ONCOLOGY ISSUES

The Journal of the Association of Community Cancer Centers
September | October 2014

Oncology Financial Navigators

Integral members of the cancer care team

ACCC Association of Community Cancer Centers 40 YEARS STRONG

GRANIX™
(TBO-FILGRASTIM)
Injection

Take a bite out of G-CSF acquisition costs*

GRANIX™ is another option in short-acting G-CSF therapy

GRANIX™ is an option for hospitals and payers to consider when determining health system budgets

- **FDA approved through the rigorous BLA† process**
- **Teva's short-acting G-CSF was first introduced in Europe in 2008 and is available in 42 countries‡[1]**
- **GRANIX J Code: J 1446-Injection, tbo-filgrastim, 5 micrograms, effective January 1, 2014**

†Biologics License Application.

‡As of February 2014.

*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.

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.
- **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. Data on file. Teva Pharmaceuticals: Filgrastim MA Approvals Worldwide. February 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 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)*]
- Potential for Tumor Growth Stimulatory Effects on Malignant Cells [*see Warnings and Precautions (5.5)*]

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.

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

There are no adequate and well-controlled studies of GRANIX in pregnant women. In an embryofetal developmental study, treatment of pregnant rabbits with tbo-filgrastim resulted in adverse embryofetal findings, including increased spontaneous abortion and fetal malformations at a maternally toxic dose. GRANIX should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

In the 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 ($AUC_{0\text{-}24}$) 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.

