. **4.** CYRAMZA (ramucirumab) [package insert]. Indianapolis, IN: Eli Lilly and Company; 2014. **5.** Garon EB, Ciuleanu T-E, Arrieta O, et al. Ramucirumab plus docetaxel versus placebo plus docetaxel for second-line treatment of stage IV non-small-cell lung cancer after disease progression on platinum-based therapy (REVEL): a multicentre, double-blind, randomised phase 3 trial. *Lancet*. 2014;384(9944):665-673.

Lilly

CYRAMZA® (ramucirumab) injection

BRIEF SUMMARY: For complete safety, please consult the full Prescribing Information.

WARNING: HEMORRHAGE

CYRAMZA increased the risk of hemorrhage, including severe and sometimes fatal hemorrhagic events. Permanently discontinue CYRAMZA in patients who experience severe bleeding.

INDICATIONS AND USAGE

Non-Small Cell Lung Cancer:

CYRAMZA, in combination with docetaxel, is indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with disease progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving CYRAMZA.

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

Hemorrhage

CYRAMZA increased the risk of hemorrhage and gastrointestinal hemorrhage, including severe and sometimes fatal hemorrhagic events. In Study 1, the incidence of severe bleeding was 3.4% for CYRAMZA and 2.6% for placebo. In Study 2, the incidence of severe bleeding was 4.3% for CYRAMZA plus paclitaxel and 2.4% for placebo plus paclitaxel. Patients with gastric cancer receiving nonsteroidal anti-inflammatory drugs (NSAIDs) were excluded from enrollment in Studies 1 and 2; therefore, the risk of gastric hemorrhage in CYRAMZA-treated patients with gastric tumors receiving NSAIDs is unknown. In Study 3, the incidence of severe bleeding was 2.4% for CYRAMZA plus docetaxel and 2.3% for placebo plus docetaxel. Patients with NSCLC receiving therapeutic anticoagulation or chronic therapy with NSAIDS or other anti-platelet therapy other than once daily aspirin or with radiographic evidence of major airway or blood vessel invasion or intratumor cavitation were excluded from Study 3; therefore, the risk of pulmonary hemorrhage in these groups of patients is unknown. Permanently discontinue CYRAMZA in patients who experience severe bleeding.

Arterial Thromboembolic Events

Serious, sometimes fatal, arterial thromboembolic events (ATEs) including myocardial infarction, cardiac arrest, cerebrovascular accident, and cerebral ischemia occurred in clinical trials including 1.7% of 236 patients who received CYRAMZA as a single agent for gastric cancer in Study 1. Permanently discontinue CYRAMZA in patients who experience a severe ATE.

Hypertension

An increased incidence of severe hypertension occurred in patients receiving CYRAMZA as a single agent (8%) as compared to placebo (3%) and in patients receiving CYRAMZA plus paclitaxel (15%) as compared to placebo plus paclitaxel (3%) and in patients receiving CYRAMZA plus docetaxel (6%) as compared to placebo plus docetaxel (2%). Control hypertension prior to initiating treatment with CYRAMZA. Monitor blood pressure every two weeks or more frequently as indicated during treatment. Temporarily suspend CYRAMZA for severe hypertension until medically controlled. Permanently discontinue CYRAMZA if medically significant hypertension cannot be controlled with antihypertensive therapy or in patients with hypertensive crisis or hypertensive encephalopathy.

Infusion-Related Reactions

Prior to the institution of premedication recommendations across clinical trials of CYRAMZA, infusion-related reactions (IRRs) occurred in 6 out of 37 patients (16%), including two severe events. The majority of IRRs across trials occurred during or following a first or second CYRAMZA infusion. Symptoms of IRRs included rigors/tremors, back pain/spasms, chest pain and/or tightness, chills, flushing, dyspnea, wheezing, hypoxia, and paresthesia. In severe cases, symptoms included bronchospasm, supraventricular tachycardia, and hypotension. Monitor patients during the infusion for signs and symptoms of IRRs in a setting with available resuscitation equipment. Immediately and permanently discontinue CYRAMZA for Grade 3 or 4 IRRs.

Gastrointestinal Perforations

CYRAMZA is an antiangiogenic therapy that can increase the risk of gastrointestinal perforation, a potentially fatal event. Four of 570 patients (0.7%) who received CYRAMZA as a single agent in clinical trials experienced gastrointestinal perforation. In Study 2, the incidence of gastrointestinal perforations was also increased in patients that received CYRAMZA plus paclitaxel (1.2%) as compared to patients receiving placebo plus paclitaxel (0.3%). In Study 3, the incidence of gastrointestinal perforation was 1% for CYRAMZA plus docetaxel and 0.3% for placebo plus docetaxel. Permanently discontinue CYRAMZA in patients who experience a gastrointestinal perforation.

Impaired Wound Healing

CYRAMZA has not been studied in patients with serious or non-healing wounds. CYRAMZA is an antiangiogenic therapy with the potential to adversely affect wound healing. Withhold CYRAMZA prior to surgery. Resume following the surgical intervention based on clinical judgment of adequate wound healing. If a patient develops wound healing complications during therapy, discontinue CYRAMZA until the wound is fully healed.

Clinical Deterioration in Patients with Child-Pugh B or C Cirrhosis

Clinical deterioration, manifested by new onset or worsening encephalopathy, ascites, or hepatorenal syndrome was reported in patients with Child-Pugh B or C cirrhosis who received single-agent CYRAMZA. Use CYRAMZA in patients with Child-Pugh B or C cirrhosis only if the potential benefits of treatment are judged to outweigh the risks of clinical deterioration.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS)

RPLS has been reported with a rate of <0.1% in clinical studies with CYRAMZA. Confirm the diagnosis of RPLS with MRI and discontinue CYRAMZA in patients who develop RPLS. Symptoms may resolve or improve within days, although some patients with RPLS can experience ongoing neurologic sequelae or death.

ADVERSE REACTIONS

Clinical Trials 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.

CYRAMZA Administered in Combination with Docetaxel

Study 3 was a multinational, randomized, double-blind study conducted in patients with NSCLC with disease progression on or after one platinum-based therapy for locally advanced or metastatic disease. Patients received either CYRAMZA 10 mg/kg intravenously plus docetaxel 75 mg/m^2 intravenously every 3 weeks or placebo plus docetaxel 75 mg/m^2 intravenously every 3 weeks. Due to an increased incidence of neutropenia and febrile neutropenia in patients enrolled in East Asian sites, Study 3 was amended and 24 patients (11 CYRAMZA plus docetaxel, 13 placebo plus docetaxel) at East Asian sites received a starting dose of docetaxel at 60 mg/m^2 every 3 weeks. Study 3 excluded patients with an ECOG PS of 2 or greater, bilirubin greater than the upper limit of normal (ULN), uncontrolled hypertension, major surgery within 28 days, radiographic evidence of major airway or blood vessel invasion by cancer, radiographic evidence of intra-tumor cavitation, or gross hemoptysis within the preceding 2 months, and patients receiving therapeutic anticoagulation or chronic anti-platelet therapy other than once daily aspirin. The study also excluded patients whose only prior treatment for advanced NSCLC was a tyrosine kinase (epidermal growth factor receptor [EGFR] or anaplastic lymphoma kinase [ALK]) inhibitor. The data described below reflect exposure to CYRAMZA plus docetaxel in 627 patients in Study 3. Demographics and baseline characteristics were similar between treatment arms. Median age was 62 years; 67% of patients were men; 84% were White and 12% were Asian; 33% had ECOG PS 0; 74% had non-squamous histology and 25% had squamous histology. Patients received a median of 4.5 doses of CYRAMZA; the median duration of exposure was 3.5 months, and 195 (31% of 627) patients received CYRAMZA for at least six months. In Study 3, the most common adverse reactions (all grades) observed in CYRAMZA plus docetaxel-treated patients at a rate of ≥30% and ≥2% higher than placebo plus docetaxel were neutropenia, fatigue/asthenia, and stomatitis/mucosal inflammation. Treatment discontinuation due to adverse reactions occurred more frequently in CYRAMZA plus docetaxel-treated patients (9%) than in placebo plus docetaxel-treated patients (5%). The most common adverse events leading to treatment discontinuation of CYRAMZA were infusion-related reaction (0.5%) and epistaxis (0.3%). For patients with non-squamous histology, the overall incidence of pulmonary hemorrhage was 7% and the incidence of ≥Grade 3 pulmonary hemorrhage was 1% for CYRAMZA plus docetaxel compared to 6% overall incidence and 1% for ≥Grade 3 pulmonary hemorrhage for placebo plus docetaxel. For patients with squamous histology, the overall incidence of pulmonary hemorrhage was 10% and the incidence of ≥Grade 3 pulmonary hemorrhage was 2% for CYRAMZA plus docetaxel compared to 12% overall incidence and 2% for ≥Grade 3 pulmonary hemorrhage for placebo plus docetaxel. The most common serious adverse events with CYRAMZA plus docetaxel were febrile neutropenia (14%), pneumonia (6%), and neutropenia (5%). The use of granulocyte colony-stimulating factors was 42% in CYRAMZA plus docetaxel-treated patients versus 37% in patients who received placebo plus docetaxel. In patients ≥65 years, there were 18 (8%) deaths on treatment or within 30 days of discontinuation for CYRAMZA plus docetaxel and 9 (4%) deaths for placebo plus docetaxel. In patients <65 years, there were 13 (3%) deaths on treatment or within 30 days of discontinuation for CYRAMZA plus docetaxel and 26 (6%) deaths for placebo plus docetaxel. Table 4 provides the frequency and severity of adverse reactions in Study 3.

Table 4: Adverse Reactions Occurring at Incidence Rate ≥5% and a ≥2% Difference Between Arms in Patients Receiving CYRAMZA in Study 3

Adverse Reactions (MedDRA) System Organ Class	CYRAMZA plus docetaxel (N=627)		Placebo plus docetaxel (N=618)	
	All Grades (Frequency %)	Grade 3-4 (Frequency %)	All Grades (Frequency %)	Grade 3-4 (Frequency %)
Blood and Lymphatic System Disorders				
Febrile neutropenia	16	16	10	10
Neutropenia	55	49	46	40
Thrombocytopenia	13	3	5	<1
Gastrointestinal Disorders				
Stomatitis/Mucosal inflammation	37	7	19	2
Eye Disorders				
Lacrimation increased	13	<1	5	0
General Disorders and Administration Site Disorders				
Fatigue/Asthenia	55	14	50	11
Peripheral edema	16	0	9	<1
Respiratory, Thoracic, and Mediastinal Disorders				
Epistaxis	19	<1	7	<1
Vascular Disorders				
Hypertension	11	6	5	2

Clinically relevant adverse drug reactions reported in ≥1% and <5% of the CYRAMZA plus docetaxel-treated patients in Study 3 were hyponatremia (4.8% CYRAMZA plus docetaxel versus 2.4% for placebo plus docetaxel) and proteinuria (3.3% CYRAMZA plus docetaxel versus 0.8% placebo plus docetaxel).

Immunogenicity

As with all therapeutic proteins, there is the potential for immunogenicity. In 19 clinical trials, 70/2131 (3.3%) of CYRAMZA-treated patients with post baseline serum samples tested positive for treatment-emergent anti-ramucirumab antibodies by an enzyme-linked immunosorbent assay (ELISA). Neutralizing antibodies were detected in 12 of the 70 patients who tested positive for treatment-emergent anti-ramucirumab antibodies. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of incidence of antibodies to CYRAMZA with the incidences of antibodies to other products may be misleading.

DRUG INTERACTIONS

No pharmacokinetic (PK) interactions were observed between ramucirumab and docetaxel.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Category C

Risk Summary

Based on its mechanism of action, CYRAMZA may cause fetal harm. Animal models link angiogenesis, VEGF and VEGF Receptor 2 (VEGFR2) to critical aspects of female reproduction, embryofetal development, and postnatal development. There are no adequate or well-controlled studies of ramucirumab in pregnant women. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, apprise the patient of the potential hazard to a fetus.

Animal Data

No animal studies have been specifically conducted to evaluate the effect of ramucirumab on reproduction and fetal development. In mice, loss of the VEGFR2 gene resulted in embryofetal death and these fetuses lacked organized blood vessels and blood islands in the yolk sac. In other models, VEGFR2 signaling was associated with development and maintenance of endometrial and placental vascular function, successful blastocyst implantation, maternal and feto-placental vascular differentiation, and development during early pregnancy in rodents and non-human primates. Disruption of VEGF signaling has also been associated with developmental anomalies including poor development of the cranial region, forelimbs, forebrain, heart, and blood vessels.

Nursing Mothers

It is not known whether CYRAMZA is excreted in human milk. No studies have been conducted to assess CYRAMZA's impact on milk production or its presence in breast milk. Human IgG is excreted in human milk, but published data suggests that breast milk antibodies do not enter the neonatal and infant circulation in substantial amounts. Because many drugs are excreted in human milk and because of the potential risk for serious adverse reactions in nursing infants from ramucirumab, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

The safety and effectiveness of CYRAMZA in pediatric patients have not been established. In animal studies, effects on epiphyseal growth plates were identified. In cynomolgus monkeys, anatomical pathology revealed adverse effects on the epiphyseal growth plate (thickening and osteochondropathy) at all doses tested (5-50 mg/kg). Ramucirumab exposure at the lowest weekly dose tested in the cynomolgus monkey was 0.2 times the exposure in humans at the recommended dose of ramucirumab as a single agent.

Geriatric Use

Of the 563 CYRAMZA-treated patients in two randomized gastric cancer clinical studies, 36% were 65 and over, while 7% were 75 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects. Of the 1253 patients in Study 3, 455 (36%) were 65 and over and 84 (7%) were 75 and over. Of the 627 patients who received CYRAMZA plus docetaxel in Study 3, 237 (38%) were 65 and over, while 45 (7%) were 75 and over. In an exploratory subgroup analysis of Study 3, the hazard ratio for overall survival in patients less than 65 years old was 0.74 (95% CI: 0.62, 0.87) and in patients 65 years or older was 1.10 (95% CI: 0.89, 1.36).

Renal Impairment

No dose adjustment is recommended for patients with renal impairment based on population PK analysis.

Hepatic Impairment

No dose adjustment is recommended for patients with mild hepatic impairment (total bilirubin within upper limit of normal [ULN] and aspartate aminotransferase [AST] >ULN or total bilirubin >1.0-1.5 times ULN and any AST) based on population PK analysis. Clinical deterioration was reported in patients with Child-Pugh B or C cirrhosis who received single-agent CYRAMZA.

Females and Males of Reproductive Potential

Fertility

Advise females of reproductive potential that CYRAMZA may impair fertility.

Contraception

Based on its mechanism of action, CYRAMZA may cause fetal harm. Advise females of reproductive potential to avoid getting pregnant while receiving CYRAMZA and for at least 3 months after the last dose of CYRAMZA.

DOSAGE AND ADMINISTRATION

Do not administer CYRAMZA as an intravenous push or bolus.

Recommended Dose and Schedule

The recommended dose of CYRAMZA is 10 mg/kg administered by intravenous infusion over approximately 60 minutes on day 1 of a 21-day cycle prior to docetaxel infusion. Continue CYRAMZA until disease progression or unacceptable toxicity

Premedication

Prior to each CYRAMZA infusion, premedicate all patients with an intravenous histamine H_1 antagonist (e.g., diphenhydramine hydrochloride). For patients who have experienced a Grade 1 or 2 infusion reaction, also premedicate with dexamethasone (or equivalent) and acetaminophen prior to each CYRAMZA infusion.

Dose Modifications

Infusion-Related Reactions (IRR)

- Reduce the infusion rate of CYRAMZA by 50% for Grade 1 or 2 IRRs.
- Permanently discontinue CYRAMZA for Grade 3 or 4 IRRs.

Hypertension

- Interrupt CYRAMZA for severe hypertension until controlled with medical management.
- Permanently discontinue CYRAMZA for severe hypertension that cannot be controlled with antihypertensive therapy.

Proteinuria

- Interrupt CYRAMZA for urine protein levels ≥2 g/24 hours. Reinitiate treatment at a reduced dose of 8 mg/kg every 2 weeks once the urine protein level returns to <2 g/24 hours. If the protein level ≥2 g/24 hours reoccurs, interrupt CYRAMZA and reduce the dose to 6 mg/kg every 2 weeks once the urine protein level returns to <2 g/24 hours.
- Permanently discontinue CYRAMZA for urine protein level >3 g/24 hours or in the setting of nephrotic syndrome.

Wound Healing Complications

- Interrupt CYRAMZA prior to scheduled surgery until the wound is fully healed.

Arterial Thromboembolic Events, Gastrointestinal Perforation, or Grade 3 or 4 Bleeding

- Permanently discontinue CYRAMZA.

For toxicities related to docetaxel, refer to the current respective prescribing information.

PATIENT COUNSELING INFORMATION

Advise patients:

- That CYRAMZA can cause severe bleeding. Advise patients to contact their health care provider for bleeding or symptoms of bleeding including lightheadedness.
- Of increased risk of an arterial thromboembolic event.
- To undergo routine blood pressure monitoring and to contact their health care provider if blood pressure is elevated or if symptoms from hypertension occur including severe headache, lightheadedness, or neurologic symptoms.
- To notify their health care provider for severe diarrhea, vomiting, or severe abdominal pain.
- That CYRAMZA has the potential to impair wound healing. Instruct patients not to undergo surgery without first discussing this potential risk with their health care provider.
- Of the potential risk for maintaining pregnancy, risk to the fetus, or risk to postnatal development during and following treatment with CYRAMZA and the need to avoid getting pregnant, including use of adequate contraception, for at least 3 months following the last dose of CYRAMZA.
- To discontinue nursing during CYRAMZA treatment.

Additional information can be found at www.CYRAMZAhcp.com.

Lilly

Eli Lilly and Company, Indianapolis, IN 46285, USA

RB-L HCP BS 17Dec2014

CYRAMZA® (ramucirumab) injection RB-L HCP BS 17Dec2014

Hierarchical Condition Categories:
Diagnosis Coding From a Different Point of View

BY CINDY PARMAN, CPC, CPC-H, RCC

Submitting claims is easy—you report the correct codes for the services performed and the cancer diagnosis; reimbursement is guaranteed. (Note: ICD-9 and ICD-10 have diagnosis codes for "unspecified malignancies," and these codes are used too often in oncology. Whenever possible, use specific cancer diagnosis codes.) And then there are your Medicare Advantage patients. If you treat this patient population, you must also know your HCCs (hierarchical condition categories) and your ICDs (International Classification of Diseases).

Medicare Advantage Plans: 101

Medicare Advantage was created in 1997 with the signing of the Balanced Budget Act and was previously referred to as Medicare Managed Care, Medicare Part C, or the Medicare+Choice program. The Medicare Modernization Act of 2003 renamed the program Medicare Advantage. New types of plans were offered, including provider-sponsored organizations (PSOs), preferred-provider organizations (PPOs), and private fee-for-service plans (PFFS).

Congress created Medicare Advantage to encourage private insurance companies to venture into the senior care market. The plans now insure 16 million elderly and disabled people, nearly a third of those eligible for Medicare.[1] These plans are popular among beneficiaries because they often provide extra benefits, such as vision and dental care, with lower out-of-pocket costs.

The traditional model for physician reimbursement has been fee-for-service; physicians get paid for each service they provide to a patient. Under fee-for-service, the CPT® procedure codes and their individual relative values drive reimbursement and the ICD-9-CM diagnostic codes support the medical necessity of those services. In 2007 the risk adjustment phase-in was completed for the participating Medicare Advantage plans and the Medicare Advantage Hierarchical Condition Categories model turns this reimbursement system upside down.

The Risk-Adjusted Reimbursement Model: 101

In the HCC system, the patient's number and severity of medical problems is factored into a capitated payment using an actuarial prediction of costs. The Centers for Medicare & Medicaid Services (CMS) pays the Medicare Advantage plans on a per-member, per-month base, adjusted for each member's medical risk score. This means that the ICD-9-CM diagnosis codes do more than support the reason for the services; they now drive CMS payments to the Medicare Advantage plans for their members. In addition, the government trusts these plans to accurately report the health status of their participants.

This risk-adjusted reimbursement model is based on chronic and cumulative conditions (or HCCs).[2] HCCs are used to adjust capitation payments to these private healthcare plans for the health expenditure risk of their enrollees. This means that the Medicare Advantage plan must ensure that all appropriate diagnosis codes are included when the claim is processed: the primary diagnosis, other signs and symptoms, patient comorbidities, side effects of treatment, etc. Proper coding results in the revenue used to pay the medical bills of the membership and to prepare for those who have unpredictable medical problems.

The CMS Risk Adjustment Model measures the disease burden using approximately 70 HCC categories, which are correlated to about 3,300 diagnosis codes. Diagnoses are classified into groups to include clinically related conditions with similar cost-of-care ramifications, called diagnostic groups (DXGs). About 80 percent of the diagnoses used in the Risk Adjustment Processing System (RAPS) originate from the claim forms submitted by physicians and hospitals.

The RAPS creates a Risk Adjustment Factor (RAF) that identifies the individual patient's status. All of this is highly influenced by the historic costs of caring for specific chronic diseases, and payments are based upon the most severe disease manifestation. Comorbidities can have a significant impact on the RAF and HCC determination, and consequently the resulting reimbursement.

Physicians, hospitals, and cancer programs must then focus attention on accurate and complete diagnosis reporting according to the ICD-9-CM Official Guidelines for Coding and Reporting[3] (such as, coding diagnoses completely and to the highest level of specificity). The codes submitted are derived from physician documentation of face-to-face encounters; only medical record documentation can be used to support an HCC. This means that a Medicare Advantage plan can use an office

visit, hospital inpatient, or hospital outpatient medical record to support the diagnosis code(s) and resulting HCC, when more than one option is available.

Underlying Principles Behind the HCC Model

The following 10 principles guided the creation of this diagnostic classification system:[4]

1. Diagnostic categories should be clinically meaningful; conditions must be sufficiently clinically specific to minimize opportunities for gaming or discretionary coding.
2. Diagnostic categories should predict medical expenditures; diagnoses in the same HCC should be reasonably homogenous with respect to their effect on both current and future costs.
3. Diagnostic categories that will affect payments should have adequate sample sizes to permit accurate and stable estimates of expenditures.
4. In creating an individual's clinical profile, hierarchies should be used to characterize the person's illness level within each disease process, while the effects of unrelated disease processes accumulate. Because each new medical problem adds to an individual's total disease burden, unrelated disease processes should increase predicted costs of care.
5. The diagnostic classification should encourage specific coding. Vague diagnostic codes should be grouped with less severe and lower-paying diagnostic categories to provide incentives for more specific diagnostic coding.
6. The diagnostic classification should not reward coding proliferation. The classification should not measure greater disease burden simply because more ICD-9-CM codes are present.
7. Providers should not be penalized for recording additional diagnoses.
8. The classification system should be internally consistent. For example, if diagnostic category A is ranked higher than category B in a disease hierarchy, and category B is ranked higher than category C, then category A should be ranked higher than category C.
9. The diagnostic classification should assign all ICD-9-CM codes; since each diagnostic code potentially contains relevant clinical information, the classification should categorize all ICD-9-CM codes.
10. Discretionary diagnostic categories should be excluded from payment models. Diagnoses that are particularly subject to intentional or unintentional discretionary coding variation or inappropriate coding by health plans/providers, or that are not clinically or empirically credible as cost predictors, should not increase cost predictions.

The HCC model is cumulative, meaning that individual patients can have more than one HCC category assigned to them. There is a hierarchy of categories, and some categories override others. In addition, Medicare Advantage plans can look backward in the medical records to correct incomplete coding. This involves reviewing the patients' medical records to look for documentation that supports any of those 3,300+ previously unreported diagnoses (unreported because they may not have been documented to support medical necessity of a previously reported service).

Oncology-Specific HCCs

The following are some of the HCCs that relate specifically to oncology:[5]

- ***HCC 8:*** Metastatic Cancer and Acute Leukemia
- ***HCC 9:*** Lung and Other Severe Cancers
- ***HCC 10:*** Lymphoma and Other Cancers
- ***HCC 11:*** Colorectal, Bladder, and Other Cancers
- ***HCC 12:*** Breast, Prostate, and Other Cancers and Tumors
- ***HCC 46:*** Severe Hematological Disorders
- ***HCC 47:*** Disorders of Immunity.

Clinical Vignette

In addition to various documents that incorporate coding instructions, CMS provides the following example:[5]

To illustrate the CMS-HCC model, we have created a hypothetical clinical vignette of a female, age 76, who lives in the community and has several chronic conditions. She received eight ICD-9-CM diagnosis codes from visits to hospitals and physicians, which are grouped into seven DXGs: acute myocardial infarction (AMI); angina pectoris; emphysema/chronic bronchitis; chronic renal failure; renal failure, unspecified; chest pain; and sprains. These seven DXGs in turn group into six CCs [condition categories], with the chronic renal failure and unspecified renal failure DXGs mapping to a single CC of renal failure. Finally, the six CCs result in three

payment HCCs—AMI, chronic obstructive pulmonary disease (COPD), and renal failure—that are used in risk adjusting Medicare capitation payments. Although this female receives CCs for both AMI and angina, she receives no payment HCC for angina because AMI is a more severe manifestation of coronary artery disease, and thus excludes angina in the coronary artery disease hierarchy. The HCCs for major symptoms and other injuries are also excluded from the payment calculation. Chest pain is a symptom associated with a variety of medical conditions ranging from minor to serious, and sprains are typically transitory, with minimal implications for next year's cost.

Along with the demographic factors of age 76 and female ($3,409), each of the three payment HCCs identified in the clinical vignette contributes additively to this person's risk profile (AMI $2,681; COPD $2,975; renal failure $2,745). Her total predicted expenditures are the sum of the individual increments, or $11,810. Her total risk score is the sum of the individual relative factors, or 1.583. [Calendar Year 2011].

HHS Study

The Medicare & Medicaid Research Review, Volume 4, Number 2 (2014) discusses "Measuring Coding Intensity in the Medicare Advantage Program."[6] According to this report, the average Medicare Advantage risk score has increased faster than the average FFS (fee-for-service) score every year. This means that the number of patients diagnosed with diseases that result in higher payment increased faster at Medicare Advantage plans than among beneficiaries enrolled in the Original Medicare. If Medicare Advantage health plans intentionally exaggerated the severity of a patient's medical condition, this would be considered "upcoding." For example, "drug and alcohol dependence" is as much as eight times more common in the highest coding Medicare Advantage plan than among patients in standard Medicare. The report states, in part:[6]

> *If MA [Medicare Advantage] enrollees are, in fact, getting sicker more quickly than FFS [Fee For Service] beneficiaries, we would expect to see MA mortality rates increase relative to FFS mortality.*

While upcoding is always a possibility, Medicare Advantage plans have a vested interest in complete diagnosis coding and they may be working harder to obtain comprehensive diagnosis information to ensure each patient is accurately classified. This report adds:[6]

> *Concerns about coding intensity in MA [Medicare Advantage] plans would be minor if coding in FFS were relatively complete, because in that case there would be little opportunity for MA [Medicare Advantage] plans to legitimately increase risk scores through efforts at increasing diagnostic reporting. However, FFS coding is known to be both incomplete and variable. Incomplete coding is evidenced by lack of persistence in coding of chronic conditions.*

Incomplete and variable coding provides ample opportunities for Medicare Advantage plans to increase risk scores of beneficiaries through coding intensity efforts, and a number of vendors actively market services that help plans to do so, often advertising high returns on investment (ROIs) for their services.

In addition to the HHS study, a whistleblower case filed under the False Claims Act has recently become public, alleging that providers and Medicare Advantage plans have defrauded the Medicare program by manipulating data to make members appear to be sicker and generate higher capitation payments.[7] According to the Kaiser Family Foundation, CMS was projected to pay Medicare Advantage plans $156 billion in calendar year 2014, accounting for about one-third of all Medicare spending.

The Bottom Line

It all boils down to the data collection process, which of course always points back to the physician's office and/or hospital and the documentation of the patient encounter. Good documentation begins at the time of the patient's face-to-face encounter with the oncologist when the physician documents the clinical findings in the medical record, and the medical record is used to determine ICD-9-CM codes. Coding Clinic, Third Quarter 2013 (authoritative coding guidance) states:[8]

Question: *Is there a guideline or rule that indicates that you should only use the medical record documentation for that specific visit/admission for diagnosis coding purposes? Does each visit or admission stand alone? Would the coder go back to the previous encounter records to assist in the coding of a current visit or admission?*

Answer: *Documentation for the current encounter should clearly reflect those diagnoses that are current and relevant for that encounter.*

Conditions documented on previous encounters may not be clinically relevant on the current encounter. The physician is responsible for diagnosing and documenting all relevant conditions. A patient's historical problem list is not necessarily the same for every encounter/visit. It is the physician's responsibility to determine the diagnoses applicable to the current encounter and document in the patient's medical record. When reporting recurring conditions and the recurring condition is still valid for the outpatient encounter or inpatient admission, the recurring condition should be documented in the medical record with each encounter/admission. However if the condition is not documented in the current health record, it would be inappropriate to go back to previous encounters to retrieve a diagnosis without physician confirmation.

This is an area where coders and/or department managers may need to educate physicians and/or practice managers on the need to include complete diagnoses when outpatient services are ordered and to continue to document chronic or longstanding conditions on each admission/encounter record. Please note this advice applies to both ICD-9-CM and ICD-10-CM.

In addition, Coding Clinic, First Quarter 2012 states:[9]

Question: *Since our facility has converted to an electronic health record, providers have the capability to list the ICD-9-CM diagnosis code instead of a descriptive diagnostic statement. Is there an official policy or guideline requiring providers to record a written diagnosis in lieu of an ICD-9-CM code number?*

Answer: *Yes, there are regulatory and accreditation directives that require providers to supply documentation in order to support code assignment. Providers need to have the ability to specifically document the patient's diagnosis, condition, and/or problem. Therefore, it is not appropriate for providers to list the code number or select a code number from a list of codes in place of a written diagnostic statement. ICD-9-CM is a statistical classification, per se, it is not a diagnosis. Some ICD-9-CM codes include multiple different clinical diagnoses and it can be of clinical importance to convey these diagnoses specifically in the record. Also, some diagnoses require more than one ICD-9-CM code to fully convey. It is the provider's responsibility to provide clear and legible documentation of a diagnosis, which is then translated to a code for external reporting purposes.*

Finally, the HHS report states:[1]

> *Coding more carefully may have real health benefits. Better identification of problems and better documentation of problems that have been identified could improve the quality of treatment provided and may even lower costs—or they may lead to unnecessary treatment and higher costs.*

The only way to be certain is for every physician, freestanding cancer center, and hospital to make an effort to accurately document and report diagnosis codes that classify the individual patient, including the reason for each patient encounter, all medical conditions treated, and all conditions that impact the treatment provided. With complete and accurate diagnosis coding, the data will reflect the complexity of patient care and the intensity of treatment. OI

Cindy Parman, CPC, CPC-H, RCC, is a principal at Coding Strategies, Inc., in Powder Springs, Ga.

References

1. Schulte F. HHS Report Finds Medicare Advantage Plans Exaggerate Members' Diseases To Make More Money. Available online at: www.kaiserhealthnews.org/news/medicare-advantage-plans-exaggerate-diseases-to-make-money-says-study. Last accessed Feb. 4, 2015.

2. CMS. Medicare Managed Care Manual. Chapter 7: Risk Adjustment. Available online at: www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/mc86c07.pdf. Last accessed Feb. 4, 2015.

3. CDC. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). Available online at: www.cdc.gov/nchs/icd/icd9cm.htm. Last accessed Feb. 4, 2015.

4. CMS. Risk Adjustment of Medicare Capitation Payments Using the CMS-HCC Model. Available online at: www.cms.gov/Research-Statistics-Data-and-Systems/Research/HealthCareFinancingReview/downloads/04Summerpg119.pdf. Last accessed Feb. 4, 2015.

5. CMS. Evaluation of the CMS-HCC Risk Adjustment Model: Final Report. Available online at: www.cms.gov/Medicare/Health-Plans/MedicareAdvtgSpecRateStats/downloads/Evaluation_Risk_Adj_Model_2011.pdf. Last accessed Feb. 4, 2015.

6. Kronick R, Welch WP. Measuring coding intensity in the Medicare Advantage Program. *MMRR.* 2014;4(2):E1-E19. Available online at: www.cms.gov/mmrr/Downloads/MMRR2014_004_02_a06.pdf. Last accessed Feb. 4, 2015.

7. Schencker L. Were patients really sicker? Lawsuits say Medicare Advantage plans inflated diagnoses to boost payments. *Modern Healthcare.* Available online at: www.modernhealthcare.com/article/20141122/MAGAZINE/311229981. Last accessed Feb. 4, 2015.

8. American Hospital Association. *Coding Clinic,* Third Quarter 2013.

9. American Hospital Association. *Coding Clinic,* First Quarter 2012.

Top 3 Takeaways about HCCs

1. Medicare Advantage plans require all relevant patient diagnosis codes for correct payment.
2. All diagnosis codes should be reported at the highest level of specificity (no unspecified codes).
3. Complete and accurate diagnosis coding reflects the complexity of care and intensity of treatment.

spotlight

Katmai Oncology Group, Anchorage, Alaska

Ellen H. Chirichella, MD

Katmai Oncology Group is the largest oncology practice, as well as the only Quality Oncology Practice Initiative (QOPI®)-certified practice, in the state of Alaska. Located in Anchorage—which is home to more than 40 percent of the state's total population—the physician-owned community oncology-hematology practice offers on-site chemotherapy and has its own laboratory facilities.

The practice is located on the third floor of the Providence Cancer Center, which is part of the Providence Alaska Medical Center campus. The practice space boasts a sweeping mountain view of the Alaskan landscape, just one of the features designed to enhance the patient experience and create a calming environment of care. Offering a holistic approach to treating the "whole patient," the practice features an integrative medicine suite with a soothing waterfall feature. Supportive care services include integrative medicine (acupuncture, massage therapy), palliative care, survivorship counseling, social services, financial counseling, and access to the only oncology-certified dietitian in the state of Alaska. Navigation services, available to all Katmai Oncology patients, are performed by clinic nurse navigators.

Bringing Quality Oncology Care to Alaska

Founded in 1973, by Dale Webb, MD, Katmai Oncology Group was the first practice of its kind to serve the patient population of Anchorage, and Dr. Webb is credited with providing medical services that were previously unavailable in Alaska. Today, Katmai Oncology Group continues to expand. The practice is now staffed by:

- Six oncologists
- Six oncology nurse practitioners
- A psychiatric nurse practitioner
- Eight clinic nurse navigators
- Infusion nurses
- A social worker
- An oncology-certified dietitian
- Two massage therapists
- An acupuncturist.

All of the practice nurses are OCN-certified.

Survivorship is a new service offered by Katmai Oncology Group as of 2014. Currently, survivorship care plans are prepared by nurse practitioners for colorectal and breast cancer patients. In the coming year, the practice intends to add survivorship services for lymphoma patients.

Practice physicians participate in a breast tumor board that meets twice a month; a brain tumor board and a thoracic tumor board, which meet monthly; and a city-wide multidisciplinary tumor board that is held weekly for any cases that do not fit into the aforementioned disease sites.

Although the Katmai Oncology Group is a completely separate entity, the clinic is housed in the Providence Cancer Center. The proximity of services does have benefits. Katmai refers patients to the Providence Cancer Center's oncology rehabilitation program, utilizes local research staff, and also works closely with the hospital's radiation oncology group (for high-dose rate brachytherapy and Tomotherapy services). This close relationship and being physically located in the cancer center ensures a smooth coordination of care.

Bridging a Care Gap

Katmai Oncology Group continues to grow to meet patient demands. In addition to serving the area surrounding Anchorage (a city with a population of 300,000), the practice also operates a satellite infusion clinic (opened in 2012) four days a week in Soldotna on the Kenai Peninsula, which is about 150 miles south of Anchorage. Offering oncology services at the Soldotna Clinic was due to patient demand, and the care access issues experienced by the rural patient population inspired Katmai to bring their services to them.

"The peninsula is definitely rural. Access to care is a barrier down there. Patients were reluctant to make the trek to Anchorage for care," said Dr. Shannon Smiley, one of Katmai's practicing oncologists. The clinic is a 15 to 20 minute flight from Anchorage or a three-hour drive. "It seemed, anecdotally, that patients coming in to the clinic were also experiencing other health issues because they may not have sought any medical care prior to a cancer diagnosis," said Dr. Smiley.

Improving Patient Access to Clinical Trials

In December 2014 Katmai Oncology Group joined the Seattle Cancer Care Alliance (SCCA) Network as its eleventh affiliate in the greater Northwest. By joining the SCCA Network, Katmai Oncology Group oncologists can now offer their patients expanded access to cancer treatment options via select

SCCA clinical studies without the patients having to travel to Seattle to participate. This affiliation also provides support for Katmai's community-based oncology services by arranging for local patients to enroll in clinical trials managed by qualified community physicians. Katmai Oncology Group currently accrues about seven percent of patients to clinical trials annually.

Incorporating New Technology

Katmai Oncology Group is working toward incorporating new technology with a goal of helping to streamline patient care access. According to Dr. Smiley, the practice hopes to begin performing telemedicine in the coming year. Achieving this goal will not only enhance the care of local patients, but may also help to ease the travel burden for patients living in rural locations. Another step in improving the patient experience is the adoption of a patient portal. Currently, the practice uses the My Care Plus patient portal. Through the portal, patients can access their personal health records at any time and view educational videos on a variety of topics including pain management, "chemo-brain," managing distress, and more. Katmai Oncology Group is also currently beta-testing a cloud-based EHR, which Dr. Smiley said would allow providers smartphone access to the EHR, a particular benefit for providers who cover a large and rural geographic area.

Select Support Services

- Navigation
- Oncology dietitian
- Financial counseling
- Palliative care
- Survivorship

Number of new analytic cases seen in 2014: 680

tools

Approved Drugs

- Novartis (www.novartis.com) announced that the U.S. Food and Drug Administration (FDA) has approved **Farydak® (panobinostat) capsules**, previously known as LBH589, in combination with bortezomib and dexamethasone for the treatment of patients with multiple myeloma who have received at least two prior regimens, including bortezomib and an immunomodulatory (IMiD) agent.

- FDA has granted accelerated approval to **Ibrance® (palbociclib)** (Pfizer, Inc., www.pfizer.com) for use in combination with letrozole for the treatment of postmenopausal women with estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer as initial endocrine-based therapy for their metastatic disease.

- Janssen Biotech, Inc. (www.janssenbiotech.com) announced that the FDA has approved **Imbruvica® (ibrutinib)** capsules as the first therapy indicated specifically for patients with Waldenstrom's macroglobulinemia (WM), a rare, indolent type of B-cell lymphoma. This represents the fourth indication for Imbruvica since its initial approval in November 2013. Imbruvica was granted Breakthrough Therapy Designation for WM by the FDA and is being jointly developed and commercialized by Janssen and Pharmacyclics, Inc.

- Eisai, Inc. (www.eisai.com) announced that the FDA has granted approval to **Lenvima™ (lenvatinib)** to treat patients with progressive, differentiated thyroid cancer (DTC) whose disease progressed despite receiving radioactive iodine therapy (radioactive iodine refractory disease). Lenvima is a kinase inhibitor, which works by blocking certain proteins from helping cancer cells grow and divide.

- The FDA has granted accelerated approval to **Lynparza™ (olaparib)** (AstraZeneca Pharmaceuticals, www.astrazeneca.com) for women with advanced ovarian cancer associated with defective BRCA genes, as detected by an FDA-approved test. Lynparza is a poly ADP-ribose polymerase (PARP) inhibitor that blocks enzymes involved in repairing damaged DNA. It is intended for women with heavily pre-treated ovarian cancer that is associated with defective BRCA genes. The FDA approved Lynparza with a genetic test called BRCAAnalysis CDx (Myriad Genetics, Inc., www.myriad.com), a companion diagnostic that will detect the presence of mutations in the BRCA genes (gBRCAm) in blood samples from patients with ovarian cancer.

- Bristol-Myers Squibb (www.bms.com) announced that the FDA has granted accelerated approval to **Opdivo® (nivolumab)** for patients with unresectable or metastatic melanoma who no longer respond to other drugs. Opdivo works by inhibiting the PD-1 protein on cells, which blocks the body's immune system from attacking melanoma tumors. Opdivo is intended for patients who have been previously treated with ipilimumab and for melanoma patients whose tumors express a gene mutation called BRAF V600, for use after treatment with ipilimumab and a BRAF inhibitor.

- Celgene Corporation (www.celgene.com) has announced that the FDA has expanded the existing indication for **Revlimid (lenalidomide)** in combination with dexamethasone to include patients newly diagnosed with multiple myeloma.

- The FDA has approved **Somatuline® Depot Injection (lanreotide)** (Ipsen Pharma, www.ipsen.com) for the treatment of patients with unresectable, well or moderately differentiated, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NETs) to improve progression-free survival.

Genetic Tests and Assays in the News

- The FDA has granted 510(k) clearance for Agendia's (www.agendia.com) **Mamma-Print® Breast Cancer Recurrence Test in FFPE** (formalin-fixed paraffin embedded) **Tissue**. The MammaPrint FFPE test uses the same 70 genes and proprietary algorithm as the previously cleared MammaPrint Fresh. Due to the larger panel of genes, both tests provide an unambiguous result of "Low vs. High risk" for recurrence of a patient's breast cancer. OI

MammaPrint FFPE
Now FDA 510(k) Cleared

agendia®
decoding cancer

Why settle for fuzzy results? Insist on a clearer picture.

MammaPrint® provides more information about your patient's breast cancer recurrence risk with definitive, High Risk/Low Risk results. **BluePrint®** classifies Luminal-type, Basal-type and HER2-type functional molecular subtypes. Together, they reveal more clinically actionable biology:

- MammaPrint + BluePrint can reclassify up to 25% of breast cancers with potential therapeutic and prognostic implications, according to a study published in *Cancer Research.*[1]
- Most recently, NBRST, a prospective neoadjuvant study, concluded that BluePrint may be a better guide than IHC-FISH tests in making decisions about how to treat early-stage breast cancer before surgery.[2]

For more clinically actionable information, order MammaPrint + BluePrint to uncover your patient's functional molecular subtype. The difference is clear.

MammaPrint + BluePrint: Better together.
Convenient online ordering available at **www.agendia.com**.

Agendia, Inc. 22 Morgan, Irvine, CA 92618 (888) 321-2732
www.agendia.com

1 Cristofanilli M, et al. *Cancer Res.* 2012;72(24 Suppl):Abstract nr P3-05-01.
2 Whitworth P, et al. *Ann Surg Oncol.* 2014 Aug 7.
[Epub ahead of print];doi: 10.1245/s10434-014-3908-y.

M-USA-044-V1

mammaprint®
70-Gene Breast Cancer Recurrence Assay

blueprint®
80-Gene Molecular Subtyping Assay

A Model Symptom Management Clinic

Aims to Improve Patient Satisfaction & Reduce Hospitalizations

BY CATHERINE BRADY-COPERTINO, BSN, MS, OCN;
MADELAINE BINNER, MBA, CRNP, DNP;
SUSANNE TAMERIS; BARRY MEISENBERG, MD;
LYNN GRAZE, RN, MSN, OCN

The future of cancer care faces many challenges, including an increase in patients due to an aging population, a shrinking oncology workforce, funding reductions, spiraling costs, and high patient expectations. In a 2013 publication, the Institute of Medicine (IOM) concluded "that meeting these challenges will require stronger core competencies for clinicians, team-based models of care, more effective communication with patients, and new payment models."[1] Economic, social, and ethical imperatives are driving the U.S. to reduce the unsustainable growth of its healthcare spending, while ensuring its citizens receive high quality, evidence-based care. Common areas that adversely affect oncology cost and quality include:

- Lack of compliance with evidence-based, cost-effective guidelines
- High cost of drug regimens with lack of transparency
- A high reliance on emergency room and hospital admissions for care.

While solutions may be found under the Affordable Care Act's episode-based or bundled payment methodology or through the organizational structure of accountable care organizations (ACOs), healthcare systems themselves must look for innovative and progressive models to meet these challenges. Community-based oncology practices and hospital-based cancer programs have a significant opportunity and obligation to lead meaningful change and demonstrate the ability to work together.

Improvement Needed

In January 2010, Anne Arundel Medical Center (AAMC), Annapolis, Md., purchased the private hematology-oncology practice, AAMC Oncology & Hematology. The practice relocated its offices to AAMC's main campus. Infusion and laboratory staff were employed and housed in AAMC's hospital-based outpatient infusion center at the Geaton and JoAnn DeCesaris Cancer Institute (DCI), while the physician practice was housed in the adjacent pavilion. The telephone triage functions shifted to the hospital outpatient department, while a 1.0 registered nurse and all other administrative staff remained in the physician pratice. The capacity of AAMC's outpatient infusion center grew overnight from 12 infusion chairs to 42. The physical separation of the infusion nurse triage functions from the practice itself was quickly identified as a quality issue by multiple stakeholders, including physicians, patients, and nurses.

> Our experience demonstrated that patients needed education on the importance of early recognition of acute symptoms related to their disease and/or associated therapies requiring urgent or emergent intervention.

The culture change from a private practice to a hospital-based program brings a number of changes—not the least is a willingness on the behalf of physicians to participate in numerous quality improvement (QI) initiatives. These QI initiatives require focused attention and time to measure, report, and implement change for a number of accrediting bodies, such as the American College of Surgeons Commission on Cancer (CoC) and The Joint Commission (TJC), and for various other QI initiatives, including the American Society of Clinical Oncology's (ASCO) Quality Oncology Practice Initiative (QOPI), ASCO/Oncology Nursing Society (ONS) Chemo Safety Standards, P4 Pathways, and Magnet nursing, as well as the implementation of electronic health records (EHRs) and Meaningful Use measures. In addition, the relocation of the practice to the hospital campus brought a 10 percent increase in new patient volume as patients reacted favorably to the sense of being involved in a community comprehensive cancer center.