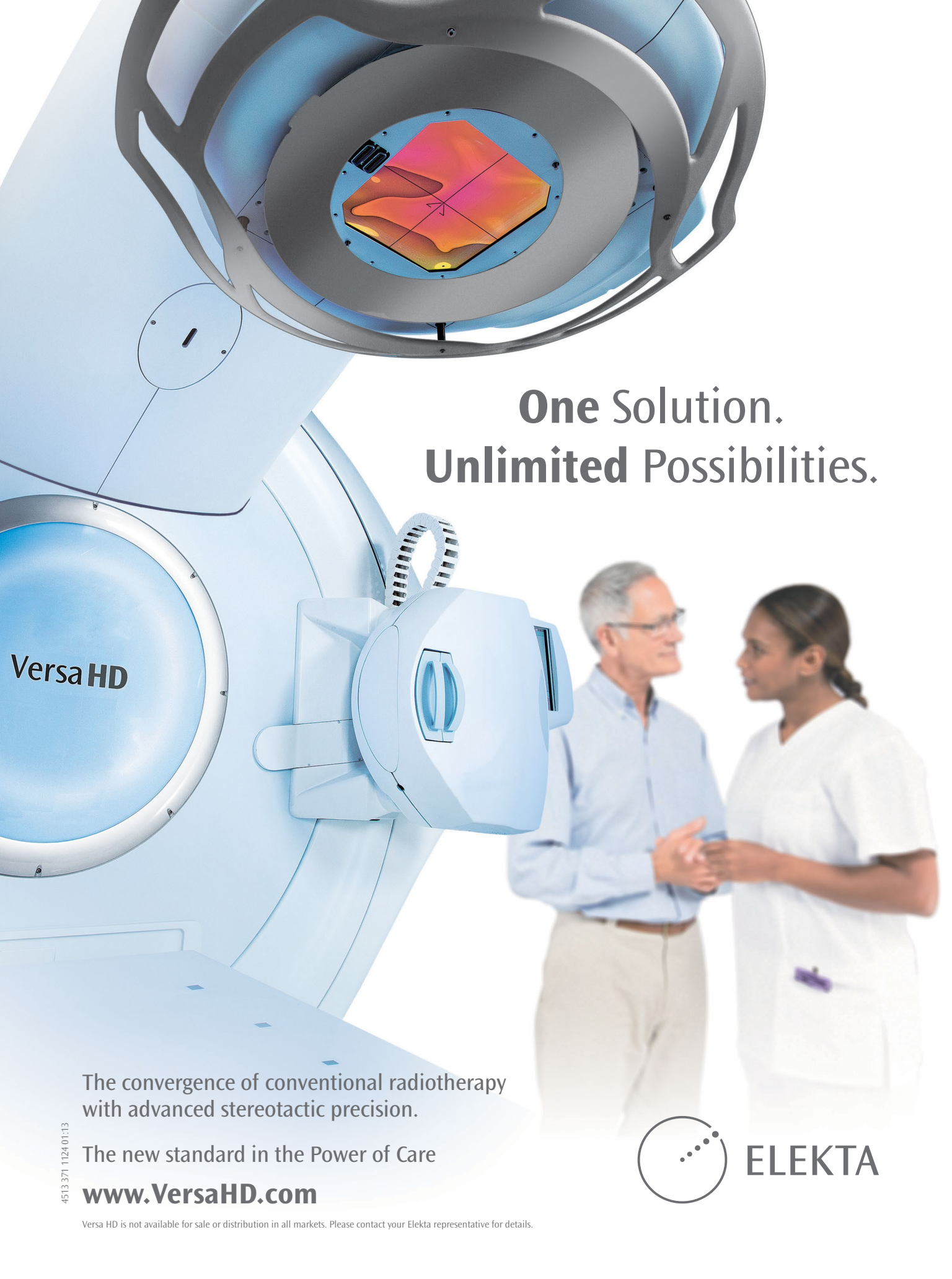
TEVA Oncology

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-40189 January 2014

This brief summary is based on TBO-003 GRANIX full Prescribing Information.



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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

Keep Your Eyes on the Road

BY CHRISTIAN DOWNS, JD, MHA

Back in high school, my old football coach was also my driver education instructor. Coach used to get particular joy in turning around his golf ball-sized, college championship ring, resting his ring hand behind the seat, and then popping his students in the head when we made a driving error. I didn't get the ring much, but I do remember one time: "Stop staring at your rear view mirror! Look out the windshield." *Pop*!

In other words, don't look at what's behind you, but focus instead on what's coming down the road. This *Oncology Issues* is just such a "look out the windshield" edition.

First, mailing with this issue are highlights from ACCC's 2014 Trends in Cancer Programs Survey. For the last five years, thanks to generous support from Lilly Oncology, ACCC has been able to produce this report—helping you to focus on the road ahead. ACCC's Trends in Cancer Programs Survey was one of the first to identify the shift in care from the physician office setting to the hospital outpatient department. This tool also demonstrated the widespread (and growing) use of dedicated financial advocates in most cancer programs.

Take some time and review these highlights. Anecdotally, we've heard that many of your colleagues use this information in strategic planning, needs assessments, and updates to the C-Suite. And starting with the next iteration of ACCC's trends survey, we will include even more "forward looking" questions that will capture data from several different disciplines.

Along with ACCC's 2014 Trends in Cancer Programs Survey, articles in this issue offer a "look through the windshield" at what's coming towards the oncology community.

For example, in line with results reported in ACCC's trends survey, author Dan Sherman's article describes the importance of oncology financial navigators to our patients *and* our programs. His financial navigation pilot project demonstrated ROI by improving access to care, removing financial barriers, improving patient distress, reducing bad debt, and saving money for the cancer program's charity program.

Next, author Kate Sweeney writes about her program's "Hub" model of care. By placing patients at the middle or "hub" with all the services they need surrounding them, this cancer program was able to improve patient access and care coordination.

An issue that nearly all of us see looming ahead is the increasing incidence of skin cancer. Authors Steven Castle, John Turner, and Tricia Cox discuss the importance of skin cancer screening. Not only is this type of screening crucial for prevention efforts, it may also be an outreach opportunity for cancer programs seeking to expand market share or increase their footprint in the local community. Read how this skin cancer screening clinic reduced patient wait times, increased awareness about the risk of skin cancer, and expanded the hospital's scope of services and marketplace brand.

Finally ACCC's 2014 ASCO Roundup, compiled by ACCC Past President Cary Presant, MD, FACP, FASCO, provides a look at what is coming down the road in terms of new treatments and technologies.

As you can see, with ACCC's 2014 Trends in Cancer Programs Survey, *Oncology Issues*, and numerous other tools and resources, ACCC members won't need coach and his ring to remind them to keep their eyes on the road ahead. And that's a good thing—believe me! OI

PRESIDENT'S MESSAGE

Cancer Quality—GP³?

BY BECKY L. DEKAY, MBA

It is so interesting to see the word "quality" becoming a mantra for so many groups—federal and state governments, and payers, providers, and patients (GP³). The quest for "quality" has been around for a long time. What is different today is the increased emphasis on quality in *cancer care*.