This increased patient volume, coupled with the sequential introduction of a new ambulatory EHR and chemotherapy ordering system, increased the workload and expectations of physicians. As a result, physician schedules were quickly booked to capacity, making it difficult to respond quickly to nurse inquiries and patient messages, which were often related to symptom

management issues. The majority of these calls waited until the end of the day for a response—after business hours. This, in turn, delayed return calls to patients until the next business morning. Other times, patients who could not reach their physicians were forced to call multiple individuals, including the on-call physician, oncology nurse navigators, outpatient infusion nurses, or other providers, to have their concerns addressed. Lack of timely communications can often result in medical complications, worsening patient conditions, and decreased patient satisfaction. Further, the literature finds that unrelieved symptoms lead to a decline in performance status, physical state, and increased suffering in patients.[2] This delay in response often left a local emergency department (ED) as the only viable choice for patients with urgent needs. Research has found that patients who go to the ED for symptom management have more than a 50 percent likelihood of being admitted for hospitalization.[3] Studies have also found that systematic nursing assessment and targeted interventions can reduce patient trips to the ED for symptom management.[4]

Studies have also found that systematic nursing assessment and targeted interventions can reduce patient trips to the ED for symptom management.[4]

Barriers to Symptom Management

Several barriers can prevent cancer patients from receiving high-quality care for symptom management. A significant barrier is patients themselves; patients often hesitate to call physicians about symptoms for fear of bothering them. Another barrier is the patient's belief that physicians and nurses will know when the symptoms are likely to appear and will intervene at the appropriate time.[5]

Lack of availability of physician appointments and/or transportation issues can also create barriers to effective symptom management. Patients who work need appointments in the early morning or late afternoon, when physician schedules are typically full. Elderly oncology patients prefer early morning to midday appointments. Repeatedly missing work for physician appointments or not keeping physician appointments can contribute to both poor clinical outcomes and financial distress. At AAMC, lack of same-day physician appointments was a significant barrier to effective symptom management. Same-day physician appointments were not readily available, resulting in care coordination managed via telephone or by referring the patient to the ED.

Lack of transportation is an important and often overlooked aspect of quality cancer care. It is reported that 13 to 14 percent of cancer patients have significant transportation difficulties.[6] Consequently, symptom management issues may escalate while patients struggle to coordinate transportation to multiple appointments.

Finally, we found that lack of patient education regarding symptoms and symptom management was a barrier. Our experience demonstrated that patients needed education on the importance of early recognition of acute symptoms related to their disease and/or associated therapies requiring urgent or emergent intervention.

Table 1. Oncology Nurse Practitioner Symptom Management Clinic Patient Symptom List

1	Fever greater than 100.4°
2	Chills with or without fever after receiving recent chemotherapy
3	New shortness of breath/dyspnea on exertion
4	New bleeding (nose, tarry stools, urine)
5	Mouth sores making it difficult to eat or drink
6	Uncontrolled nausea and vomiting (not responding to home medications)
7	Diarrhea not controlled by home medications (unresponsive to Imodium/Lomotil)
8	New abdominal pain with or without constipation
9	New swelling in arms or legs
10	Redness or tenderness of port site
11	Swelling, pain, redness at peripheral IV site
12	New rash
13	Need for increased pain management or new site of bone pain
14	Dysuria or urinary frequency
15	Excessive fatigue
16	Excessive thirst
17	Dizziness or vertigo
18	Weakness of arms or legs
19	Neuro issues (double vision, headache)

Development & Implementation of a Symptom Management Clinic

Oncology physicians and nursing leadership recognized the need to be creative when developing an improved business and practice model that would provide value and benefit to patients by ensuring their needs were met. Research has demonstrated the importance of symptom management and the optimization of the health and comfort of patients undergoing cancer therapy, resulting in improved function and quality of life (QOL). Excellent symptom management also leads to improved quality metrics, such as utilization of medical care, patient and/or caregiver comfort and productivity, and family cohesion.[7]

Recognizing the difficulty of implementing multiple changes simultaneously, these accountable leaders chose a more manageable approach and prioritized the development of an evidence-based Symptom Management Clinic. Our early goals were to improve symptom management and patient satisfaction, and to reduce the number of ED visits and hospital admissions. In 2012, the Medical Oncology Executive Committee, which includes physicians representing the medical oncology physician practice, and medical, nursing, and executive oncology leadership, developed a plan for a Symptom Management Clinic.

That same year, AAMC's Symptom Management Clinic was embedded in the medical oncology practice and managed by 2.0 FTE telephone triage nurses and a 1.0 FTE oncology nurse practitioner (NP). Telephone triage nurses were experienced infusion nurses who rotated regularly from the hospital-based outpatient infusion department to the Symptom Management Clinic. The rotation provided patient-centered continuity of care, as the infusion nurses were already familiar with individual patients.

The NP worked with AAMC's oncology nurses to develop:

- Symptom criteria (Table 1, above)
- Standard protocols of care

(continued on page 27)

Figure 1. Symptom Management Clinic NP Evaluation Preventing ED Visits

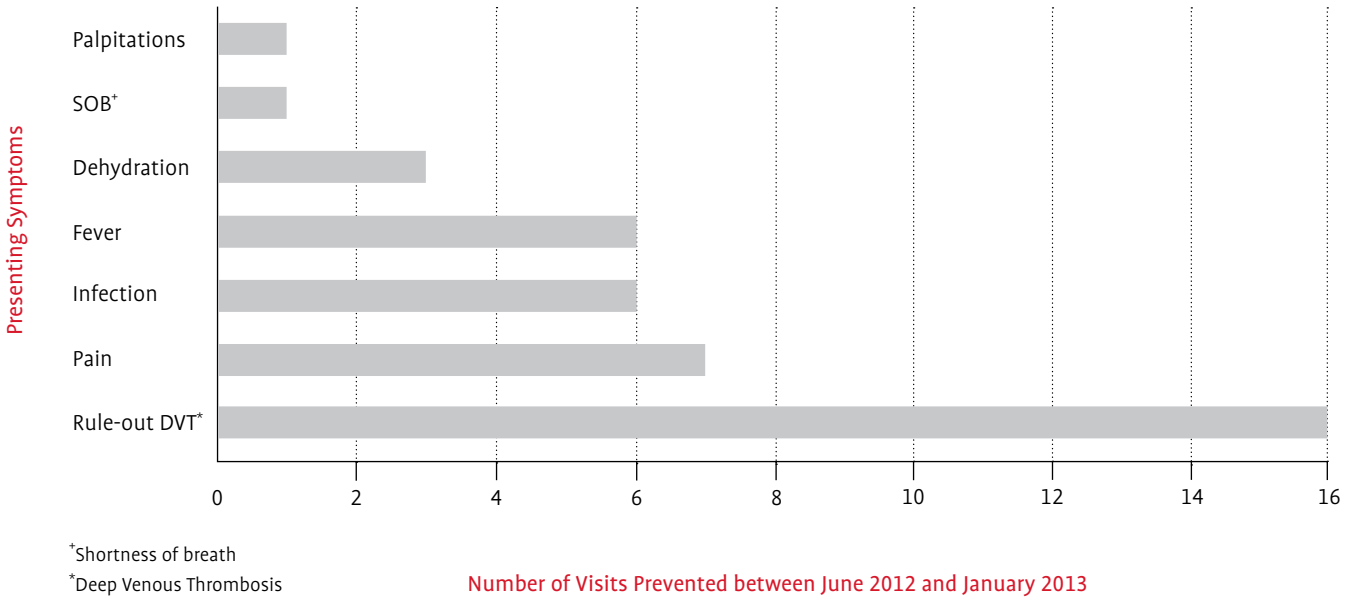
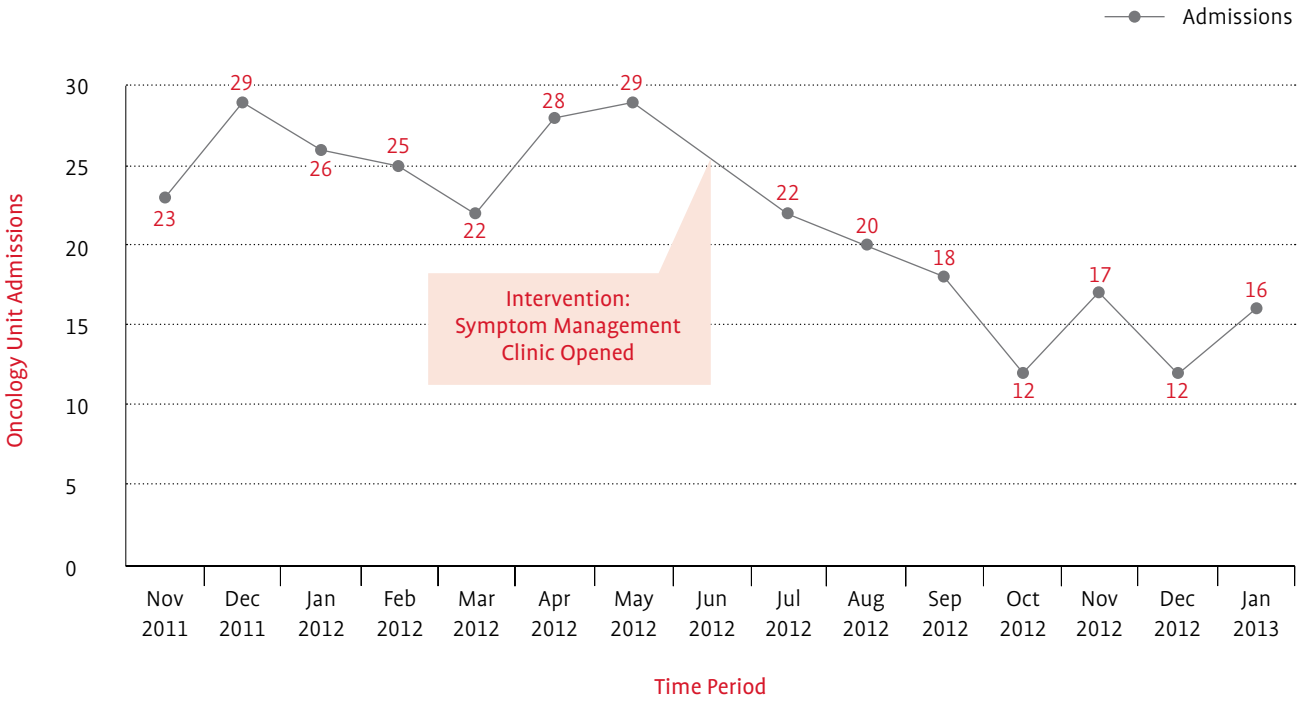


Figure 2. Oncology Unit Admissions Related to Symptoms of Pain and Weakness



(continued from page 25)

- Hours of operation
- A scheduling process
- Patient and caregiver education materials.

If a patient met the criteria, triage nurses would automatically prioritize and schedule an appointment with the NP. The office phone lines were opened 30 minutes prior to office hours, allowing for early patient calls and appointments in the Symptom Management Clinic.

Our Results

Data from the first eight months of AAMC's Symptom Management Clinic, July 2012 to February 2013, demonstrated effective interventions. On average, the clinic saw 41 patients per month. The most commonly treated symptoms were pain, weakness, nausea, vomiting, diarrhea, swelling, and fever. Due to effective and efficient triage, the Symptom Management Clinic did not manage any life-threatening emergencies. Based on clinical appropriateness, 65 percent of the patients were seen the same day, 25 percent were seen the next day, and the remaining 10 percent were seen in two or more days. Oncology ED visits associated with pain and weakness were reduced from 26 per month to 17, a 35 percent reduction. Out of 337 patients evaluated by the NP at the Symptom Management Clinic:

- 284 patients (84%) were sent home including 4 patients (1%) who were referred to hospice as a result of the visit
- 42 patients (12%) were referred to the outpatient infusion center for fluids or blood transfusions
- 11 patients (3%) were directly admitted to the hospital
- 3 patients (<1%) were sent to the emergency department.

Figure 1, left, shows ED visits prevented by presenting symptom. Figure 2, left, shows oncology unit admissions related to symptoms of pain and weakness.

Hospital readmissions are viewed as indicators of poor quality of care.[8] Indeed, a recent chart review of AAMC oncology readmissions suggested that 29 percent (unpublished observation)

Our Program At-a-Glance

Founded in 1902, Anne Arundel Medical Center is a 384-bed regional referral center located on a 57-acre campus in Annapolis, Md. It has a medical staff of more than 1,000 providers, including a 245 health system-employed provider medical group. AAMC includes the not-for-profit hospital with more than 30,000 inpatient admissions, 95,000 ED visits, and 100,000 outpatient visits annually, and a mental health and substance abuse center. AAMC serves an area of more than one million people and is the state's third busiest hospital, based on inpatient discharges. AAMC operates five diagnostic imaging facilities that together perform 159,000 imaging studies annually. Five regional pavilions with multispecialty services, including medical oncology, are strategically located throughout the market.

AAMC's Geaton and JoAnn DeCesaris Cancer Institute is a comprehensive community cancer program and includes a breast center, a four-vault radiation oncology center, a 42-chair outpatient infusion center, nurse navigation, a survivorship clinic, and psychosocial programs. Since 2007 there has been steady growth in the primary and extended market in medical, radiation, and surgical oncology. More specifically, over the past seven years, the number of new cases evaluated at the DeCesaris Cancer Institute has increased 50 percent to a total of 1,800 with over 300 ambulatory patients treated in the institute each day, making it one of the largest cancer programs in Maryland.

AAMC is the recipient of numerous awards and certifications, including an ACCC 2012 Innovator Award for its Rapid Access Chest and Lung Assessment Program, an ACCC 2014 Innovator Award for the Symptom Management Clinic described in this article, and Magnet® recognition by the American Nurses Credentialing Center in 2014.

Table 2. Ambulatory Care RN Role Dimensions for Healthcare	
1	Work with established evidence-based care management protocol (EBP).
2	Lead or participate in development and refinement of EBPs.
3	Collaborate on development of process and outcome indicators for EBPs.
4	Monitor (assessment and evaluation) current status of patients, often using telehealth modalities.
5	Make adjustments to treatment plan with specified EBP parameters.
6	Collaborate and communicate with healthcare team regarding patient status and needs.
7	Document all patient encounters in the EHR.
8	Refer patients who are out of alignment to MD/NP.
9	Maintain a long-term supportive relationship with patients and families.
10	Act as a resource and advocate for patients and families.
11	Collaborate on measurement of patient and family outcomes of care.
12	Find resources in the community.

were potentially preventable. One primary reason: crisis admissions that could have been anticipated and avoided with improved symptom management. Early data from primary care medical homes suggest that about 50 percent of hospital readmissions and 50 to 69 percent of ED visits can be prevented with even more comprehensive programs.[9,10]

Conclusion & Discussion

While the literature describes similar Symptom Management Clinics, these clinics are often based at academic programs, for single tumor types, offer weekly not daily appointments, and lack telephone triage nurses. Since 2012, a handful of oncology pioneers are participating in accountable care transformative models; however, there is a stunning lack of data on their patient-reported outcomes.

Research has demonstrated that improved symptom management benefits patients through:[11]

- Fewer dose modifications
- Fewer delayed treatments
- Increased access to supportive care
- Increased education exchanges for patients and caregivers
- Improved medication adherence
- Earlier treatment of symptoms
- Improved quality of life.

Haas and Hackbarth have identified 12 ambulatory care RN dimensions (Table 2, above) that allow nurses to be successfully integrated into ACOs and Patient-Centered Medical Homes (PCMHs).[12] Our oncology nurses are poised to lead and implement innovative strategies to deliver high-quality, lower-cost healthcare. They manage complex, chronic, and acute symptoms, as well as coordinate and serve as the patient advocate and communication link with the multispecialty team. Nurses must assume additional leadership responsibilities, identify processes for efficient resource utilization, and implement and track quality improvement, thereby increasing safety and potential value to patient-centered care.

Research suggests that systematic nursing assessments and interventions for patients result in better patient outcomes and increased quality of life.[13,14] For the concept to succeed, the entire management team must take responsibility for the comprehensive care of the oncology patient. The need to identify a system-wide approach to proactively reach out to high-risk patients must be developed.

The DeCesaris Cancer Institute is focusing on additional quality metrics and program development to support the value proposition, including:

- Financial and psychosocial distress management
- Transparency and cost awareness of drug regimens
- Expansion of its patient portal
- Reporting and tracking of patient-reported outcomes
- Advance care planning
- Survivorship care planning
- Expansion of triage hours for 24/7 coverage.

Results from AAMC's Symptom Management Clinic represent the first step towards a value-based model. To be comprehensive, both clinical and administrative changes must take place within the practice and hospital, as well as within our community providers. The oncology nurse is well-positioned to help guide us to this value-based model through enhanced use of major ambulatory care roles and skills such as advocacy, telehealth, patient education, care coordination, transitional care, and community outreach. OI

Catherine Brady-Copertino, RN, MS, OCN, is executive director of the DeCesaris Cancer Institute; Madelaine Binner, MBA, CRNP, DNP, is a nurse practitioner at the Survivorship Clinic; Susanne Tameris is practice manager, AAMC Oncology & Hematology; Barry Meisenberg, MD, is medical director of the DeCesaris Cancer Institute; Lynn Graze, MSN, OCN, is director of the Infusion Center at Anne Arundel Medical Center, Annapolis, Md.

References

1. Institute of Medicine. Levit LA, Balogh FEP, Nass SJ, Ganz PA (eds.) Delivering High-Quality Cancer Care: Charting a New Course for a System in Crisis. Washington, D.C. National Academics Press; 2013. Available online at: www.iom.edu. Last accessed Jan. 29, 2015.

2. Mori A, Yamaoka K, Tango T, Matsuda T, et al. Effectiveness of psychoeducation support on quality of life in early-stage breast cancer patients: A systematic review and meta-analysis of randomized controlled trials. *Qual Life Research*. 2014; 23(1):21-30.

3. Vandyk AD, Harrison MB, Mccartney G, Ross-White A, et al. Emergency department visits for symptoms experienced by oncology patients: a systematic review. *Support Care Cancer*. 2012; 20(8):1589-1599.

4. Mayer GG, Villaire M, Connell J. Ten recommendations for reducing unnecessary emergency department visits. *J Nurs Admin*. 2005;35(10):428-430.

5. Berry DL. Patient-reported symptoms and quality of life integrated into cancer care. *Semin Oncol Nurs*. 2011;27(3):203-210.

6. Zulig LL, Jackson GL, Provenzale D, Griffin JM, et al. Transportation: a vehicle roadblock to cancer care for VA colorectal cancer patients. *Clin Colorectal Cancer*. 2012;11(1):60-65.

7. Cleeland CS. Moving Beyond 'Best Supportive Care;' 2011. Available online at: www.endocrinologynetwork.com/articles/moving-beyond-best-supportive-care. Last accessed Jan. 26, 2015.

8. Earle CC, Landrum MB, Souza JM, Neville BA et al. Aggressiveness of Cancer Care Near the End of Life: Is it a Quality-of-Care Issue? *J Clin Oncol*. 26: 3860-3866, 20089.

9. Sprandio JT, Flounders BP, Lowry M and Tofani S. Data-Driven Transformation to an Oncology Patient-Centered Medical Home. *J Oncol Prac*. 9(3):130-132, 2013

10. Kuntz G, Tozer JM, Snegosky J, Fox J, Meumann K. Michigan Oncology Medical Home Demonstration Project: First-Year Results. *J Oncol Prac*. 10(5):294-297, 2014.

11. Coolbrant A, Van den Heede K, Vanhove E, DeBom A, et al. Immediate versus delayed sef-reporting symptoms and side effects during chemotherapy: does timing matter? *Eur J Oncol Nurs*. 201;15 (2):130-136.

12. Haas S, Hackbath DP. Dimensions of the staff nurse role in ambulatory care: Part III-using research data to design new models of nursing care delivery. *Nurs Econ*. 1995;13(4):230-241.

13. Oncology Nursing Society. Putting Evidence into Practice: Improving Oncology Patient Outcomes. J Tipton and L Eaton (eds). Pittsburgh; 2009.

14. Fessele K, Yendro S, Mallory G. Setting the bar: developing quality measures and education programs to define evidence-based, patient-centered, high quality care. *Clin J Oncol Nurs*. 2014;18(suppl.):7-11.


PCSP
RECOGNITION

BY SUSAN VAN DER SOMMEN, MHA, CMPE, FACHE

Patient-Centered Specialty Practice

How Bassett Healthcare achieved PCSP recognition

From 1980 to 2000, the U.S. population grew by 23 percent, from an estimated 227 million to 279 million.[1] During the same period, the incidence of cancer rose 66 percent from 807,000 to 1.34 million.[1] Approximately 14 million people are currently "cancer survivors," with an expectation that this number will increase to 18 million by 2022;[1] the current estimate of 1.6 million cancer diagnoses per year is expected to rise to 2.3 million by 2030.[1] Of additional concern is the fact that the cost of cancer care is rising at a rate faster than other disciplines.[1] From 2004 to 2010, the cost of cancer care in this country rose dramatically from $72 billion to $125 billion.[1] This trend is expected to continue, with estimated costs growing 39 percent by 2020 to $173 billion.[1]

Uneasiness over our healthcare system's ability to provide care to this increasingly complex population has been steadily rising over the past decade. A model that fails to provide adequate transition of care can result in less than optimal outcomes and wasteful spending.[2] In 2011 avoidable medical complications and hospital readmissions cost the U.S. between $25 billion and $45 billion of unnecessary expenditures.[2]

Taken together, it has become clear that the U.S. healthcare model as we know it is simply unsustainable.

In its publication, *Crossing the Quality Chasm: A New Health System for the 21st Century*, the Institute of Medicine (IOM) states that patient care should be safe, effective, evidence-based, patient-centered, timely, efficient, and equitable.[3] The IOM report notes that patients who leave one care setting for another often receive minimal information with regard to medications, self-care, and whom to seek out for answers to questions.[3] Further, the IOM developed 13 recommendations for improving the delivery of healthcare in this country (see Table 1, pages 35-36).

In 2010 the American College of Physicians (ACP) endorsed the Patient-Centered Medical Home Neighbor (PCMH-N) concept, recognizing that to attain a comprehensive, coordinated model of care that meets the aims of the IOM report, there must be bi-directional communication between primary care physicians and their specialist counterparts.[4] This model of care is particularly relevant to patients with a cancer diagnosis, the advent of which can bring about great fear, anxiety, and uncertainty to a population presently receiving care in a system that is fragmented and not adequately structured to meet their needs.[1] Unfortunately, the complex nature of a cancer diagnosis encumbers treating physicians as they seek to provide accurate, evidence-based, and timely care, and often leaves patients with questions about their treatment plan, goals, and likelihood of survival.

Why PCSP Recognition?