Quality measures for acute myocardial infarction, congestive heart failure, and total hip replacement have been in existence since the late 80s, early 90s. While patients with those conditions are unique—many with co-morbidities—the treatment and outcome for these patient populations are very similar and predictable for at least the proverbial 80 percent of cases.

In contrast, cancer providers treat more than 100 diseases in various stages and with varying tumor markers, differing genetic structure, and individual tolerances for many toxic drugs. Choosing the appropriate quality measures for this patient population has proven to be a daunting task. Even more formidable is how to communicate quality to the stakeholders who want to understand what "quality" cancer care really means.

In June, I attended ACCC's Institute for the Future of Oncology in Chicago. Two topics were on the agenda: "Organizational Leadership" and "Communicating Quality." Stakeholders held lively discussions around both topics, which will lead to white papers you'll hear more about later, but I found it very interesting how the topic of quality in cancer care bubbled to the top during the discussion of "Organizational Leadership." This experience illustrates perfectly how quality cannot be separated from other discussions. In fact, quality should take a central role, along with the patient, in any discussions related to cancer care.

I'd like to highlight two recent articles I read that touch on quality in very different ways. First was an article published online July 8, 2014, from the *Journal of Oncology Practice*, "Changing Physician Incentives for Affordable, Quality Cancer Care: Results of an Episode Payment Model." Among much interesting information about the study itself, this statement stood out to me: "Multiple quality measures were monitored, and none of them provided an early signal that quality of care was different than controls." (Quality measures monitored included ER and hospitalization rates, average drug cost per episode, survival rates, and many others.)

The second was a perspective in *The ASCO Post*, published June 25, 2004, titled "Sharing 50 Years of Christmas: A Quality Metric?" The author points out that clear-cut metrics, such as mortality, morbidity, hospital length of stay, and readmissions are closely monitored and hospitals and providers fall somewhere along the quality spectrum. He speaks of a 68-year old woman who was referred to him with biopsy-proven liver metastasis from primary colon cancer. After consultation with his patient, who had lost her husband of 49 years a few months earlier, and her daughter, a nurse by profession, they agreed upon a right hepatectomy. Surgery was uneventful but the patient suffered marked pulmonary problems post-surgery due to her history of smoking. The problems were reversible and easily treatable, but after a few days the patient and daughter decided to withdraw all active interventions. She was transitioned to comfort care and passed away surrounded by her family.

The author stated the patient's providers felt that they satisfied all of the quality metrics—appropriate assessment, uneventful surgery, appropriate post-operative care, site-of-service transition, and respect for the family wishes. His point: the person sitting at a remote computer assessing the quality of care objectively may believe this mortality was negative since the metric is "yes" or "no." To the patient and her daughter, the fact that the patient would spend the 50th Christmas with her husband was a much better metric of "quality" than mortality.

These two articles exemplify the wide chasm that exists when trying to capture quality in cancer care; what is important to the many stakeholders, including GP³. It is not too late to join in this important conversation at the ACCC 31st National Oncology Conference, October 8-10, in San Diego. Add your voice to the collective! OI

Coming in Your 2014–2015 *ONCOLOGY ISSUES*

- What to Do When Our Staff Becomes Our Patients
- The N.E.T. (Non-Emergency Transportation) Program
- Improving the Patient Experience with the Chemotherapy Process
- FUN (Fitness, Understanding, Nutrition) for Life Program
- The Journey to Cultural Competence
- A Model Oncology Rehabilitation Program
- An Innovative Breast Cancer Survivor Retreat
- Cancer Clinical Trials: Enhancing Infrastructure & Accrual
- Patient Education & Consent for Oral Chemotherapy
- A Value-Driven Symptom Management Clinic
- Closing the Gap: An Outpatient Nutrition Clinic
- Capturing Quality Data to Improve Palliative Care
- COME HOME—A Model Oncology Medical Home

more online @ www.accc-cancer.org

fast

LISTEN

Reimbursement Outlook for 2015?

Did you miss ACCC's call on the proposed 2015 HOPPS and PFS rules? Log into mynetwork@accc-cancer.org and enter the key words "OPPS 2015" or "PFS 2015" in the search box to listen to the archived call.

INFO

To Extend or Not to Extend?

ACCC's newest education resource examines the costs and benefits of extending practice hours, including a practical tool where cancer programs input their own data to help develop a value proposition for making this programmatic change. www.accc-cancer.org/resources/pdf/Patient-Centered-Scheduling.pdf.