Care coordination and communication between and among providers are among the core tenets of the National Committee for Quality Assurance's (NCQA's) evaluation program for specialty practices: Patient-Centered Specialty Practice (PCSP). The program is designed to formalize processes that are often already in place. PCSP sets standards and provides accountability for those caring for our patients—from front-line staff to physicians, in both the specialty and primary care practices. PCSP intends to reduce dissatisfaction among patients due to incomplete communication and fragmented care, as well as to reduce waste and improve outcomes.[5] These reductions are accomplished through:[5]

- Agreements between caregivers—both formal and informal
- Standards and guidelines for referrals, including expectations of the referring and receiving providers
- Information about the care team and defined quality improvement measures.

...the goals of the PCSP are, ultimately, to enhance communication and coordination of care, resulting in increased patient satisfaction, reduced waste, and improved outcomes.

Though PCSP is proven to generate cost savings, providers are not always interested in pursuing a new model of care.[2] Pursuing institutional approval and provider buy-in to seek PCSP recognition fosters conversation about an enhanced model of care that is a sound structural fit with oncology practices and many aspects of healthcare reform. Additionally, it provides an opportunity to analyze an oncology practice and determine ways to improve patient care.

PCSP Goals

As noted earlier, the goals of the PCSP are, ultimately, to enhance communication and coordination of care, resulting in increased patient satisfaction, reduced waste, and improved outcomes. In many ways, the objectives are aligned with the American College of Surgeons Commission on Cancer (CoC) patient-centered standards, particularly those that were phased in this year—psychosocial distress screening, patient navigation, and survivorship care planning.

Oncology practices that have implemented PCSP standards have reported increased efficiency in their practices, fewer ER visits and hospital admissions, and a decreased length of stay.[1] Enhanced efficiency is obtained by ensuring each staff member works to the highest level of his or her competency, as well as licensure. Additionally, increased care coordination results in less duplication of services, which adds to increased clinical effectiveness and reduction in unnecessary costs.

PCSP: The Next Stage of Continuous Improvement at Bassett Healthcare

In 2014, despite being part of an integrated network accredited by The Joint Commission and the CoC, Bassett Healthcare recognized that care coordination among and between its physician groups was not optimal. Our referring physicians were very pleased with the care their patients were getting at Bassett Cancer Institute; they just wanted more information. For example, one physician shared what happened when he did not know that a long-time patient had recently succumbed to his cancer. After running into the patient's wife in the local grocery store, the physician asked the woman how her husband was doing and was embarrassed to learn that he had recently passed away.

According to the NCQA, primary care providers (PCPs) report sending patient information to specialists 70 percent of the time; specialists report receiving the information only 35 percent of the time.[5] Conversely, specialists report sending a report to the PCP 81 percent of the time, whereas PCPs report receiving it only 62 percent of the time.[5] Additionally, between 25 to 50 percent of referring physicians did not know if their patients had seen a specialist.[5] Clearly this communication gap is problematic for the providers and leaves patients vulnerable.

Patients, too, expressed their frustration to us, *"It would have been nice to have someone help me through the system, most of which I did on my own. I am a doctor. I have worked in this hospital for many years. I know who to call…but I am not the doctor and don't want to be. I want to be a patient."*

Another patient stated, *"I felt that communication often got lost…I traveled from one department to another with no one looking at all aspects of my care. This lack of continuity often caused me more angst than the actual diagnosis."*

Many of our primary care practices are certified Patient-Centered Medical Homes and have had great success in better managing their patients' care. With their success for inspiration and a shared vision for communication, Bassett Healthcare decided to pursue early adoption of the Patient-Centered Specialty Practice, with the goal of better care coordination and increased patient satisfaction.

Attaining & Sustaining the PCSP Model of Care

There are six standards in the PCSP application, each with its own elements—approximately 22 in total (see Table 2, page 37). Among these elements are "must pass" standards. If a practice cannot adequately demonstrate that it meets these critical elements within the domain, no credit is granted. There are a total of 100 points, and recognition may be granted with as few as 25 points. Of importance, policies and procedures that are created to meet these standards must be in place three months before a PCSP application is submitted. Therefore, we strongly advise careful review and consideration of the application in advance. While Bassett Cancer Institute's application results were strong, they clearly identified areas we could focus on for additional quality improvement (QI) efforts. We share our results below.

PCSP 1: Track & Coordinate Referrals

(20/22 Points)

A key feature of the Patient-Centered Specialty Practice is the concept of a "neighborhood"—that is, ensuring a smooth transition of care from the primary care provider to the specialist. At the Bassett Cancer Institute, our team developed a referring provider agreement with a select group of primary care practices

as a pilot for receiving PCSP recognition. The agreement clearly outlines the reason for the referral (consult, second opinion, transfer of care) and the urgency of the referral. Essentially, the neighborhood is a commitment between the primary care physician and the specialist to work together to provide evidence-based, safe, effective, and coordinated care to patients.

To meet this element we strongly urge programs to *leverage their electronic health record* (EHR)! Our practice provides patients with a care plan prior to their treatment and prints an after-visit summary, which details the care provided. Our information technology (IT) team amended the EHR specialty referral form to allow options—second opinion, consult, care during treatment, or full assumption of care. Additionally, our referral has a free-form text field so that a referring clinician can offer additional information, as warranted.

PCSP 2: Provide Access & Communication

(9/18 Points)

In our practice, we have a clinician (usually a physician) who is identified as the "doctor of the day." Each provider (via a rotating daily schedule) is responsible for taking add-ons and urgent referrals, answering questions, and speaking to patients who may call or stop in, in addition to his or her full clinic schedule.

As a performance improvement project, our team developed a new patient handbook that clearly delineates the roles of our specialists, the availability of interpreter services, social work, dietary services, etc. Additionally, we enhanced Bassett Cancer Institute's website to ensure patients had access to information about their diagnosis and educational websites.

Despite having these processes in place, our surveyor stated we did not sufficiently document that patients received same-day appointments, timely clinical advice after hours, and non-visit consultations with referring clinicians. These are areas that we will continue to address through QI initiatives.

PCSP 3: Identify & Coordinate Patient Populations

(7/10 Points)

Many of the requirements in this element are captured in demographic information and/or Meaningful Use measures. Practices that are not yet in Meaningful Use-Stage 2 (we were not at the time) may struggle with certain aspects of this measure, namely generating a list of patients and providing a "proactive" reminder of caring for a healthcare condition. The condition does not necessarily need to be oncology specific, but is, in fact, more focused on primary care.

PCSP 4: Plan & Manage Care

(17/18 Points)

Our team identified a variety of resources to help us meet this measure, most of which are common in oncology practices.

Members of the Bassett Healthcare team that worked to achieve Patient-Centered Specialty Practice recognition. (L to R) Robin Abbass, RT(T), manager, Radiation Oncology; Bertine McKenna, PhD, chief operating officer and executive vice-president; Frank Panzarella, FACHE, vice president, Operations; James Leonardo, MD, PhD, division chief, Medical Oncology; Sue van der Sommen, FACHE, administrative director; Christine Conkling, medical oncology and community outreach manager; Kelly Morris, RN, OCN, nurse manager; and Tom Manion, director, Musculoskeletal Services (formerly the practice and business manager at the cancer center).

These resources include our psychosocial needs assessment, chemo education packet, and patient fund assistance applications, as well as examples of sharing information through our EHR.

PCSP 5: Track & Coordinate Care

(3/16 Points)

Clearly, we fell short in this area, despite it being a key success factor in the "medical neighborhood." Some of the elements included tracking secondary referrals, which are defined as referrals generated when an oncologist refers a patient to another specialist. Additionally, our oncologists do not have referral agreements with specialists to whom they refer. Having these agreements in place would be an added benefit to our patients. For continuity of care, this referral information must be provided to the primary care physician. In our present practice, it is not. This definitely represents an area targeted for improvement.

Another aspect of care is the long-sought after "care transition" model. We could not effectively demonstrate a process for tracking our patients when they go to the emergency department (ED) or are admitted to the hospital. Although we often know this information—it is the inherent nature of an oncology practice to know

the status of its patients—we do not have a formal process for effectively tracking this information.

Recognizing these gaps in our care model and the value that enhanced care coordination will add to our practice, our senior leaders recently approved a nurse navigator position. We are confident that the addition of a skilled navigator will assist our team in improving our patients' experience. Again, this highlights how the pursuit of the Patient-Centered Specialty Practice model can assist cancer administrators and practitioners in identifying opportunities for improvement and seeking solutions to improve the patient experience. If you apply for PCSP recognition and have a plan to hire a navigator in the future, be sure to include that information in the application.

PCSP 6: Measure & Improve Performance

(12/16 Points)

This element is largely focused on performance improvement, patient and family engagement, and setting goals to improve access to care. Bassett Cancer Institute uses Press Ganey to assess our overall patient satisfaction levels. Since clinician-specific scores are available, we share this information with our providers. In addition, our oncology team hosts patient focus groups to understand how our patients feel about our program—from our new patient handbook to the colors in our waiting area.

For programs interested in achieving PCSP recognition, this element provides an opportunity to leverage CoC standards 4.7 and 4.8: Studies of Quality.

We have found that coordinating improvement initiatives with our primary care colleagues is an area that requires further attention.

Leverage Existing Structures & Accreditations

Oncology practices are well suited for the PCSP model, particularly those that participate in CoC accreditation, QOPI (or other performance improvement initiatives), NAPBC, and/or Meaningful Use—which is a key component of PCSP measurement. Many components from these various accreditations and recognitions can be cross-walked with the PCSP scoring model, including, but not necessarily limited to, patient navigation, survivorship, and psychosocial distress screening.

Patient Focus, Measurable Results

The ultimate goal, of course, is always to provide exceptional, evidence-based care for our patient population by partnering with patients and referring providers. Additionally, the PCSP care model will better position oncology practices for health-care reform and to meet the challenges of the Institute for Healthcare Improvement's triple aim—improving the patient experience, enhancing the health of the population, and reducing the costs of care. OI

Susan van der Sommen, MHA, CMPE, FACHE, is administrative director of the Bassett Cancer Institute, Bassett Healthcare, Cooperstown, N.Y.

References

1. National Research Council. *Delivering High-Quality Cancer Care: Charting a New Course for a System in Crisis*. Washington, DC: The National Academies Press, 2013.

2. Burton R. Health policy briefs: improving care transitions. *Health Affairs;* Sept. 13, 2012. Available online at: www.healthaffairs.org/healthpolicybriefs/brief.php?brief_id=76. Last accessed Jan. 13, 2015.

3. Institute of Medicine. *Crossing the Quality Chasm: A New Health System for the 21st Century*. Washington, DC: National Academy Press, March 2001.

4. American College of Physicians. The Patient-Centered Medical Home Neighbor: The Interface of the Patient-Centered Medical Home with Specialty/Subspecialty Practices; 2010. Available online at: www.acponline.org/advocacy/current_policy_papers/assets/pcmh_neighbors.pdf. Last accessed Jan. 13, 2015.

5. NCQA. *Patient-Centered Specialty Practice Recognition.* Available online at: *www.ncqa.org/Portals/0/Newsroom/2013/PCSP%20Launch/PCSPR%202013%20White%20Paper%203.26.13%20formatted.pdf.* Last accessed Jan. 13, 2015.

Our Program At-a-Glance

Bassett Healthcare Network is an integrated healthcare system spanning over 5,600 square miles throughout an eight-county region in rural upstate New York. The network includes six affiliated hospitals and over 40 community and school-based health centers. Bassett Medical Center, the network's flagship site, is located in Cooperstown, N.Y., overlooking beautiful Otsego Lake.

Bassett Cancer Institute is a comprehensive community cancer center comprised of medical oncology, an ACRO-accredited radiation oncology department, and hematology. Having been continuously accredited by the CoC since 1947, it is one of the longest-standing accredited cancer centers in the country, and most recently achieved Gold Status.

Bassett Cancer Institute includes five infusion centers and two linear accelerators, with 1,244 accessioned cases in 2013. The cancer institute also provides screening services via a mobile medical coach, which, in July of 2014, received the Community Health Improvement Award from the Healthcare Association of New York State.

Table 1. IOM Recommendations for Improving Healthcare Delivery in the U.S.[3]

Recommendation 1	All healthcare organizations, professional groups, and private and public purchasers should adopt as their explicit purpose to continually reduce the burden of illness, injury, and disability, and to improve the health and functioning of the people of the United States.
Recommendation 2	All healthcare organizations, professional groups, and private and public purchasers should pursue six major aims; specifically, healthcare should be safe, effective, patient-centered, timely, efficient, and equitable.
Recommendation 3	Congress should continue to authorize and appropriate funds for, and the Department of Health and Human Services should move forward expeditiously with the establishment of, monitoring and tracking processes for use in evaluating the progress of the health system in pursuit of the above-cited aims of safety, effectiveness, patient-centeredness, timeliness, efficiency, and equity. The Secretary of the Department of Health and Human Services should report annually to Congress and the President on the quality of care provided to the American people.
Recommendation 4	Private and public purchasers, healthcare organizations, clinicians, and patients should work together to redesign healthcare processes in accordance with the following rules: 1. Care based on continuous healing relationships 2. Customization based on patient needs and values 3. The patient as the source of control 4. Shared knowledge and the free flow of information 5. Evidence-based decision making 6. Safety as a system property 7. The need for transparency 8. Anticipation of needs 9. Continuous decrease in waste 10. Cooperation among clinicians.
Recommendation 5	The Agency for Healthcare Research and Quality (AHRQ) should identify not fewer than 15 priority conditions, taking into account frequency of occurrence, health burden, and resource use. In collaboration with the National Quality Forum (NQF), the agency should convene stakeholders, including purchasers, consumers, healthcare organizations, professional groups, and others, to develop strategies, goals, and action plans for achieving substantial improvements in quality in the next 5 years for each of the priority conditions.
Recommendation 6	Congress should establish a Healthcare Quality Innovation Fund to support projects targeted at: 1. Achieving the six aims of safety, effectiveness, patient-centeredness, timeliness, efficiency, and equity; and/or 2. Producing substantial improvements in quality for the priority conditions. The fund's resources should be invested in projects that will produce a public-domain portfolio of programs, tools, and technologies of widespread applicability.
Recommendation 7	AHRQ and private foundations should convene a series of workshops involving representatives from healthcare and other industries and the research community to identify, adapt, and implement state-of-the-art approaches to addressing the following challenges: • Redesign of care processes based on best practices • Use of information technologies to improve access to clinical information and support clinical decision making • Knowledge and skills management • Development of effective teams • Coordination of care across patient conditions, services, and settings over time • Incorporation of performance and outcome measurements for improvement and accountability. (*continued on page* 36)

Table 1. IOM Recommendations for Improving Healthcare Delivery in the U.S.[3] *(continued)*

Recommendation 8	The Secretary of the Department of Health and Human Services should be given the responsibility and necessary resources to establish and maintain a comprehensive program aimed at making scientific evidence more useful and accessible to clinicians and patients. In developing this program, the Secretary should work with federal agencies and in collaboration with professional and healthcare associations, the academic and research communities, and the NQF and other organizations involved in quality measurement and accountability.
Recommendation 9	Congress, the executive branch, leaders of healthcare organizations, public and private purchasers, and health informatics associations and vendors should make a renewed national commitment to building an information infrastructure to support healthcare delivery, consumer health, quality measurement and improvement, public accountability, clinical and health services research, and clinical education. This commitment should lead to the elimination of most handwritten clinical data by the end of the decade.
Recommendation 10	Private and public purchasers should examine their current payment methods to remove barriers that currently impede quality improvement, and to build in stronger incentives for quality enhancement.
Recommendation 11	The Health Care Financing Administration (HCFA) and AHRQ, with input from private payers, healthcare organizations, and clinicians, should develop a research agenda to identify, pilot test, and evaluate various options for better aligning current payment methods with quality improvement goals.
Recommendation 12	A multidisciplinary summit of leaders within the health professions should be held to discuss and develop strategies for: 1. Restructuring clinical education to be consistent with the principles of the 21st Century health system throughout the continuum of undergraduate, graduate, and continuing education for medical, nursing, and other professional training programs; and 2. Assessing the implications of these changes for provider credentialing programs, funding, and sponsorship of education programs for health professionals.
Recommendation 13	The Agency for Healthcare Research and Quality should fund research to evaluate how the current regulatory and legal systems: 1. Facilitate or inhibit the changes needed for the 21st Century healthcare delivery system, and 2. Can be modified to support healthcare professionals and organizations that seek to accomplish the 6 aims set forth in Chapter 2.

Table 2. PCSP Recognition: 6 Standards, 22 Elements[5]

1. Track & Coordinate Referrals (22 pts)	*A. Referral process and agreements B. Referral content *C. Referral response
2. Provide Access & Communication (18 pts)	A. Access B. Electronic access C. Specialty practice responsibilities D. Culturally and linguistically appropriate services (CLAS) *E. The practice team
3. Identify & Coordinate Patient Populations (10 pts)	A. Patient information B. Clinical data C. Coordinate patient populations
4. Plan & Manage Care (18 pts)	A. Care planning and support self-care *B. Medication management C. Use of electronic prescribing
5. Track & Coordinate Care (16 pts)	A. Test tracking and follow-up B. Referral tracking and follow-up C. Coordinate care transitions
6. Measure & Improve Performance (16 pts)	A. Measure performance B. Measure patient and family experience *C. Implement and demonstrate continuous quality improvement D. Report performance E. Use of certified EHR technology

Recognition starts with 25 points. *Indicates "must pass" elements.

From Distress Screenings to Solutions

BY LORI MCMULLEN, RN, MSN, OCN

January 1, 2015, marked the implementation date for several new standards required of cancer programs seeking accreditation from the American College of Surgeons Commission on Cancer (CoC), including Standard 3.2, psychosocial distress screening. This standard requires that "the cancer committee develops and implements a process to integrate and monitor onsite psychosocial distress screening and referral for the provision of psychosocial care."[1] The CoC permits for some flexibility in the screening process by allowing cancer programs to select their own screening tool and to determine the best time to screen, as long as cancer patients are screened at least once during a pivotal medical visit. If the screening identifies distress, the cancer program must provide a link to psychosocial services, either onsite or by referral.[1]

The Institute of Medicine (IOM) in its 2008 report *Cancer Care for the Whole Patient: Meeting Psychosocial Health Needs* revealed that between 29 to 43 percent of cancer patients report psychosocial distress.[3] One of the issues in recognizing distress as a concern for cancer patients is that distress is discounted as being a normal consequence of a cancer diagnosis.[4] Additionally, the topic of distress is not usually a topic of conversation during a medical visit. "Communication regarding psychosocial issues may be hampered by competing expectations as to who should take the lead in initiating such discussions"—the physician or the patient.[5]

At the Edward and Marie Matthews Center for Cancer Care, Plainsboro, N.J., the process for developing and implementing Standard 3.2 began in January 2013. The Matthews Center for Cancer Care is the community cancer program of the Princeton Healthcare System. Two medical oncologists and one radiation oncologist deliver outpatient oncology care with 950 abstracted cases annually. The center houses radiation oncology and an outpatient infusion room. The cancer program is supported by an FTE oncology nurse navigator, an American Cancer Society patient-navigator (8 hours a week), and a registered dietitian (2 hours per week); outpatient social service referrals are made to Cancer*Care*®.

dis·tress (dĭ-strĕs´)

an unpleasant experience of an emotional, psychological, social, or spiritual nature that interferes with the ability to cope with cancer treatment. It extends along a continuum, from common normal feelings of vulnerability, sadness, and fears, to problems that are disabling, such as true depression, anxiety, panic, and feeling isolated or in spiritual crisis.

NATIONAL COMPREHENSIVE CANCER NETWORK[2]

Developing a Distress Screening Tool

The first step in developing the distress screening process was to form a workgroup from members of the Cancer Committee. The workgroup included the cancer program director, the outpatient infusion room assistant nurse manager, the cancer program manager, the oncology practice nurse, the breast health nurse, the inpatient clinical nurse leader, the inpatient nurse manager, the oncology nurse navigator, and the radiation oncology nurse; the inpatient social worker (who is the psychosocial representative on the Cancer Committee) was available as a consultant.

Top: University Medical Center of Princeton at Plainsboro, Plainsboro, N.J.
Bottom: The entrance to the Edward and Marie Matthews Center for Cancer Care.

The workgroup's underlying goal: to design a process for distress screening that could be easily incorporated into daily routine, across the entire healthcare system, and using the support resources currently available to be compliant with CoC standard 3.2. Despite the ease of using the NCCN Distress Thermometer, which has already been validated, the planning team felt that the tool itself was redundant with questions pertaining to physical symptoms. These questions are already reviewed at medical appointments, and while patients could clearly indicate their degree of distress on the thermometer, there was no way of knowing what was causing the distress unless patients only mark one symptom. The workgroup quickly made the decision to develop its own distress screening tool.

The workgroup started by conducting a literature review to see how other cancer programs were incorporating distress screening. The literature review revealed a 2012 article written by Kendall, Hamann, and Clayton, "Oncology Distress Screening: Distress Prevalence, New Standards, and Implementation," published in *Oncology Issues*.[6] The article reviewed the process that was established at the Simmons Cancer Center in Dallas, Tex. The oncology nurse navigator, who was the team lead for the project, contacted the lead author, Jeffrey Kendall. Their subsequent phone conversation helped guide the workgroup in the development of its own distress screening tool.

With permission from Kendall, the workgroup remodeled the tool used by the Simmons Cancer Center into a format that would allow for the best use of our support services. Our final product was a paper and pencil distress screening tool (Figure 1, pages 41 and 42). After learning from our literature review that having the definition of distress on the tool itself is helpful,[7] the workgroup added the definition to the top of its tool.

The distress screening tool identifies six areas most likely to cause distress in our patients:

1. Weight
2. Sadness
3. Anxiety
4. Concerns about children and/or family
5. Concerns about significant others
6. Financial concerns.

There is also an area where patients can identify an "other" concern that is not represented on the distress screening tool.

The workgroup decided to use a 0-5 Likert-type scale rather than a 0-10 scale. While some programs have established a referral process for lower scores on the scale, such as written information for a response of 3-5, referral to the appropriate professional within 48 hours for a response of 6-8, and immediate referral for a response of 9-10, we were looking to offer referrals to patients with significant levels of distress—a 4 or 5 on our scale. That said, patients have the option to refuse a referral or to request a referral without an identified distress trigger. The nurse who administers the distress screening tool is responsible for making the appropriate referrals. Therefore, the back of the tool has space for the staff to document who administered the tool and what educational materials or referrals were made. Our goal: to contact patients within 24 hours.

The workgroup's next step involved establishing referral pathways to the appropriate professional and timing protocols for administering the tool.