VIDEO

It Takes a Team

In this brief video, your peers from across the country answer the questions—when, why, and how to reach out to one of ACCC's Community Resource Centers. www.accc-cancer.org/resources/CRC.asp#video2.

MEETING

One-Day Financial Advocacy Meetings

Interactively discuss case studies, successful strategies, and practical solutions related to financial advocacy and patient assistance. Join us in San Diego, Calif. (Oct. 8); Schaumburg, Ill. (Nov. 6), and Seattle, Wash. (Dec. 9). Register today at www.accc-cancer.org/financialadvocacy.

GPOs generate up to $55 billion in annual cost savings for hospitals, Medicare & Medicaid.

GPOs are expected to reduce healthcare spending by up to $864 billion over the next 10 years.

Source. Dobson DaVanso & Associates, LLC. A 2014 Update of Cost Savings and Marketplace Analysis of the Health Care Group Purchasing Industry Healthcare Supply Chain Association. https://c.ymcdn.com/sites/higpa.site-ym.com/resource/resmgr/research/hsca_cost_savings_group_purc.pdf.

A Look at ACA Open Enrollment

- **10.3** million uninsured Americans got coverage during open enrollment*
- **57%** of ACA enrollees were previously uninsured+
- After enrollment, the adult uninsured rate fell from **21%** to **16.3%***
- The largest decline in uninsured Americans occurred among **Latinos, blacks,** and **adults ages 18-34**—groups targeted for outreach.*

Sources. *Sommers BD, et al. Health reform and changes in health insurance coverage in 2014. *NEJM*. Published online at www.NEJM.org. +Kaiser Family Foundation. Survey of Non-Group Health Insurance Enrollees. http://kaiserfamilyfoundation.files.wordpress.com/2014/06/survey-of-non-group-health-insurance-enrollees-findings-final1.pdf.

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facts

10 Questions to Guide End-of-Life Conversations

1. Thinking about your death, what do you value most about your life?
2. If you were diagnosed with cancer, would you want to pursue every possible cure?
3. Do you imagine wanting to stop curative efforts if they were unsuccessful?
4. What kinds of aggressive treatments would you want (or not want)?
5. Do you want to die at home?
6. How do you feel about an extended hospitalization?
7. How much pain is acceptable to you?
8. Do you want to be with your family when you die?
9. What decisions regarding care do you want to entrust to others?
10. What do you hope for most regarding your death?

Source. Hospice Foundation of America. www.hospicefoundation.org.

U.S. Cancer Survivors Face Significant Economic Burden

- From 2008–2011, male cancer survivors had annual medical costs of more than **$8,000** per person, and productivity losses of **$3,700** compared to males without a history of cancer at **$3,900** and **$2,300** respectively.
- Female cancer survivors had **$8,400** in annual medical costs per person and **$4,000** in productivity losses compared to females without a history of cancer at **$5,100** and **$2,700**.
- Cancer survivors were more likely to be female, non-Hispanic white, have multiple chronic conditions, or to be in fair or poor health.
- Employment disability accounted for about **75%** of lost productivity among cancer survivors.
- Among survivors who were employed at the time of their diagnosis, cancer and its treatment interfered with physical tasks (**25%**) and mental tasks required by the job (**14%**); almost **25%** of cancer survivors felt less productive at work.

Source. CDC. Medical Costs and Productivity Losses of Cancer Survivors: United States, 2008-2011. www.cdc.gov/mmwr.

BUZZ ACCC

Stay (or Get) Engaged!

Member engagement is *everything* to ACCC. In addition to the committees highlighted on your right, here are some other ways you can stay engaged.

Follow ACCC on Twitter

Here is just a sample of our recent tweets:

Check out highlight videos from our 2014 Innovator Award Winners to learn about their game-changing care strategies, http://ow.ly/ACff8.

ACCC's Question of the Week: How Will Biosimilars Impact Cancer Care? Take our quick poll here: http://ow.ly/AxJgE #biosimilars.

Congrats to ACCC-member Helen F. Graham Cancer Center & Research Institute on 5-year, $8.2 million NCORP grant, http://ow.ly/Auv3k .

Like ACCC on Facebook

Here's a look at what's on our wall:

CMS announced that the Open Payments system is reopened so that physicians can register, review, and, as needed, dispute financial payment information received from healthcare manufacturers, under the Sunshine Act Open Payments program.

Join ONS for #whentostop tweet chat about prolonged cancer treatment this Thursday, August 14, from 12-1 pm EST.

Coming again this fall: ACCC's Oncology Reimbursement Meetings—the free meetings it pays to attend! More info, registration, and complete agendas here: www.accc-cancer.org/meetings/ReimbursementMeetings.asp.

Join ACCC on Linked In

Don't be late to the party! More than 2,000 of your colleagues have already joined.

Pick Up Your Pen!

Do you enjoy reading this journal? Then maybe it's time to contribute! *Oncology Issues* accepts unsolicited manuscripts of interest to our readers. It's easy. Simply send a query email to mmarino@accc-cancer.org with one or two paragraphs about your intended topic and its relevance to the oncology community. Or maybe you would like to provide input into future topics? If so, ACCC's Editorial Committee might be just the venue. Email volunteerinfo@accc-cancer.org to find out more.

Are You in the Know?

As the leading education and advocacy organization for the multidisciplinary cancer care team, ACCC relies heavily on the shared expertise of its membership and a cadre of dedicated volunteers. Are you "in the know" about the issues and challenges affecting today's cancer programs? Then ACCC wants to hear from you! Help provide input into future meeting agendas. Email apowell@accc-cancer.org to share your knowledge.

fast facts

Raise Your Voice!

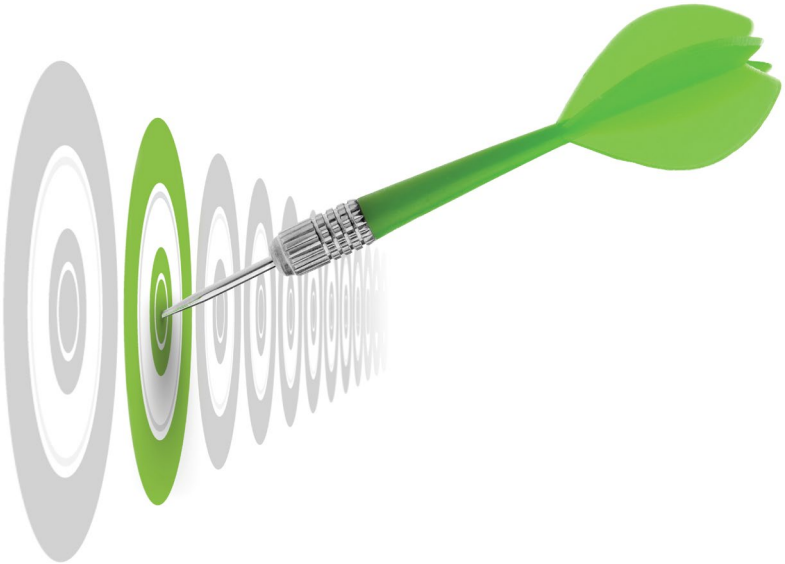
Healthcare reform. The Affordable Care Act. State health exchanges. New payment models. Accountable Care Organizations. Quality reporting. These are just a few of the challenging (and sometimes scary) changes the oncology community is facing. Do you want a voice in shaping the future of the oncology landscape? If so, get involved in ACCC's advocacy efforts by emailing mfarber@accc-cancer.org.

We're Looking for a Few Good Men and Women!

ACCC is governed by a Board of Trustees comprised of 15 elected members: President, President-Elect, Immediate Past President, Secretary, Treasurer, and ten trustees. ACCC's Nominating Committee helps solicit nominees who are representative of the different programs, chapters, and professions that make up ACCC's multidisciplinary membership; reviews the qualifications of the nominees; and then selects appropriate candidates to be placed on the ballot. Want a say in nominating future leaders? Email volunteerinfo@accc-cancer.org.

Like to Strategize?

Like any well-run organization, ACCC develops and follows a strategic plan to help guide day-to-day operations and decision-making. Each year ACCC's Strategic Planning Committee reviews the long-range goals, strategies, and milestones; obtains approval from the Board of Trustees if changes need to be made; and reports the Board-approved strategic plan to ACCC's House of Delegates. If you're interested in helping set the future course for ACCC and its membership, consider volunteering for this important committee. Email volunteerinfo@accc-cancer.org to learn more.



It's that Time of Year Again...

BY MATTHEW FARBER, MA

That's right. Even though memories of backyard barbecues, pools and beaches, and celebratory fireworks are still fresh in our minds, summer is officially over. For ACCC, the end of summer means it's time to comment on two 2015 rules proposed by the Centers for Medicare & Medicaid Services (CMS).