To make the referral process as seamless as possible, the workgroup worked with support services to create an algorithm with parameters for potential referrals (Figure 2, page 44). The algorithm guides the clinician who administers the distress screening tool to the appropriate support service. A second algorithm addresses when distress screening should take place (Figure 3, page 45). As timing is critical, the workgroup made the decision not to administer screening during "high points" of patient

(continued on page 43)

Figure 1. Matthews Center for Cancer Care Distress Screening Tool (*continued on back*)

Distress: "An unpleasant experience of an emotional, psychological, social, or spiritual nature that interferes with the ability to cope with cancer treatment. It extends along a continuum, from common normal feelings of vulnerability, sadness, and fears, to problems that are disabling, such as true depression, anxiety, panic, and feeling isolated or in spiritual crisis."

(NCCN practice guidelines for the management of psychosocial distress. National Comprehensive Cancer Network. Oncology (Williston Park)13(5A): 113-47, 1999. [PUBMED Abstract]

The staff of the Matthews Center for Cancer Care recognizes that cancer care is more than just receiving treatments. Peace of mind and a sense of well-being are essential for you to achieve long-term success. Please tell us how you are doing today by completing this screening tool.

☐ Check this box if there are no changes since the last time you completed this survey.

STEP 1. Please circle the number for each symptom that best describes how you feel now:

(0=no complaints; 5=severe complaints).

No weight loss	0	1	2	3	4	5	Significant weight loss
No sadness	0	1	2	3	4	5	Significant sadness
No anxiety	0	1	2	3	4	5	Severe anxiety
No concerns about children/family	0	1	2	3	4	5	Significant concerns about children/family
No concerns about your significant other	0	1	2	3	4	5	Severe concerns about your your significant other
No financial concerns	0	1	2	3	4	5	Severe financial concerns
Other problems	0	1	2	3	4	5	Tell us: _____

_____

_____

STEP 2. If you want to be contacted by one of our professionals, please check the box next to the professional and he or she will contact you.

☐ Cancer Dietitian ☐ UMCPP Chaplain ☐ Nurse Navigator ☐ Financial Services

☐ Check this box if you do not want to be contacted by a support service staff member.

Your name: (*please print*) _____ Date: _____

Best contact method (*phone or email address*): _____

Name of your treating physician: _____

(*continued on page 42*)

For Staff Use Only:

Date of Assessment	Provider Signature	(Any Response) Educational Materials	(Response of 4 or 5) Patient Referred to:	MD Notified and Date
			Referred to: Facility name:	
			Referred to: Facility name:	
			Referred to: Facility name:	

Referral Contact Information

Cancer Dietitian
(*Name, phone number, and email*)

UMCPP Chaplain Office
(*Name, phone number, and email*)

Cancer*Care* Social Worker
(*Name, phone number, and email*)

Breast Navigator
(*Name, phone number, and email*)

Breast Resource Center
(*Name, phone number, and email*)

Nurse Navigator
(*Name, phone number, and email*)

American Cancer Society Patient Navigator
(*Name, phone number, and email*)

UMCPP Financial Counselor
(*Name, phone number, and email*)

Support Groups
(*Name, phone number, and email*)

*For referrals to homecare, palliative care, and/or hospice, contact treating physician.

(continued from page 40)
distress, for example, the day patients are given their cancer diagnosis. The workgroup also took into consideration the workflow of the areas where the distress screening tool would be administered; nursing units with more than 15 minutes face-to-face time with patients were identified as the primary administrators of the distress screening tool.

The distress screening tool was piloted from March 2013 through August 2013. The workgroup wanted an opportunity to work out any issues surrounding the implementation or referral process prior to presenting its work. The final product was presented to the Cancer Committee for approval in October 2013.

Once the distress screening tool is complete, the oncology nurse navigator collects copies of the distress screening tool and enters the responses and referrals into a spreadsheet. Original copies of completed tools are kept in the patient's medical chart. When distress screening is conducted in radiation oncology, the collaborating medical oncologist is notified when patients report any distress level of 4-5, including what interventions were initiated. The oncology nurse navigator reports distress screening metrics quarterly to the Cancer Committee.

Once the workgroup felt that the distress screening process was complete, staff received face-to-face education about their responsibilities for completing the distress screening tool, as well as a list of "helpful hints" for introducing the distress screening tool into conversations with patients (see page 46).

Pilot Outcomes

Over a six-month period, the oncology nurse navigator collected the distress screening tool from departments that participated in the pilot, including radiation oncology, outpatient infusion, the Breast Health Center, the inpatient oncology unit, and the medical oncologist practice. She checked for completion and that appropriate referrals had been made. The oncology nurse navigator then followed up with patients—either in person or by phone—to confirm that patients had completed the referral process. It quickly became apparent that patients were not taking the initiative to contact the support staff on their own, and the decision was made to have cancer program staff initiate contact with support staff, providing the patient's contact information.

Our data revealed that 41 percent of our patients required referrals for distress symptoms, which is concordant with the 2008 IOM report. The workgroup was satisfied that it had accomplished its goal.

Anecdotally, our patients reported that the distress screening tool is user-friendly. Nurses who reviewed the completed tool with the patients reported that the distress screening tool only added about 15 minutes to their daily routine.

One result we did not anticipate: an additional 20 percent of the patients who took the distress screening tool self-referred to our support services, which included the chaplaincy department, a department that had not previously seen outpatient cancer patients.

The oncology nurse navigator discusses financial resources with a patient.

Improving the Process

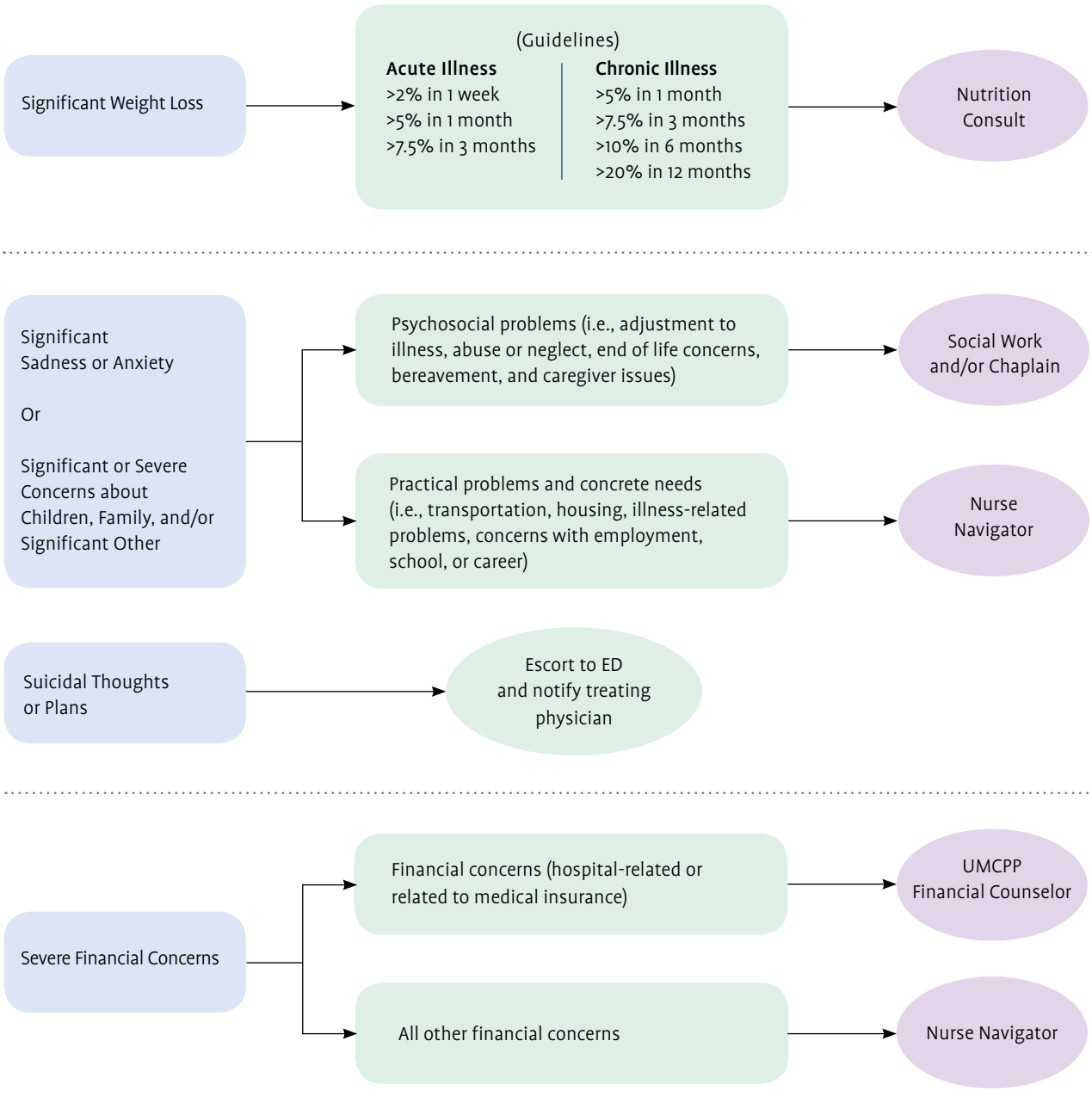
The workgroup's final task was to write a policy and procedure for administration of the distress screening tool. Since Princeton Healthcare System is a Magnet facility, the policy was reviewed and approved by the Clinical Practice Committee, as well as the Cancer Committee. (View this policy online at www.accc-cancer.org/oncology_issues/MA2015.asp).

Inpatient staff who administered the distress screening tool identified one challenge: the tool is paper and pencil, and inpatient staff chart exclusively in an EHR. The inpatient nurses who were part of the workgroup took on this challenge, working with the IT department to make the distress screening tool part of the EHR. In April 2014, following a hospital-wide education program, the distress screening tool was launched as part of the EHR. Now the distress screening tool is entered into the system by the staff as a direct order when the patient is identified as a cancer patient. This process improvement has made it possible for a cancer patient admitted anywhere in the Princeton Healthcare System to be screened for distress, if appropriate.

A second challenge was educating staff to take full ownership of the distress screening tool, including completing the tool and identifying the appropriate referrals to support services. In the first month of the pilot, the oncology nurse navigator found that 25 percent of distress screening tools were incomplete. Our solution: identifying a staff member to act as "volunteer champion."

(continued on page 45)

Figure 2. Matthews Center for Cancer Care Distress Tool Pathways



Acknowledgements

The author of this article was part of the initial interdisciplinary team that developed and implemented the distress screening tool. She would like to thank her fellow workgroup members: Judy Neuman, CTR, cancer program director; Deborah Richey, RN, MSN, OCN, nurse manager, cancer program; Beth Beckett, RN, BSN, OCN, OPI assistant nurse manager; Sheryl Smolesky, RN, OCN, radiation nurse; Monica Lyle, RN, BSN, OCN, clinical practice nurse; Inez Brandon, MSN, RN, OCN, CHPN, CNL, MNO, clinical nurse leader; Audrey Amir, MSN, RN, CNL, PCCN, MNO, clinical nurse leader; Humility Samayang, RN, BSN, BC, nurse manage; Britni Walton, BSN, RN, OCN, WCC; Nune Mehrabyan, RN, BC, MS, IT Department; and Mary Kiensicki, RN, CBCN, breast health nurse.

(continued from page 43)

This individual was then tasked with ensuring that all distress screening tools placed in the folder for the oncology nurse navigator to collect were complete with appropriate referrals. (Fortunately, the volunteer champion was able to "retire" from her position at the conclusion of the pilot.)

Patient-Centered Care

Although implementation of the distress screening tool required a commitment of time from Princeton Healthcare System nursing staff, we have successfully implemented psychosocial distress screening to become compliant with CoC standard 3.2 without adding an FTE to our budget.

Staff who are responsible for administering the distress screening tool have observed that it has improved our delivery of patient-centered care. For example, screening patients for distress has created an opportunity to open dialogue and engage our patients beyond their clinical needs. This benefit is apparent in the number of referrals to support services and resources that are triggered as a result of distress screening. Since the distress screening tool is usually first administered just after diagnosis or early in the treatment process, concerns are identified and communicated to the care team, allowing for prompt interventions that can promote a positive effect before these concerns become insurmountable or paralyzing.

The distress screening tool has also improved care coordination by expanding the circle of multidisciplinary support for our patients. For example, both the registered dietitian and social worker have reported an increase in referrals since distress screening was implemented. OI

Lori McMullen, RN, MSN, OCN, is senior oncology nurse navigator, University Medical Center of Princeton at Plainsboro, Edward and Marie Matthews Center for Cancer Care, Plainsboro, N.J.

References

1. American College of Surgeons. Cancer Program Standards 2012: Ensuring Patient-Centered Care, Version 1.1.2, Standard 3.2 Psychosocial Distress Screening. Chicago, IL, 2012 Available online at: www.facs.org/cancer. Last accessed Oct. 6, 2014.

2. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines Version 2.2014, Distress Management. Available online at www.nccn.org. Last accessed March 7, 2014.

3. Institute of Medicine. Cancer Care for the Whole Patient: Meeting Psychosocial Health Needs. Washington, DC: The National Academies Press; 2008. Available online at: http://www.nap.edu/openbook.php?record_id=11993. Last accessed Sept. 7, 2014.

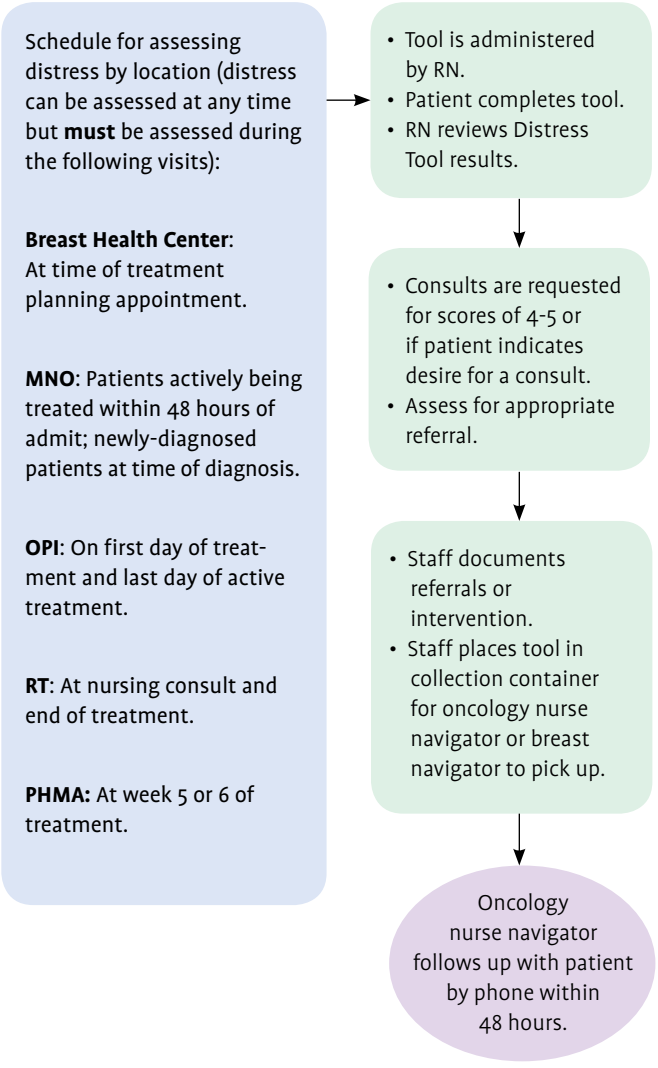
4. Fallowfield L, Ratcliff D, Jenkins V, Saul J. Psychiatric morbidity and its recognition by doctors in patients with cancer. *British J Cancer*. 2001;84 (8):1011-1015.

5. Detmar SB, Aaronson LDV, Weaver M, Muller, Schornagel, J H. How are you feeling? Who wants to know? Patients' and oncologists' preferences for discussing health-related quality-of-life issues. *J Clin Oncol*. 2000;18(18):3295-3301.

6. Kendall J, Hamann H, Clayton S. Oncology distress screening: Distress prevalence, new standards, and implementation. *Oncol Issues*. 2012; 27(6): 22-28.

7. Fulcher C, Gosselin-Acomb T. Distress assessment: Practice change through guideline implementation. *CJON*. 2007;11(6): 817-821.

Figure 3. Matthews Center for Cancer Care Distress Tool Administration Pathway



(continued on page 46)

FACTS AND HELPFUL HINTS FOR ADMINISTERING THE DISTRESS TOOL (DT)

The American College of Surgeons (ACoS) Commission on Cancer (CoC), the accrediting body for cancer programs, has added standard 3.2 Psychosocial Distress Screening as a requirement for achieving accreditation. The standard promotes patient-centered care with the goal of improving the quality of cancer care.

Why is Distress Screening Important?

- 20 to 47 percent of newly-diagnosed and recurrent cancer patients show significant levels of distress
- Failure to recognize and treat distress can lead to:
  - Trouble making decisions about treatment
  - Extra visits to the ED or physician's office
  - Poor quality of life and have a negative impact on survival.

- Early evaluation and screening of distress:
  - Improves medical management
  - Ensures appropriate referrals to psychosocial resources that can lead to lower levels of stress in three months compared to those without screening and referral
  - Better adherence to treatment
  - Better communication
  - Fewer calls and visits to MD office
  - Avoidance of anger and development of severe anxiety or depression.

Suggestions for Introducing Distress Screening

In screening patients for distress, our goal is to provide them with the best resource to address their problem(s). As you introduce the tool:

- Build rapport and trust before expecting the patient to talk about something personal and revealing.
- Make it clear that this is a normal, routine assessment rather than something unusual.
- Take your time and talk generally about how things are going before introducing the distress screening tool. For example, *"How have you been managing with your diagnosis and treatment?"*
- If the patient identifies a distressing issue, move from the general to the specific. For example, *"You've put down weight loss. Can you tell me a bit more about this?"* And then follow up with, *"What do you think is causing you to lose weight?"*
- Explore how the patient is using their own resources in managing their distressing issue. For example, *"Can you tell me what you are doing at home to manage your weight loss?"*
- Acknowledge achievements and build on things that are going well.
- Focus on a solution to the problem rather than the problem itself.
- Offer (and encourage) appropriate referrals.

Resources

1. American Cancer Society. Distress in People with Cancer; 2012. Available online at: www.cancer.org/acs/groups/cid/documents/webcontent/002827-pdf.pdf. Last accessed Jan. 28, 2015.

2. Brennan J. A Manual for Screening and Responding to Cancer Distress using the Distress Thermometer and Problem Checklist; 2009. Available online at: www.ncsi.org.uk/wp-content/uploads/DT-Instruction-Manual-Bristol-method.pdf. Last accessed Jan. 28, 2015.

3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines Distress Management, Version 2.2013. Available online at: www.nccn.org.

Edward & Marie Matthews Center for Cancer Care
University Medical Center of Princeton *at Plainsboro*

ACCC: MEETING YOUR NEEDS

Gear up for a full menu of meetings with need-to-know information for the entire cancer care team. Don't miss out on unparalleled opportunities to advance your learning in critical areas, and earn CE credits. Be sure to share this information with your colleagues who can benefit from these events.

ACCC
Association of Community Cancer Centers

FINANCIAL ADVOCACY REGIONAL MEETINGS

Bridging the Gap between Patient Needs and Financial Resources
These FREE one-day meetings help sharpen the skills and knowledge base of financial advocates.

Tuesday, May 5, 2015
Tampa, Florida

Tuesday, June 2, 2015
Silver Spring, Maryland

Tuesday, June 23, 2015
Burlingame, California

ONCOLOGY REIMBURSEMENT MEETINGS

Any member of the cancer care team who deals with oncology business and reimbursement will benefit from these FREE one-day meetings. Gain a full-spectrum perspective with sessions on payment reform; the latest trends in coding and billing; proper management of financial data; and the practical application of radiation oncology CPT codes.

Thursday, April 16, 2015
Chicago, Illinois

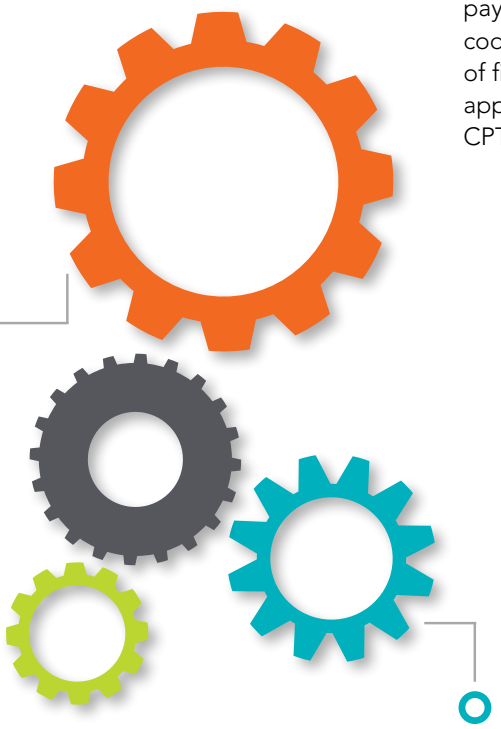
Tuesday, April 28, 2015
Raleigh, North Carolina

Tuesday, May 19, 2015
Scottsdale, Arizona

Tuesday, August 25, 2015
Indianapolis, Indiana

Tuesday, November 17, 2015
Boston, Massachusetts

Thursday, December 10, 2015
Birmingham, Alabama



ONCOLOGY PHARMACY EDUCATION NETWORK REGIONAL MEETINGS

These two-day meetings provide take-away tools and information to oncology pharmacists and members of the cancer care team in pharmacy operations.

May 15–16, 2015
New Brunswick, New Jersey

June 26–27, 2015
Fort Lauderdale, Florida

July 10–11, 2015
Charlotte, North Carolina

Stay Tuned!

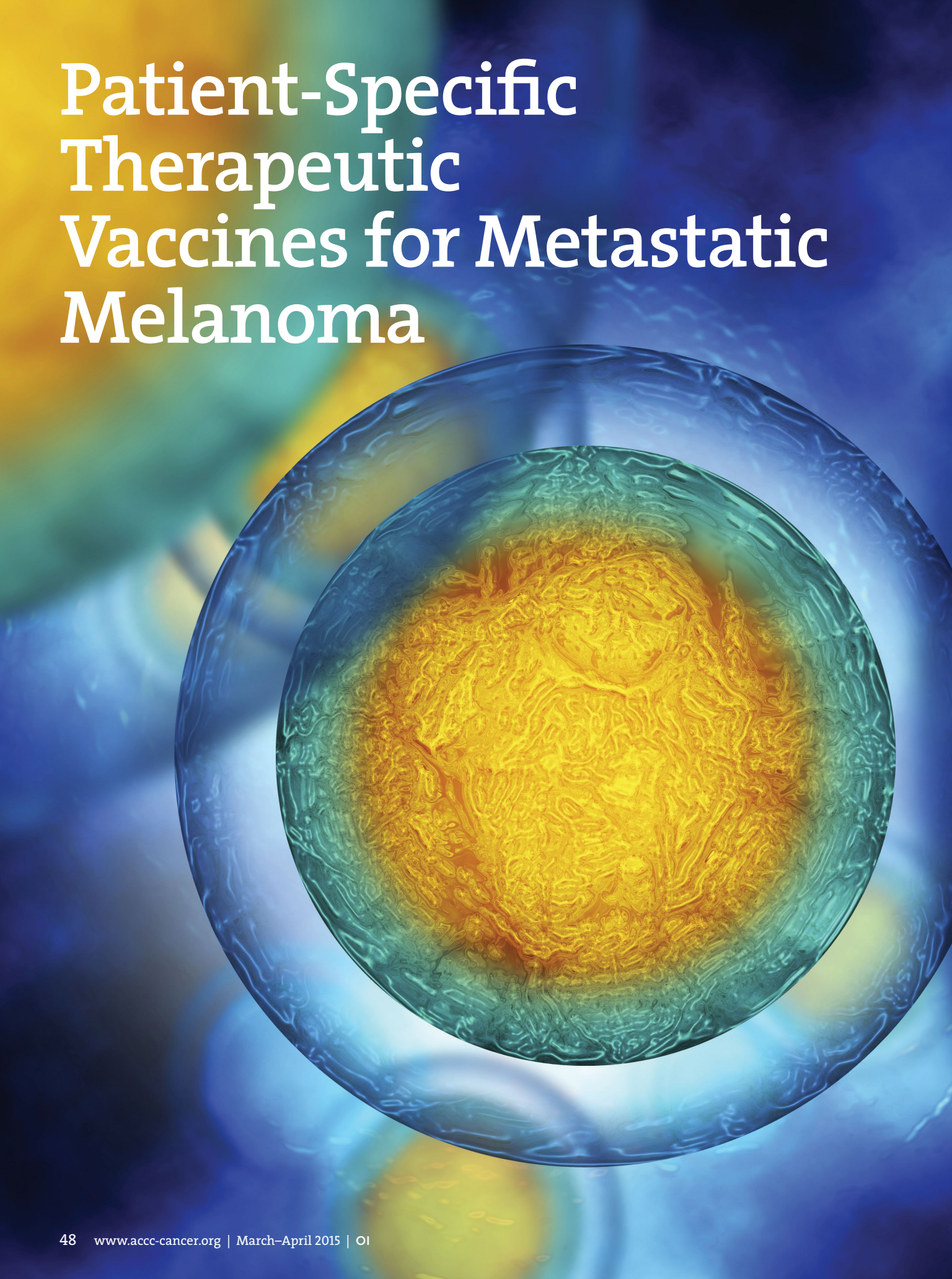
32ND NATIONAL ONCOLOGY CONFERENCE

The ACCC National Oncology Conference delivers innovative ideas, solutions, and strategies to implement in your cancer program.

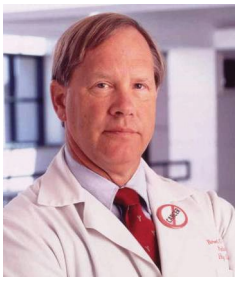
October 21–24, 2015
Portland Marriott Downtown Waterfront
Portland, Oregon

For details on all ACCC meetings go to www.accc-cancer.org/meetings

Patient-Specific Therapeutic Vaccines for Metastatic Melanoma



BY ROBERT O. DILLMAN, MD



The only standard treatments for metastatic melanoma that have been associated with long-term overall survival (OS) are surgical resection, and immunotherapies that include the immune-stimulating cytokine interleukin-2 (IL2), the anti-cytotoxic T lymphocyte antigen-4 (CTLA-4) monoclonal antibody ipilimumab, and the anti-programmed death 1 (PD1) monoclonal antibodies nivolumab and pembrolizumab (aka lambrolizumab). Long-term OS has not been enhanced by classical chemotherapy, or agents that target enzymes associated with *BRAF* and MET. Until recently, 5-year OS rates for patients with unresectable metastatic melanoma were less than 10 percent.[1,2] For many years dacarbazine or temozolomide chemotherapy alone, or in combination with other chemotherapies, was the most frequently used treatment for patients with metastatic melanoma. In randomized trials, 2-year survival rates with these agents were less than 20 percent;[3-6] 5-year OS rates were not reported. Combinations of chemotherapy also failed to improve long-term survival.[3, 7-10]

Surgical Resection

The Society for Immunotherapy of Cancer (SITC) guidelines for treatment of metastatic melanoma recommend surgical resection as the treatment of choice in patients whose disease can be completely resected.[11] Surgical resection of metastatic disease is associated with 5-year OS rates of between 25 and 35 percent, depending on patient selection and the sites of metastases.[12-14] This approach is limited to patients who are fit for surgery, and typically to those who have either a single metastatic site, or a few metastases limited to a single organ that can be readily resected (e.g., lung segmentectomy, section of bowel, lymph node station, or hepatic lobe), or readily accessible solitary sites in two or three separate organs. It has been assumed that an underlying immune response makes long-term OS possible in post-metastasectomy patients, many of whom undergo repeated resections of recurrent metastases over the course of their disease. Such patients were the focus of randomized trials testing a vaccine derived from allogeneic tumor cell lines,[15] and granulocyte-macrophage colony stimulating factor (GM-CSF), and/or melanoma peptides gp100, MART-1, and tryosinase.[16] Unfortunately none of these improved survival compared to placebo-based control arms.

BRAF and MET Inhibitors

In patients whose tumors express V600 *BRAF* mutations, oral, targeted enzyme inhibitors are useful for gaining rapid control of widespread or rapidly progressing metastatic disease.[17] For aberrant epidermal growth factor signal transduction, *BRAF* inhibitors,[5,18,19] and MET inhibitors,[20] both have activity as single agents, but the combination of *BRAF* and MET inhibitors, such as dabrafanib plus tremitinib,[21] or vemurafinib plus cobimetinib,[22] is preferred. These combinations not only produce higher response rates, but actually decrease the risk of secondary cutaneous tumors. With these combinations, an objective response rate (ORR) in the range of 75 to 85 percent has been observed. Unfortunately only about 10 percent of patients exhibit complete responses, and resistance tends to develop within a few months,[23] such that median progression-free survival (PFS) is only one year. In randomized trials, these enzyme inhibitors were superior to dacarbazine or temozolomide in terms of ORR and PFS, but they had no significant impact on long-term OS. Treatments that enhance recognition of tumor associated antigens (TAA) may prolong the benefit of these agents, and it has been suggested that *BRAF* mutations are associated with increased TAA expression.[24] For these reasons, and their limited impact on long-term OS, many melanoma thought-leaders recommend immunotherapy as first-line treatment of unresectable metastatic melanoma patients, even if they have the V600E mutations.[11,25]

Interleukin-2

Interleukin-2 (or IL2) has been commercially available since 1992, but was not specifically approved for marketing as melanoma therapy until 1998, based on pooled data on 270 patients from 8 Phase II trials.[26] Although the ORR was only 16 percent, about half were complete responses that were quite durable. Various high-dose IL2 trials have confirmed 5-year OS rates of 15 percent in patients with metastatic melanoma.[27-29] Combining chemotherapy with IL2 results in higher ORR, and more toxicity, but does not prolong OS compared to sequencing of such therapies.[30,31] Unfortunately IL2 itself is quite toxic and requires hospitalization for administration and monitoring.[32] However, the side effects tend to reverse quickly once treatment is discontinued. The typical

treatment plan involves no more than two cycles of therapy over two months.[33] Most patients have stable disease rather than an objective response three months after starting treatment. IL2 works by stimulating existing immune responses to TAA via both the innate immune system (natural killer cells) and the adaptive immune system (cytotoxic T lymphocytes). Therefore, it is also a treatment that might be more effective if TAA recognition is enhanced by vaccination. In a randomized trial IL2 plus gp100 vaccine was associated with a higher response rate and longer PFS compared to IL2 alone, but 5-year OS was still only 15 percent in both arms,[29] which was similar to results for 131 melanoma patients treated in 3 Phase II trials with IL2 plus gp100.[28] In a retrospective analysis, 5-year OS rates were three times longer (39 percent vs 13 percent) in patients treated with IL2 plus an autologous vaccine than with IL2 alone.[34]

Monoclonal Antibodies

Recently there has been unprecedented success in the treatment of unresectable melanoma with monoclonal antibodies that target immune-inhibitory checkpoint molecules, such as cytotoxic T lymphocyte antigen-4 (CTLA-4) and programmed death molecules (PD1) or PD ligands.[35,36] In a recent study by Hodi et al., despite a relatively low ORR, the anti-CTLA-4 antibody ipilimumab, with or without gp100 peptide vaccine, was associated with a longer OS than the control arm of gp100 in patients who had progressed despite prior immunotherapy (IL2 or interferon) or chemotherapy (dacarbazine or temozolomide).[37] Patients treated in 3 Phase II trials testing various doses of ipilimumab had a 4-year survival rate of about 20 percent from the start of treatment.[38] Ipilimumab is administered as four infusions over three months. Its major drawback is immune-related adverse events (IRAE) associated with the release of repressed autoimmune responses.[39] These IRAE include colitis, dermatitis, hepatitis, iritis, hypophysitis, pneumonitis, and nephritis. IRAE are problematic, and can be severe to life-threatening in up to one-third of patients, although they are reversible if recognized in a timely manner and treated appropriately.

More recently there has been great excitement over monoclonal antibodies that block PD1 and PDL1, which, like CTLA-4, are associated with immune suppression. In patients with metastatic melanoma, antibodies that block these checkpoint inhibitors have been associated with ORR of 25 to 35 percent,[40-43] and 2-year OS rates of more than 40 percent.[44] Similar to what was seen with ipilimumab, some patients have experienced delayed responses, or even early disease progression followed by tumor regression.[45] Long-term disease control has been documented after discontinuation of therapy. Five-year survival rates are projected to be about 30 to 40 percent. Nivolumab and pembrolizumab also cause IRAE, but the severity is usually much less than observed with ipilimumab, except possibly for pneumonitis. Response rates associated with anti-PD1 inhibitors are similar or slightly higher in patients previously treated with ipilimumab.[43] Concurrent administration of the anti-CTLA-4 ipilimumab plus the anti-PD1 nivolumab was associated with an ORR of 40 percent, but also had a 53 percent rate of severe and life-threatening IRAE.[46]

Vaccines & Checkpoint Inhibitors

The checkpoint molecules are key mediators in the suppression of anti-TAA immune responses that are part of the cancer versus immunity evolutionary battle.[35,36,47,48] CTLA-4 interferes with the interaction between antigen presenting cells and T lymphocytes, while the binding of PDL1 to PD1 causes anergy (a state of immune unresponsiveness) in T cells and other immune cells. In tumors, PDL1 is found on the surface of tumor cells, and in the extracellular space. PD1 and PDL1 are both expressed on dendritic cells. Interference with the binding of PDL1 to PD1 can be accomplished by giving antibodies that block either molecule. Metaphorically speaking, interference with these interactions effectively takes the brakes off of existing host anti-cancer immune responses that have been repressed. Unfortunately, not all patients benefit from these checkpoint inhibitor immunotherapies, and it appears that 5-year OS rates following such therapies will be less than 50 percent; so adjunctive nontoxic therapies for patients with metastatic melanoma are still needed. Because of persisting concerns regarding IRAE, it is not clear whether the anti-checkpoint agents will have a role as adjunctive therapies after metastasectomy.

When anti-checkpoint therapies are ineffective, the explanation may be the absence of recognition of TAA. One way to enhance TAA recognition is vaccination. Experiments in M16 melanoma animal models have demonstrated a benefit for adding a GM-CSF secreting vaccine with both anti-CTLA-4,[49] and anti-PD1 antibodies;[50] the combinations were superior to vaccine alone and to either anti-checkpoint antibody alone. This is why the placebo-controlled randomized trial that led to approval of ipilimumab randomized patients 3:1:1 to ipilimumab plus gp100 vaccine, gp100 vaccine alone, and ipilimumab alone because of the belief that the combination (of ipilimumab plus gp100 vaccine) would be the best.[37] However, study results showed no benefit associated with adding gp100.[37] In contrast, a trial of high-dose IL2 with or without gp100 found a higher ORR and longer PFS when gp100 was added to IL2, and a trend for OS benefit.[29]

Genome analyses have demonstrated that melanomas express hundreds to thousands of mutations,[51] many of which can produce mutated TAA.[52] Many of these mutated antigens, which are unique to each individual rather than shared, can be recognized by the immune system and effectively targeted with massive numbers of helper or cytotoxic T lymphocytes.[53,54] However, vaccination approaches with one or a few TAA or allogeneic cell lines have yielded disappointing clinical results,[55] and are unlikely to produce optimal immunization because of TAA heterogeneity among patients. For these reasons attention is focusing increasingly on autologous TAA.

Although inducing inflammation of an *in vivo* metastasis may enhance TAA recognition in some patients,[56,57] a better approach may be the use of pure autologous tumor cell lines as a source of TAA.[58] Use of autologous tumor cell lines may be the only way to capture unique TAA expressed on early self-renewing and proliferating tumor cells that make up a short-term cell line. This approach has all of the advantages of allogeneic cell lines combined with the autologous nature of the antigens, which overcomes the

Table 1. Common Features among Clinical Trials Testing Vaccines Derived from Autologous Tumor Cell Lines
Eligible patients had experienced distant metastatic melanoma or recurrent stage III melanoma.
A cell line had been established in the Hoag Cell Biology Laboratory from tissue obtained at the time of resection of a metastatic lesion.
Patients with hepatitis B or C, human immunodeficiency virus were not eligible.
Pregnant patients were not eligible.
Patients with known auto-immune disease were not eligible.
Patients had no significant hematologic, hepatic, or renal laboratory abnormalities.
Patients had good performance status (ECOG 0-1).
Patients originated from all over the U.S.
Patients with controlled brain metastases were eligible.
Patients were eligible regardless of whether they were anergic to standard skin tests.
Patients were referred for treatment by their managing physician.
At the time of treatment, patients were allowed to have no-evidence disease, detectable but non-measurable disease, or measurable disease.
Concurrent anti-cancer treatment was not allowed.
Patients were injected with a single subcutaneous injection of vaccine weekly for 3 weeks and then monthly for 4 months at weeks 8, 12, 16, 20, and 24.

limitations related to inter-patient heterogeneity and the negative effects of allogeneic antigens.[58,59]

Clinical Trials Using Vaccines Derived from Autologous Tumor Cell Lines

From 1990 to 2011 research teams working in the Hoag Cancer Center in Newport Beach, Calif., focused on growing autologous tumor cell lines for use as patient-specific vaccines.[60-67] Most of this work focused on patients with metastatic melanoma. Four sets of clinical data have been reported:

1. 74 patients injected with irradiated tumor cells (TC) with various adjuvants[65]
2. 54 patients injected with dendritic cells (DC) loaded with antigens from irradiated TC (DC-TC) and suspended in GM-CSF[66]
3. 42 patients treated in a randomized Phase II trial that compared DC-TC to TC, with both products suspended in GM-CSF[67]
4. A retrospective comparison of patients who were treated with IL2 or IL2 with an autologous TC or DC-TC vaccine before or after IL2.[34]

Critical eligibility criteria and features common to all 3 of these clinical trials are summarized in Table 1, above, and results of these trials are shown in Table 2, page 52. The most common toxicities were grade 1 or 2 local injection site reactions that occurred in about 75 percent of patients, similar to what is seen with single injections of GM-CSF. Objective tumor regressions were rare, as would be predicted for an immune effect targeting early proliferating cells more than differentiated tumor cells. Historical comparisons and the randomized trial suggested that the DC-TC product was associated with better OS than TC.[66,67] The effect on PFS was not nearly as impressive as the effect on OS. One durable complete response was noted, but could not be declared until nearly nine months after completion of therapy, after months of stable disease.[67,68] That patient previously had never been disease-free despite multiple surgeries, IL2, sorafenib and chemotherapy, and Gamma Knife treatment of brain metastases.

One question left unanswered was whether the apparent survival benefit associated with this therapy is dependent on tumor burden. In other words, is benefit seen both in patients who have no evidence of disease at the time of treatment and in those who have detectable disease at the time of treatment? To address this question, all 72 patients treated with DC-TC were compared to a more favorable subset of 71 of the 98 patients treated with TC. For patients who had no evidence of disease when treatment was started, 5-year survival rates were 73 percent for DC-TC (n=33) vs 43 percent for TC (n=37) (p=0.015).[69] The 43 percent survival rate for the TC arm is similar to that observed in other vaccine trials for patients who had been rendered disease free by surgery; 5-year OS rates were 40 to 45 percent for such patients treated with various peptide vaccines,[70] and BCG or BCG plus allogeneic tumor cells.[15] Among patients who had detectable disease, OS was again superior in the DC-TC arm (n=39) compared to TC (n=34),

Table 2. Results from Clinical Trials Testing Vaccines Derived from Autologous Tumor Cell Lines

NAME	74 TC	54 DC-TC	42 (DC-TC vs YC)
TRIAL	Phase I/II	Phase I/II	Phase II randomized
WHEN	1990–2001	2000–2006	2007–2011
ELIGIBILITY	• Metastatic melanoma • Successful TC line • MD decision to Rx	• Metastatic melanoma • Successful TC line • MD referral for Rx	• Metastatic melanoma • Successful TC line • MD referral for Rx
PRODUCT	Irradiated tumor cells (TC) as source of tumor-associated antigens (TAA)	DC loaded with TAA from irradiated autologous TC to produce DC-TC & suspended in GM-CSF	DC loaded with TAA from irradiated autologous TC to produce DC-TC & suspended in GM-CSF
PROTOCOL DESIGN AND # OF PATIENTS	Open label: up to 40 measurable patients and 40 non-measurable patients	Open label: up to 40 measurable patients and 40 non-measurable patients	Randomized, open label: 200 patients stratified by measurable disease and most advanced stage
PRIMARY EFFICACY ENDPOINTS	• Tumor skin test conversion • Objective response • Overall survival	• Tumor skin test conversion • Objective response • Overall survival	Overall survival α =p<.05, β =0 .80 40% difference, 2-tailed
ACCRUAL	• CBRG 90-08:TC-BCG (n=7) • CBRG 92-12 randomized phase II: TC + injections of GM-CSF v IFN-γ (n=38) • Compassionate use: other adjuvants (n=29)	• 15 measurable • 39 non-measurable	• Terminated early • 24 TC • 18 DC-TC
SCHEDULE	Subcutaneous weekly x 3 & monthly x 5	Subcutaneous weekly x 3 & monthly x 5	Subcutaneous weekly x 3 & monthly x 5
CELLS PER INJECTION	10 million (2 million to 24 million)	15 million (4 million to 35 million)	3 million DC-TC (5-23) 12 million TC (7-22)
MEDIAN AGE	50	51	DC-TC 58, TC 58
MALE : FEMALE	44:30	34:20	DC-TC 11:7, TC 16:8
HIGHEST STAGE EVER	Stage IV=44 (59%) Stage III=23 (31%) Unknown=7 (9%)	Stage IV= 44 (81%) Stage III= 10 (19%)	Stage IV=33 (79%) Stage III= 9 (21%)
STAGE @ Rx	Not adjusted for LDH	IIIa & Ib to Ic by LDH	IIIa & IVb to IVc by LDH
NED	35 (47%)	25 (46%)	19 (45%)
M1a	8 (11%)	3 (6%)	4 (10%)
M1b	13 (18%)	7 (13%)	6 (14%)
M1c	17 (22%)	19 (35%)	13 (31%)
% Rx AT HOAG	35/74 (47%)	54/54 (100%)	42/42 (100%)

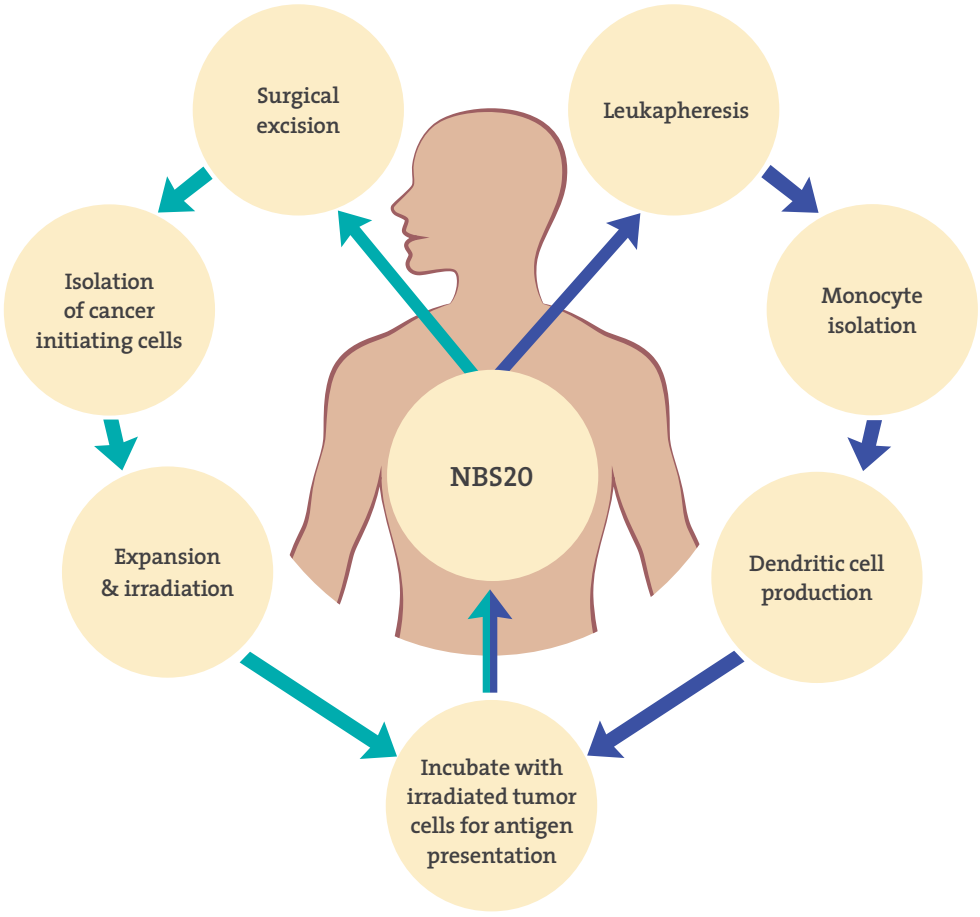
with a median OS of 39 vs 15 months, and 5-year OS of 33 percent vs 20 percent.[71] In a smaller subset of 32 patients who had measurable disease by RECIST criteria at the time of vaccine therapy, there was also a superior OS associated with DC-TC.[71]

Manufacturing NBS20, a DC-TC Candidate for Metastatic Melanoma

It is one scenario to develop a treatment such as this in a specialized translational research laboratory, but quite another scenario to make it a potential commercial product for practical delivery in the community. In other words, while research on NBS20

Figure 1. Sequence of Events Associated with the Creation of Patient-Specific NBS20

This schema illustrates the steps from tumor acquisition to treatment with patient-specific vaccine consisting of autologous dendritic cells loaded with antigens from an autologous tumor cell line, and injected s.c. (subcutaneous) with granulocyte-macrophage colony stimulating factor. The tumor cell production process takes about six weeks. The production of dendritic cells and loading with antigen takes about one week, and quality assurance procedures for product release take another two weeks.



began at the Hoag Cell Biology Laboratory, bringing it to market was another story. In 2011 California Stem Cell, Inc., Irvine, Calif., acquired Hoag Cell Biology Laboratory and the rights to NBS20. Then, in 2014, California Stem Cell was bought by NeoStem, Inc., N.Y. The sequence of events associated with the creation of each patient-specific product are summarized in Figure 1, above. The seven critical steps are:

1. ***Obtaining and shipping tumor tissue.*** Metastatic melanoma lesions are frequently resected as part of the standard of care, but for a biological product such as NBS20, the tissue must be collected in a manner that maintains sterility and viability, and processed in a manner that allows cryopreservation of cells that will be viable when thawed in the future, and/or processed for an effort to establish a tumor cell line.[72] To accomplish this, transport kits containing tissue culture media and antibiotics are provided. A viable portion of tumor tissue is selected by the surgeon and/or pathologist and sterilely placed into a media-containing vial, placed in the transport kit, and then sent by special delivery so that the tissue can be processed within 24 to 72 hours of the surgical resection. The quantity of tissue requested is about 1 cubic cm, but quality is more important than quantity. Viable well-vascularized tissue on the periphery of a mass is preferred to necrotic tissue; non-pigmented is preferred to pigmented tissue because melanin production is associated with more differentiated melanoma cells. A smaller lesion is preferred to a large lesion, because there may be a higher proportion of tumor stem cells or progenitor cells in a smaller lesion. Using these procedures, researchers have successfully established cell lines from tissues received up to 72 hours after resection and transported from Brazil, Switzerland, and Australia.

2. ***Processing tumor tissue.*** Once received, the tumor tissue has to be maintained under sterile conditions. Standard operating procedures are in place for digesting and mincing the tumor into cell suspension and placing cells into tissue culture for efforts to grow a cell line, or with DMSO (dimethylsulfoxide) and media for cryopreservation in the vapor phase of liquid nitrogen at less than -135° C.
3. ***Growing cell lines.*** The methods used in the Hoag Cell Biology Laboratory were not sufficient for a commercial product. Success rates over the years were about 50 percent for more than 600 specimens and were similar regardless of the cell biologists and laboratory technicians who worked with the samples.[65-67] It also took a long time to establish a cell line; the median time for success was about 4 months, with a range from 2 to 11 months.[73] As stated previously, in 2011 the assets and intellectual property of the Hoag Cell Biology Laboratory were acquired by California Stem Cell, Inc. The company applied its expertise in growing stem cells to increase the success rate and decrease the time required to establish tumor cell lines. In fact, cell lines have been established within 6 weeks from 80 percent of cryopreserved melanoma samples (personal communication with Andrew Cornforth of Stem Cell, Inc.), even though historically it took longer to grow a cell line from a frozen than fresh sample. This percentage has included successful growth of cell lines from samples that previously could not grow cell lines.
4. ***Irradiating tumor cells.*** Tumor cells are treated with high doses of radiation to inhibit the proliferative capability of the cells to reduce the slim chance that viable tumor cells might be injected back into the patient. Such radiation also induces apoptosis in a manner that facilitates phagocytosis and antigen processing by DC. Proteins are partially digested and then expressed on the surface of the DC in the context of histocompatibility molecules to initiate a new anti-TAA immune response or enhance an existing immune response.
5. ***Collecting peripheral blood mononuclear cells (PBMC).*** Dendritic cells (DC) are derived from PBMC. DC are now appreciated as being the most efficient of the antigen presenting cells (APC) that communicate with T cells in the adaptive immune system. Animal and human studies suggest that TAA presentation by DC that have been loaded with antigen *ex vivo*, result in better immune responses and better clinical outcome than simply injecting TAA with a cytokine or adjuvant.[67] PBMC are collected in the process of leukapheresis (a procedure in which white blood cells are separated from a sample of blood) that is performed using machines designed for collection of different blood elements and plasma on the basis of differential centrifugation. Many physicians are familiar with leukapheresis because of collection of hematopoietic stem cells for autologous or allogeneic bone marrow transplants, the intravenous dendritic-cell immunotherapy sipuleucel-T for prostate cancer,[74] and various vaccine clinical trials that require generation of DC. The procedure itself typically involves a 10 liter exchange over four to five hours. Good venous access is required so that blood can be removed from the body, PBMC segregated and removed, and the rest of the blood product returned to the patient. Patients must have adequate veins to withstand the draw pressures so the veins do not collapse. When collecting PBMC for autologous or allogeneic transplants, central lines are required in most patients because of the draw pressures. Fortunately, central lines are generally not required when collecting PBMC from which to generate DC.

   During leukapheresis, anti-coagulation with citrate is required to avoid clotting, and it can cause symptomatic hypocalcemia, especially in patients with mild Vitamin D deficiency, such as that commonly associated with metabolic syndrome. Mild symptoms such as perioral (around the mouth) tingling are usually easily controlled with calcium carbonate (e.g., Tums®) and/or milk products. Intravenous calcium chloride may be required for patients that have more severe or persistent symptoms of hypocalcemia.

   For multicenter trials, PBMC can be collected by any appropriately certified pheresis facility, placed in a transfer kit, and then shipped to the NeoStem facility in Irvine, Calif. (formerly California Stem Cell, Inc.). Many cancer programs have their own leukapheresis facilities, especially if they are involved in bone marrow transplants or cell-based biological therapies. However, there are commercial pheresis entities that provide this service, including the American Red Cross, HemaCare, and Blood Centers of America. In contrast to the sipuleucel-T product for prostate cancer that requires three leukaphereses,[74] only one pheresis procedure is needed to derive enough cells for all eight planned injections of NBS20. Further purification of the PBMC and growth in interleukin-4 and GM-CSF results in production of immature DC in about 6 days.
6. ***Combining DC and TC.*** NBS20 (DC-TC) consists of autologous DC cells loaded with TAA from the irradiated autologous TC by co-incubation for 12 to 18 hours. During this time DC phagocytose (engulf and destroy) the TC and present antigenic fragments in the context of HLA histocompatibility proteins for presentation to T lymphocytes. Each dose contains TAA derived from about 10 million self-renewing, proliferating, autologous TC. The loading process is associated with maturation of DC, which helps optimize presentation of TAA to T lymphocytes. Quality testing for product release currently requires an additional two weeks. The final product is divided into aliquots containing 5 million to 20 million cells for each of the intended 8 injections and stored in a cryovial. The time from leukapheresis to availability of NBS20 for treatment is 4 weeks, or about 1 month.
7. ***Storage, preparation, and administration of NBS20.*** All doses are shipped in a cryopreserved state to the treatment site for storage in the vapor phase of liquid nitrogen in a dewar (a tank designed for this purpose) which needs to be at or very near the treatment site. There are companies that provide a refill service to maintain the desired liquid nitrogen level for the dewar. Alternatively, it is possible to send each dose in its own dewar containing sufficient liquid nitrogen to last for several days. The cell product is maintained in this manner until just prior to administration, when one conical vial is thawed at room temperature (approximately 68°-75° F, 20°-24° C) under

a sterile hood. Next, 500 microgram of GM-CSF is reconstituted in 0.5 ml of saline and injected into the cryovial to suspend the DC-TC product. The final 1.1 ml volume of GM-CSF and DC-TC is drawn into a 3.0 ml syringe and 1.0 ml of liquid and cells is injected subcutaneously via 25-gauge needle into one of the patient's extremities for each administration. Once thawed, the cell product should be injected as soon as possible, and within five hours.

The INTUS Trial

The U.S. Food and Drug Administration (FDA) granted NBS20 orphan drug status and a special protocol assessment and fast track designation in 2013. (Breakthrough status was not warranted because there is no standard therapy for comparison that is recognized as adjunctive treatment for patients with metastatic melanoma.) GM-CSF has been used in similar patients, but clinical benefit from this approach was not confirmed in randomized trials.[75, 76]

The INTUS trial, NCT01875653, which opened for enrollment in late October 2014, is a double-blinded, placebo-controlled, randomized trial for patients with distant metastatic melanoma or recurrent stage III melanoma. The randomization is 2:1 for the study agent NBS20 to control. The plan is to randomize and treat 250 patients. The control arm is autologous monocytes (MC) in order to facilitate the double-blind design. Leukapheresis is performed shortly after randomization to collect PBMC from which DC or MC are derived. Both treatment products, DC-TC and MC, become available about one month after leukapheresis, and are suspended in 500 µg GM-CSF for injection. Entry criteria are similar to those used in the previous trials as summarized in Table 1, page 51. There are no restrictions related to prior or subsequent therapies, but concurrent therapy is not allowed. Managing physicians and patients should recognize that pre-enrollment screening can take up to a month, and it takes another month from the time of randomization and leukapheresis to availability of the treatment product.

Patients are stratified based on the extent of disease at the time of randomization as follows:

1. No evidence of disease
2. Presence of non-measurable or equivocal disease
3. Measurable disease with a serum lactate dehydrogenase (LDH) that is in the normal range
4. Measurable disease with an elevated LDH.

RECIST criteria are used to define the appropriate strata for each patient,[77] but determination of ORR or PFS are not endpoints for this trial. Based on theoretical considerations, and observations made in earlier trials, the only endpoint is death for determination of OS. If most of the anti-tumor effect is on the small number of tumor stem cells present in various lesions, then a response can only be determined once more differentiated cells that do not express these antigens have ceased replicating and die off; therefore, objective responses are likely to be rare, and delayed, which is consistent with what has been seen in previous trials.

Similarly, if we are targeting a small population of cells in a given tumor mass, untargeted cells will continue to grow and the lesion is likely to enlarge for a period of time until the more differentiated tumor cells die off; therefore, PFS is unlikely to be prolonged, which is consistent with what was observed in earlier trials. Targeting a small subset of such cells can eliminate established tumors in animal models.[78] Even though OS potentially could be confounded by other therapies, it is the only meaningful endpoint for an immune response that should persist for many years, if not indefinitely; therefore a randomized, double-blinded, placebo-controlled trial with overall survival as the endpoint is the appropriate study design. OI

Robert O. Dillman, MD, is vice president of Oncology, NeoStem, Inc., and clinical professor of Medicine, University of California Irvine. Dr. Dillman became vice-president of Oncology for NeoStem, Inc., in May 2014 when it acquired California Stem Cell, Inc., where he was chief medical officer from 2012–2014. During 2011–2014 he also served as executive medical director of the Hoag Hospital Institute for Research and Education, in Newport Beach, Calif. Prior to that, Dr. Dillman was executive medical director of the Hoag Family Cancer Institute (2008–2011), and medical director of the Hoag Cancer Center (1989–2008) where he directed the translational cell biology research laboratory focused on bench-to-bedside patient-specific cell therapies, which was acquired by California Stem Cell in 2011.

References

1. Balch CM, et al. Final version of 2009 AJCC melanoma staging and classification. *J Clin Oncol*. 2009;27(36):6199-6206.

2. American Joint Committee on Cancer. Edge SB, Byrd DR, Comton CC, et al., eds. Melanoma of the skin. In *AJCC Cancer Staging Handbook, 7th ed.*; New York: Springer; 2010;387-415.

3. Chapman PB, et al. Phase III multicenter randomized trial of the Dartmouth regimen versus dacarbazine in patients with metastatic melanoma. *J Clin Oncol*. 1999;17(9):2745-2751.

4. Middleton MR, et al. Randomized phase III study of temozolomide versus dacarbazine in the treatment of patients with advanced metastatic malignant melanoma. *J Clin Oncol*. 2000;18(1):158-166.

5. Chapman PB, et al. Improved survival with vemurafenib in melanoma with *BRAF* V600E mutation. *N Engl J Med*. 2011;364(26):2507-2516.

6. Robert C, et al. Ipilimumab plus dacarbazine for previously untreated melanoma. *N Engl J Med*. 2011;364(26):2517-2526.

7. Eton O, et al. Sequential biochemotherapy versus chemotherapy for metastatic melanoma: results from a phase III randomized trial. *J Clin Oncol*. 2002;20(8):2045-2052.

8. Atkins MB, et al. Phase III trial comparing concurrent biochemotherapy with cisplatin, vinblastine, dacarbazine, interleukin-2, and interferon alfa-2b with cisplatin, vinblastine, and dacarbazine alone in patients with metastatic malignant melanoma (E3695): a trial coordinated by the Eastern Cooperative Oncology Group. *J Clin Oncol*. 2008;26(35):5748-5754.

9. Hauschild A, et al. Results of a phase III, randomized, placebo-controlled study of sorafenib in combination with carboplatin and paclitaxel as second-line treatment in patients with unresectable stage III or stage IV melanoma. *J Clin Oncol*. 2009;27(17):2823-2830.

10. Kim KB, et al. BEAM: a randomized phase II study evaluating the activity of bevacizumab in combination with carboplatin plus paclitaxel in patients with previously untreated advanced melanoma. *J Clin Oncol*. 2011;30(1):34-41.

11. Kaufman HL, et al. The Society for Immunotherapy of Cancer consensus statement on tumour immunotherapy for treatment of cutaneous melanoma. *Nat Rev Clin Oncol*. 2013;10:588-98.

12. Essner R, et al. Contemporary surgical treatment of advanced-stage melanoma. *Arch Surg*. 2004;139(9):961-966.

13. McLoughlin JM, et al. Treatment options for limited or symptomatic metastatic melanoma. *Cancer Control*. 2008;15(3):239-247.

14. Howard JH, et al. Metastasectomy for distant metastatic melanoma: analysis of data from the first Multicenter Selective Lymphadenectomy Trial (MSLT-I). *Ann Surg Oncol*. 2012;19(8):2547-2555.

15. Morton DL, et al. An international, randomized, phase III trial of bacillus Calmette-Guerin (BCG) plus allogeneic melanoma vaccine (MCV) or placebo after complete resection of melanoma metastatic to regional or distant sites. *J Clin Oncol*. 2007;25:474s (abstr 8508).

16. Lawson DH, et al. E4697: Phase III cooperative group study of yeast-derived granulocyte macrophage colony-stimulating factor (GM-CSF) versus placebo as adjuvant treatment of patients with completely resected stage II-IV melanoma. *J Clin Oncol*. 2010;28:15s (suppl; abstr 8504).

17. Flaherty KT, et al. Inhibition of mutated, activated *BRAF* in metastatic melanoma. *N Engl J Med*. 2010;363(9):809-819.

18. Sosman JA, et al. Survival in *BRAF* V600-mutant advanced melanoma treated with vemurafinib. *N Engl J Med*. 2012;366(8):707-714.

19. Hauschild A, et al. Dabrafenib in *BRAF*-mutated metastatic melanoma: a multicenter, open-label phase III randomized controlled trial. *Lancet*. 2012;380:1893-1901.

20. Flaherty KT, et al. Improved survival with MEK inhibition in BRAF-mutated melanoma. *N Engl J Med*. 2012;367(2):107-114.

21. Flaherty KT, et al. Combined *BRAF* and MEK inhibition in melanoma with *BRAF* V600 mutations. *N Engl J Med*. 2010;367(18):1694-1703.

22. Ribas A, et al. Combination of vemurafenib and cobimetinib in patients with advanced *BRAF*(V600)-mutated melanoma: a phase 1b study. *Lancet Oncol*. 2014;15:954-965.

23. Solit DB, et al. Resistance to *BRAF* inhibition in melanoms. *N Engl J Med*. 2011;364:772-774.

24. Frederick DT, et al. *BRAF* inhibition is associated with enhanced melanoma antigen expression and a more favorable tumor microenvironment in patients with metastatic melanoma. *Clin Cancer Res*. 2013;19(5):1225-1231.

25. Dillman RO, et al. Should high-dose interleukin-2 still be the preferred treatment for patients with metastatic melanoma? *Cancer Biother Radiopharm*. 2012;27(6):337-343.

26. Atkins MB, et al. High-dose recombinant interleukin 2 therapy for patients with metastatic melanoma: analysis of 270 patients treated between 1985 and 1993. *J Clin Oncol*. 1999;17(7):2105-2116.

27. Atkins MB, et al. High-dose recombinant interleukin-2 therapy in patients with metastatic melanoma: long-term survival update. *Cancer J Sci Am*. 2000;6(suppl 1): S11-S14.

28. Sosman JA, et al. Three phase II Cytokine Working Group trials of gp100 (210M) peptide plus high-dose interleukin-2 in patients with HAL-A2-positive advanced melanoma. *J Clin Oncol*. 2008;26:2292-2298.

29. Schwartzentruber DJ, et al. Gp100 peptide vaccine and interleukin-2 in patients with advanced melanoma. *N Engl J Med*. 2011;364(22):2119-2127.

30. Eton O, et al. Sequential biochemotherapy versus chemotherapy for metastatic melanoma: results from a phase III randomized trial. *J Clin Oncol*. 2002;20(8):2045-2052.

31. Atkins MB, et al. Phase III trial comparing concurrent biochemotherapy with cisplatin, vinblastine, dacarbazine, interleukin-2, and interferon alfa-2b with cisplatin, vinblastine, and dacarbazine alone in patients with metastatic malignant melanoma (E3695): a trial coordinated by the Eastern Cooperative Oncology Group. *J Clin Oncol*. 2008;26:5748-5754.

32. Schwartz RN, et al. Managing toxicities of high-dose interleukin-2. *Oncol*. 2002;16(11 Suppl 13):11-20.

33. Lindsey KR, et al. Impact of the number of treatment courses on the clinical response of patients who receive high-dose bolus interleukin-2. *J Clin Oncol*. 2000;18(9):1954-1959.

34. Dillman RO, et al. High-dose IL-2 in metastatic melanoma: better survival in patients immunized with antigens from autologous tumor cell lines. *Cancer Biother Radiopharm*. 2014;29:53-57.

35. Pardoll D. The blockade of immune checkpoints in cancer immunotherapy. *Nature Cancer Reviews*. 2012;12:252-264.

36. Dolan DE, et al. PD-1 pathway inhibitors: changing the landscape of cancer immunotherapy. *Cancer Control*. 2014;21:231-237.

37. Hodi FS, et al. Improved survival with ipilimumab in patients with metastatic melanoma. *N Engl J Med*. 2010;363:711-723.

38. Wolchok JD, et al. Four-year survival rates for patients with metastatic melanoma who received ipilimumab in phase II clinical trials. *Ann Oncol*. 2013; 24:2174-2180.

39. Weber J. Ipilimumab: controversies in its development, utility and autoimmune adverse events. *Cancer Immunol Immunother*. 2009;58:823-830.

40. Topolian SL, et al. Safety, activity, and immune correlates of anti-PD-1 antibody in cancer. *N Engl J Med*. 2012;366:2443-2454.

41. Brahmer JR, et al. Safety and activity of anti-PD-L1 antibody in patients with advanced cancer. *N Engl J Med*. 2012;366:2455-2466.

42. Hamid O, et al. Safety and tumor responses with lambrolizumab (Anti-PD-1) in melanoma. *N Engl J Med*. 2013;369:134-144.

43. Robert C, et al. Anti-programmed-death-receptor-1 treatment with pembrolizumab in ipilimumab-refractory advanced melanoma: a randomised dose-comparison cohort of a phase 1 trial. *Lancet*. 2014;384(9948):1109-1117.

44. Topalian SL, et al. Survival, durable tumor remission, and long-term safety in patients with advanced melanoma receiving nivolumab. *J Clin Oncol*. 2014;32,1020-1030.

45. Wolchok JD, et al. Guidelines for the evaluation of immune therapy activity in solid tumors: immune-related response criteria. *Clin Cancer Res*. 2009;15:7412-7420.

46. Wolchok JD, et al. Nivolumab plus ipilimumab in advanced melanoma. *N Engl J Med*. 2013;369:122-133.

47. Chen DS, Mellman I. Oncology meets immunology: the cancer-immunity cycle. *Immunity*. 2013;39:1-10.

48. Mittal D, et al. New insights into cancer immunoediting and its three component phases—elimination, equilibrium and escape. *Curr Opin Immunol*. 2014;27:16-25.

49. Van Elsas A, et al. Combination immunotherapy of B16 melanoma using anti-cytotoxic T lymphocyte-associated antigen 4 (CTLA-4) and granulocyte/macrophage colony- stimulating factor (GM-CSF)-producing vaccines induces rejection of subcutaneous and metastatic tumors accompanied by autoimmune depigmentation. *J Exp Med*. 1999;190:355–366.

50. Li B, et al. Anti-programmed death-1 synergizes with granulocyte macrophage colony-stimulating factor—secreting tumor cell immuno-

therapy providing therapeutic benefit to mice with established tumors. *Clin Cancer Res*. 2009;15:1623–1634.

51. Lawrence MS, et al. Mutational heterogeneity in cancer and the search for new cancer genes. *Nature*. 2013;499:214-218.

52. Robbins PF, et al. Mining exomic sequencing data to identify mutated antigens recognized by adoptively transferred tumor-reactive T cells. *Nat Med*. 2013;19:747-752.

53. Tran E, et al. Cancer immunotherapy based on mutation-specific CD4+ T cells in a patient with epithelial cancer. *Science*. 2014;344:641-645.

54. Lu Y-C, et al. Efficient identification of mutated cancer antigens recognized by T cells associated with durable tumor regressions. *Clin Cancer Res*. 2014;20:3401-3410.

55. Dillman RO. Melanoma Vaccines: Trials and Tribulations. *Vaccine Dev Ther.* 2013;3:57-78.

56. Andtbacka RHI, et al. OPTiM: A randomized phase III trial of talimogene laherparepvec (T-VEC) versus subcutaneous (SC) granulocyte-macrophage colony-stimulating factor (GM-CSF) for the treatment (tx) of unresected stage IIIB/C and IV melanoma. *J Clin Oncol*. 31, 2013 (suppl; abstr LBA9008).

57. Postow MW, et al. Immunologic correlates of the abscopal effect in a patient with melanoma. *N Engl J Med*. 2012;366:925-931.

58. Dillman RO, et al. Establishing in vitro cultures of autologous tumor cells for use in active specific immunotherapy. *J Immunother.* 1993;14:65-69.

59. Dillman RO, et al. Cancer stem cell antigen-based vaccines: the preferred strategy for active specific immunotherapy of metastatic melanoma? *Expert Opin Biol Ther*. 2013;13:643-656.

60. Dillman RO, et al. The feasibility of using short-term cultures of ovarian cancer cells for use as autologous tumor cell vaccines as adjuvant treatment of advanced ovarian cancer. *Cancer Biother Radiopharm*. 1999;14:443-449.

61. Dillman RO, et al. Irradiated cells from autologous tumor cell lines as patient-specific vaccine therapy in 125 patients with metastatic cancer: induction of delayed-type hypersensitivity to autologous tumor is associated with improved survival. *Cancer Biother Radiopharm*. 2002;17:51-66.

62. Dillman RO, et al. Autologous tumor cell line-derived vaccine for patient-specific treatment of advanced renal cell carcinoma. *Cancer Biother Radiopharm*. 2004;19:570-580.

63. Dillman RO, et al. Phase I/II trial of autologous tumor cell line-derived vaccine for recurrent or metastatic sarcomas. *Cancer Biother Radiopharm*. 2004;19:581-588.

64. Dillman RO, et al. Patient-specific dendritic cell vaccines for metastatic melanoma. *N Engl J Med*. 2006;355:1179-1181.

65. Dillman RO, et al. Patient-specific vaccines derived from autologous tumor cell lines as active specific immunotherapy: results of exploratory phase I/II trials in patients with metastatic melanoma. *Cancer Biother Radiopharm*. 2007;22:309-321.

66. Dillman RO, et al. Phase II trial of dendritic cells loaded with antigens from self-renewing, proliferating autologous tumor cells as patient-specific anti-tumor vaccines in patients with metastatic melanoma: Final Report. *Cancer Biother Radiopharm*. 2009;24:311-319.

67. Dillman RO, et al. Tumor stem cell antigens as consolidative active specific immunotherapy: a randomized phase II trial of dendritic cells versus tumor cells in patients with metastatic melanoma. *J Immunother*. 2012;35:641-649.

68. Dillman RO, et al. Durable complete response of refractory, progressing metastatic melanoma after treatment with a patient-specific vaccine. *Cancer Biother Radiopharm*. 2010;25:553-557.

69. Dillman RO, et al. 5-year survival for patients with metastatic melanoma who had no evidence of disease at time of treatment with patient specific tumor stem cell vaccines. 105th Annual Meeting of the American Association for Cancer Research, 06 April 2014. *Proc Am Assoc Cancer Res*. 55: 2014. (abstract #197)

70. Tagawa ST, et al. Survival analysis after resection of metastatic disease followed by peptide vaccines in patients with stage IV melanoma. *Cancer.* 2006;106:1353-1357.

71. Dillman RO, et al. 5-year survival for patients with detectable metastatic melanoma at time of treatment with patient-specific tumor stem cell vaccines. American Society of Clinical Oncology 50th Annual Meeting, Chicago, IL. 01 June 2014. *J Clin Oncol*. 32:2014. (abstract #3090).

72. Dillman RO, et al. Tissue banking in community cancer centers. *Oncol Issues*. 2008;23:22-26.

73. Selvan SR, et al. Establishment of stable cell lines for personalized melanoma cell vaccine. *Melanoma Res*. 2010;20:280-292.

74. Kantoff PW, et al. Sipuleucel-T immunotherapy for castration-resistant prostate cancer. *N Engl J Med*. 2010;363:411-422.

75. Spitler LE, et al. Adjuvant therapy of stage III and IV malignant melanoma using granulocyte-macrophage colony-stimulating factor. *J Clin Oncol*. 2000;18:1614-1621.

76. Spitler LE, et al. Recombinant human granulocyte-macrophage colony-stimulating factor (GM-CSF, sargramostim) administered for 3 years as adjuvant therapy of stages II(T4), III, and IV melanoma. *J Immunother.* 2009;32:632-637.

77. Therasse P, et al. New guidelines to evaluate the response to treatment in solid tumors. European Organization for Research and Treatment of Cancer, National Cancer Institute of the United States, National Cancer Institute of Canada. *J Natl Cancer Inst.* 2000;92:205-216.

78. Schmidt P, et al. Eradication of melanomas by targeted elimination of a minor subset of tumor cells. *Proc Natl Acad Sci USA*. 2011;8:108:2474-2479.

AS OUR UNDERSTANDING OF TUMOR BIOLOGY and microenvironment evolves and an increasing number of immunotherapy approaches become available in oncology, immuno-oncology therapy is poised to revolutionize patient care by developing therapies that put the body's own immune system to work to fight cancer. In 2014 the Association of Community Cancer Centers established the Institute for Clinical Immuno-Oncology (ICLIO) to educate providers about immuno-oncology and its implementation and delivery in the community setting. The project is made possible by a charitable donation from Bristol-Myers Squibb.

To learn more about ICLIO's clinical scholars engagement program, monthly e-newsletter, series of educational webinars, and national education conference, Oct. 2, 2015, Philadelphia, Pa., go to www.accc-cancer.org/ICLIO or email Lorna Lucas, MS, ACCC's senior manager for ICLIO at llucas@accc-cancer.org.

Ask ACCC's Community Resource Centers: *Myelofibrosis*

Myeloproliferative neoplasms (MPNs) are a cluster of chronic myleoproliferative diseases that are technically classified as malignancies wherein the bone marrow produces cells that are in some way abnormal. Myelofibrosis can arise on its own (as in primary myelofibrosis, PMF), or as a progression of polycythemia vera (post-PV-MF) or essential thrombocythemia (post-ET-MF). According to Timothy Tyler, PharmD, FCSHP, director of Pharmacy, Lab and Oncology Supportive Care Services at Desert Regional Medical Center, Palm Springs, Calif., MF is not a hematologic cancer in the classic sense, and certainly not a big attention-getter, like an acute leukemia or even a chronic leukemia, but MF does generate a great deal of symptomatology and is best managed by a hematologist with a comprehensive supportive care team.

MF is a chronic blood cancer in which excessive scar tissue forms in the bone marrow and impairs its ability to produce normal blood cells. It is thought to be caused by abnormal blood stem cells in the bone marrow. The abnormal stem cells produce more mature cells that grow quickly and take over the bone marrow, causing fibrosis (scar tissue formation) that results in chronic inflammation. As a byproduct of this scarring, the bone marrow loses the ability to generate normal blood cells, and other organs, such as the spleen, may become the primary producers of blood cells. MF is generally a disease of the elderly, with average patients typically in their 60s and 70s. Younger patients can develop MF—especially if there has been environmental exposure—but, overall, MF is a disease of old age.

Limited Options

For many years, MPNs were a discouraging cauldron of indolent disease; clinicians had very few options with regard to active therapy and certainly nothing that was in any sense a "targeted" therapy. Drugs that might help to manage MF symptoms were few and far between—with no clear coverage guidelines outside of the compendia. In essence, providers and payers tried their best to manage this group of very fatigued (feeling tired, weak, or short of breath are among the symptoms of MF) patients. While transfusions of blood products can be indicated for this patient population, after taking into account indications and even cautions from blood provider agencies, clinicians often used transfusions as agents of last resort.

The manifestations of PMF, post-PV-MF, and post-ET-MF are virtually identical and treatment is generally the same for all three. Until recently, supportive care focused on fatigue management and use of hydroxyurea (Hydrea®), a drug that has been around since the 1960s. While some clinicians attempted to treat MF symptoms with erythropoietin stimulating agents (ESAs), the lack of a medical indication often resulted in reimbursement challenges. There has been some success in a limited pool of patients who are eligible and desire transplant, but as the vast majority of patients are elderly with a loss of functioning protoplasm, this therapy is not widely done. Simply put, for many years the challenges caused by MF and its hematologic cousins—primarily fatigue and a lack of energy—did not have a targeted therapy and so symptom management was key.

Our Supportive Care Model

During this period of limited treatment and management options for patients with MF, The Comprehensive Cancer Center at the Desert Regional Medical Center looked to its strong oncology supportive care services to augment the paucity of drug therapy options. For example, our psychologist is available by appointment to counsel MF patients one-on-one about energy conservation, pursed lip breathing in patients with obstructive pulmonary complications, and other strategies to manage general fatigue and lack of energy. Dietitian consults help ensure our MF patients receive education about proper nutrition; social workers can intervene regarding living situations that no longer work for elderly MF patients—many of whom are used to being self-sufficient. Bottom line: our oncology supportive care team plays an active role in managing our MF patients as compared with their role with our more "traditional" solid tumor patients.

New Hope

With the introduction of JAK inhibitors, improvement in MPN disease-related symptoms has emerged as a realistic expectation of therapy and an integral measure of clinical efficacy.[1] At the end of 2011, the U.S. Food and Drug Administration (FDA) approved ruxolitinib (Jakafi®) for the treatment of myelofibrosis; late last year, the FDA expanded this indication to include polycythemia vera. This targeted agent has breathed new hope in the treatment of these diseases, demonstrating significant reductions in symptom burden, with consequent improvements in QoL (quality of life) measures.[1]

Positive data from stage I of an adaptive two-stage Phase II trial of PRM-151, a novel anti-fibrotic immunotherapy, demonstrated reduction of bone marrow fibrosis by at least one grade observed in 42 percent of patients, which was associated in most patients with improvements in anemia and/or thrombocytopenia and, in some patients, by transfusion independence lasting at least 24 weeks.[2] These study results were presented in an oral presentation by principal investigator Srdan Verstovsek, MD, PhD, at the American Society of Hematology (ASH) 2014 Annual Meeting, Dec. 8, 2014.

In the end, while these new and emerging therapies begin to increase our treatment options for patients with MF, supportive care—an experienced clinician talking one-on-one with these often elderly patients and ensuring they receive comprehensive symptom management education—remains key. OI

References

1. Mesa RA, Scherber RM, Geyer HL. Reducing symptom burden in patients with myeloproliferative neoplasms in the era of JAK inhibitors. *Leuk Lymphoma*. 2015 Feb 3:1-39. [Epub ahead of print]

2. Stein BL, Verstovsek S. Abstract 634. Myeloproliferative Syndromes: Clinical: JAK Inhibitors and Their Combinations. Oral and Poster Abstract. ASH 2014.

Case Study

B.Q. is a 58-year-old male with a long-standing history of thrombocytopenia since his late twenties. Originally diagnosed with essential thrombocythemia, B.Q. was put on the clinical research trial for anegralide. At some point after completion of the clinical trial, B.Q. was unable to be maintained on anagrelide and was switched to hydroxyurea. While on hydroxyurea, B.Q. developed profound anemia and became quite symptomatic. He was treated with blood transfusions; epoetin alfa was successfully used for symptom management. B.Q. also met regularly with our psychologist to work on supportive care measures. (In fact, over the past six years, this patient has logged almost 100 sessions with our psychologist, working on supportive care issues directly related to his myelofibrosis.)

Over the last few years, B.Q.'s disease has transformed into a myeloproliferative disease. The patient did benefit from red-cell growth factors initially, but is presently unable to afford his co-pay due to a change in his primary insurance. In researching assistance options, the patient improved to the point where he was satisfied that growth factors could be used if necessary. For the past year, the patient's hemoglobin and hematocrit are stable and his platelet count is adequate. B.Q. has not taken hydroxyurea for the past year and his last flow cytometry revealed 1 percent blasts. The patient has been intermittently transfused and is concerned that his disease is progressive. B.Q. is considering our recommendation to initiate therapy with a JAK2 inhibitor. His physician's clinical opinion is that the disease is stable, but would likely benefit from a trial of a JAK2 inhibitor, such as ruxolitinib.

FINANCIAL ADVOCACY NETWORK

Comprehensive resources to reduce the cost burden of cancer care–for your patients & your staff

ACCC's newly-revamped and expanded Financial Advocacy Network provides a robust portfolio of tools and resources for your financial advocates–easily accessible online, in print, or at free regional meetings. Looking to expand your program? We've got you covered.

Explore this one-stop destination:

www.accc-cancer.org/FinancialAdvocacy

ONLINE COURSES

Effectively Communicating with the Patient and Multidisciplinary Team

Justifying the Financial Advocate Position

Maximizing Reimbursement

ONLINE INTERACTIVE FORUM

What should I know about ICD-10?

How do I make a case for hiring a financial advocate?

How can I improve processes to leverage copay programs?

Are there strategies to help maximize reimbursement?

PROGRAMMATIC TOOLS

Job descriptions

Flowcharts to help streamline financial advocacy services

Resources to help with payer issues, including pre-authorizations, denials and appeals

Staffing models

Financial tracking and reporting tools

FREE* REGIONAL MEETINGS

May 5 - Tampa, FL
June 2 - Silver Spring, MD
June 23 - Burlingame, CA

Agenda topics include:
Help Patients Manage the Financial Toxicity of Cancer

What's the Right Financial Advocacy Model for My Program?

Maximizing Reimbursement

**Free to ACCC members: $69 for non-members*

ACCC
Association of Community Cancer Centers

ACCC Welcomes its Newest Members

Jewish Hospital Mercy Health Cancer Program
Cincinnati, Ohio
Delegate Rep: Susan Brown, PhD, RN
Website: www.e-mercy.com

Katmai Oncology Group
Anchorage, Alaska
Delegate Rep: Terri Tope
Website: www.katmaioncology.com

Kentucky One Cancer and Blood Specialist
Louisville, Ky.
Delegate Rep: Carrie Dunn
Website: www.kentuckyonehealth.org

Ohio Valley Medical Center Cancer Center at OVMC
Wheeling, W. Va.
Delegate Rep: Breezie Ogilbee, RT, BA
Website: www.ovmc.ovrh.org

Polyclinic Cancer Program
Seattle, Wash.
Delegate Rep: Kelly Shaw, MPH
Website: www.polyclinic.com

Regional Cancer Care Center
Berlin, Md.
Delegate Rep: Irene White
Website: www.atlanticgeneral.org/Main/Home.aspx

Tampa General Hospital Cancer Center
Tampa, Fla.
Delegate Rep: Shelia Jandrlich
Website: www.tgh.org

Cancer and Careers

BY REBECCA V. NELLIS, MPP

When you think about your place of employment, many words come to mind: a paycheck, benefits, security—but also, camaraderie, fulfillment, identity. When you think about the word cancer, different words and feelings are evoked. In the past, people did not necessarily think about these words together or the symbiotic relationship between the two. The focus after a cancer diagnosis was on getting well, and rightfully so. Yet medical advancements in the past 15 years have created an enormous, ever-growing population of survivors who must think about what comes after cancer—especially with regards to their current and future employment.

The statistics are staggering; one in two men and one in three women will face a cancer diagnosis and its aftermath. For most people today, a cancer diagnosis means getting up and going to work, despite any treatment-related challenges. To do so, however, most people will need a little help along the way.

I'd like to share some of the statistics that motivate why I get up and go to work every day:

- 42 percent of cancer survivors are of "working age"
- Many cancer survivors face unemployment challenges
- One to five years post-diagnosis, approximately 20 percent of cancer survivors still report workplace limitations
- 79 percent of respondents to a 2012 Harris Poll/Cancer and Careers survey said that cancer recovery was aided by the routine nature of work.

Cancer and Careers

Employment after a cancer diagnosis and treatment is a challenging, often uphill battle into the unknown—yet necessary. This statement is the underlying reason why Cancer and Careers (www.cancerandcareers.org) was started. Of the many excellent programs and services dedicated to cancer support, we are the only organization in the U.S. solely focused on helping people with cancer thrive at their place of employment. For nearly 15 years, we have been at the forefront of supporting working people affected by cancer, as well as their health-care providers, employers, and caregivers. Our "workspace" is that busy, messy intersection where life with cancer, and life on the job, collide.

In Their Own Words

To start to understand firsthand the complexity of the issue, here are a few quotes from people who have attended our events and used our programs and services:

- Joan. *"As a colorectal cancer survivor, the challenge came when I had to keep taking time off for scans and follow-up appointments. My employer began to berate me, and just really made it difficult and uncomfortable for me to make those appointments, and of course attend them. I was eventually let go."*
- Kurt. *"I am 51-years-old. I had a brain tumor partially removed in 2011 and was stable until May 2013. Just a couple of weeks after the cancer came back, I was laid off work. My career is high-level, and I acknowledge that my memory skills are being impacted by the tumor and treatments."*
- Erik. *"I worked in the film industry for 15 years, but stopped after being diagnosed with cancer. I'm struggling to find work and am open to any job. I can't really return to film because I'm not as quick as I used to be before treatment."*

Cancer and Careers is fueled by these voices. We are tenacious about moving the awareness needle on the employment challenges people with cancer face, what needs to be done to help meet these challenges—and why this issue matters.

So, What Do *We* Do?

At Cancer and Careers, we help people with cancer take control of their work situation; we refer to it as "being the boss over cancer." For instance, if the person is currently employed, we can help him or her create an action plan after the cancer diagnosis. Our services include:

- Insight on how to share the news of a cancer diagnosis with managers or co-workers.
- Assistance in designating a "point person" at the workplace for when the person with cancer is out of the office.
- Help arranging a more flexible work schedule (if possible).
- If not, help transitioning the individual back to work after having to take time off during cancer treatment.
- Legal and financial education, with referrals to additional resources to help individuals with cancer make informed decisions and plans.
- A resume review service to help people with cancer "stand out on paper."

- Advice on managing online reputations on commonly used social media platforms, such as Facebook and LinkedIn.
- Strategies to help "swivel" people away from pesky interview questions that may send them off track.

In a nutshell, Cancer and Careers aims to put power in the hands of people with cancer, and to "have their backs" with support, and the goal of propelling them forward to succeed in the workplace.

So, What Can *You* Do?

At Cancer and Careers, we believe that healthcare professionals are our "insiders," and an important part of the cancer and employment equation. An oncology nurse, social worker, or patient advocate can be a key ally, eliminating some of the uncertainty about balancing work and cancer early in a person's cancer journey.

Since 2009, Cancer and Careers has trained more than 1,700 professionals, offering free tools, accredited events, and specialized instruction. For example, our Education Series for Healthcare Professionals offers several get-down-to-basics webinars on what it means to work through cancer treatment, how to decipher the legalese that surrounds employment issues, and how to come back to work (smoothly) after taking time off for recovery.

We know people with cancer often have employment-related questions. We understand that these people and their caregivers need an individual or an organization they trust to answer these questions and offer follow-up resources when more questions come up during their cancer journey. Bottom line: working men and women with cancer need a map and a guide, and a healthcare professional is uniquely positioned to help with both.

Strategies to Succeed

Now let's zoom back a little and talk about what works on a macro-level. What simple practices cultivate a climate of support?

- When the patient, healthcare team, and employer all work together to create a plan of action.
- When prospective employers focus on the skills and experiences of qualified candidates, regardless of their health history or resume gaps.
- When people who can no longer do a certain job because of the effects of their cancer treatment are able to find new work opportunities and not made to feel that they will never be able to support themselves, or their families, again.
- When cancer patients understand their rights and how to exercise them via existing laws.
- When employers lead the charge in developing supportive workplace policies because they recognize the value in retaining quality staff members and make it a priority to do so.

As chief mission officer for Cancer and Careers, I oversee all mission-related plans and goals, and we have an exciting year ahead. We will continue our efforts to reach underserved regions in the U.S. because our free resources are particularly important to those with less access to information or support. We have hosted patient events and in-service trainings in remote communities from Hawaii to Alaska, and our 2015 travel plans include stops in New Mexico, Nebraska, and Wyoming.

We are also in the midst of piloting a cancer support program for employers since we know one of the biggest predictors of workplace success for cancer survivors returning to employment is workplace accommodations. The program, Workplace Transitions for People Touched By Cancer, is a collaborative effort between Cancer and Careers, several major U.S. companies, such as Anthem and Pfizer, and the U.S. Business Leadership Network, to help employers offer the support necessary for their employees who are cancer survivors.

Lastly, our fifth National Conference on Work & Cancer will take place June 12 in New York City. This accredited, full-day event will include presentations, Q&A sessions, and discussions from an esteemed group of oncologists, cancer rights attorneys, medical social workers, career experts, and others. Admission is free, and we offer travel scholarships for those needing financial help to attend.

There is always more to talk about on the issue of employment after cancer. As cancer care providers, we thank you for spreading the word, staying in touch, and keeping the conversation going!

Rebecca V. Nellis, MPP, is the chief mission officer for Cancer and Careers, a national nonprofit addressing the intersection of work and cancer. For more information, tools, and programs visit www.cancerandcareers.org.

careers

MANAGER CLINICAL TRIALS
Knoxville, Tennessee

The Manager of Clinical Trials will be responsible for the administration, planning, and direction of all research operations, assuring that clinical studies are performed according to Standard Operating Procedures and Good Clinical Practice Guidelines. In addition, the Manager of Clinical Trials will be responsible for staff education, development, financial matters, and quality outcomes. This manager may assume project line management responsibilities and act as the local Project Manager for certain designated research studies—reporting directly to the Clinical Director of Thompson Cancer Survival Center.

Requirements: Full time position. Current Tennessee RN license and Oncology Certification (OCN). A Bachelor of Science, Nursing, or equivalent work experience in oncology nursing. A minimum of three (3) years management in the oncology setting. Must have knowledge of clinical trials regulatory requirements, as well as clinical trials process and study site management. Must be willing to travel between all TCSC/TOG sites.

Preferred Qualifications: A successful candidate will need to be organized, self-directed, and have the ability to work with multidisciplines in order to provide excellent patient care. We prefer candidates within the Association of Clinical Research Professional or Society of Clinical Research Associates and a minimum of five (5) years relevant clinical research experience.

THOMPSON CANCER SURVIVAL CENTER
Covenant HEALTH

Apply online at: https://careers-covenanthealth.icims.com/jobs/10174/manager-clinical-trials/job.

ADVERTISER'S INDEX

MEDICAL DIRECTOR
Towson, Maryland

The Sandra & Malcolm Berman Cancer Institute (BCI) at Greater Baltimore Medical Center (GBMC) seeks a Medical Director to work collaboratively with the Executive Director of Oncology Services to lead the strategic and operational direction of GBMC's oncology service line. The Medical Director, considered the equivalent of a department Chair will maintain a clinical practice and administer and coordinate clinical activities of the oncology service line including education, research, and programmatic development. The ideal candidate will be Board Certified in any specialty of oncology with the ability to qualify for the appropriate level of membership on the Medical Staff of GBMC.

To Apply contact: Jane Fischer, Tyler & Company, 610-558-6100, or jfischer@tylerandco.com.

When it comes to oncology solutions, there is only one.

Bridging the gap between strategy and execution

We are Oncology Solutions, the nation's largest and most experienced cancer consultancy. Our services span the lifecycle of program development, from visioning and strategic conception through implementation and execution.

Our collaborative and comprehensive approach has been proven over four decades, with more than 1,800 successful cancer program engagements. Contact us today to find out how our experts can partner with your health care organization to deliver impactful, lasting results.

ONCOLOGY SOLUTIONS
Innovation. Collaboration. Results.

Program Planning & Development • Facility & Technology Planning • Operational Assessments of Oncology Practices/Departments
Information Technology Planning • Hospital-Physician Alignment • Clinical Program Development • Community-Tertiary Care Center Affiliations

(404) 836-2000 // consulting@oncologysolutions.com // www.oncologysolutions.com

insightful cancer data
at your fingertips

CHAMPS insight$_2$oncology™

Transform your cancer data into actionable information for strategic planning, operational and financial decisions with CHAMPS Oncology's new web-based analytics system.

insight$_2$oncology™ provides you with a new perspective of your current market position and the unique insight to manage and improve your cancer service line.

i$_2$o™ allows you to collaborate with CHAMPS to analyze and interpret your cancer data in order to identify gaps, retain and attract patients, and make informed decisions with confidence.

"CHAMPS i$_2$o™ is changing the way our healthcare system is managing its practices both operationally and strategically," said one i$_2$o™ beta tester.

CHAMPS Oncology

become 1 of 10 early adopters | insight2oncology.com