As it often does, CMS released its proposed Physician Fee Schedule (PFS) and Hospital Outpatient Prospective Payment System (HOPPS) rules right before the July 4 holiday. The public is then given 60 days to read the rules and submit comments, which means that comments were due right around Labor Day. (Isn't it interesting how the rules correspond to holidays? And to add one more, the final rules are usually released around Thanksgiving.)

The proposed rules for 2015 are a mixed bag, as they usually are. There are proposals that we like, and others that we do not. In its comments, ACCC has communicated to CMS how these proposed changes will affect its membership—both the negatives and the positives. (Sometimes showing support for a proposal can be just as important as speaking out against a proposal.) Overall, however, there seemed to be fewer "ground-breaking" changes proposed for 2015, especially compared to 2014.

If you recall, last year in both rules CMS included significant proposals that—if implemented—could have meant significant changes to oncology. In the 2014 HOPPS proposed rule, the agency proposed to collapse E&M clinic visit codes and to bundle chemotherapy administration codes. In the 2014 PFS proposed rule, it was the proposal to lower the reimbursement rates for more than 200 codes to the same levels found in other sites of service that likely would have had serious negative consequences for oncology practices. As it turned out, in the final 2014 HOPPS and PFS rules, only one of these proposals was finalized for calendar year 2014 (the collapse of the five E&M codes into one clinic visit code), largely because groups such as ACCC commented to CMS about the possible implications of the agency's proposed changes.

By the time you read this column, ACCC will have submitted its comments on both rules. (You can read the comment letters in the Advocacy section at www.accc-cancer.org.) And while there are not as many significant proposals for 2015, here are a few of the issues ACCC commented on.

In the 2015 proposed PFS ACCC spoke out on:

- The modifier for "off-campus services." ACCC plans to work with CMS to ensure this requirement will not cause undue burdens on members and also explore how the agency can best use the data gathered.
- Revision of equipment costs, which will have a negative impact on radiation oncology and radiology reimbursement.
- Changes to digital mammography and prostate biopsy codes. ACCC will monitor these changes to see how they may potentially affect membership.
- Potentially mis-valued codes.
- The elimination of the CME exemption from Sunshine Act reporting.
- A chronic care management code. ACCC intends to work with CMS on this issue.
- Changes to colorectal cancer screening, which will hopefully make it easier for patients to access this important service.
- Changes to the value-based modifier.

In the 2015 proposed HOPPS rule, ACCC commented on:

- Drug reimbursement. ACCC supported the proposed rate of ASP+6 percent (unchanged from 2014).
- Packaging of drugs and services, which holds both benefits and drawbacks for ACCC members.
- E&M codes. ACCC raised issues related to the negative impact of the 2014 E&M code changes.
- Comprehensive APCs, another area with both benefits and drawbacks for the oncology community.
- Future proposals to package drug administration. ACCC intends to work with CMS on this critical issue.
- The modifier for "off-campus services."

As in years past, ACCC also testified before a CMS advisory panel on many of these issues. If you have any questions on these proposals or ACCC's comments, please contact me at mfarber@accc-cancer.org. OI

Matt Farber, MA, is ACCC's director of provider economics & public policy.

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Medical Scribes

BY CINDY PARMAN, CPC, CPC-H, RCC

According to a January 12, 2014, article in *The New York Times*, physicians once pinned their hopes on computers to help them manage the overwhelming demands of office visits.[1] Instead, this article postulates that electronic health records (EHRs) have become a disease in need of a cure, as physicians do their best to diagnose and treat patients while continuously feeding the data-hungry computer.

Medical Scribe Do's & Don'ts

According to the American Medical Association (AMA), the medical scribe industry is poised for significant growth in the next few years.[2] The Joint Commission (TJC) defines a scribe as an unlicensed individual hired to enter information into the EHR or chart at the direction of the physician or licensed independent practitioner. Of importance, the individual acting as a scribe *does not*:

- Evaluate the patient in any clinical capacity
- Assist directly with patient care
- Make independent decisions
- Interject their personal observations or impressions in the documentation.

The primary function of a scribe is collaborating with the physician in the creation and maintenance of the patient's medical record in a timely manner, which is performed under the supervision of the attending physician.[3] Additional functions of a scribe may include performing other clerical and information technology functions for the physician.[4] For example, the medical scribe may:

- Accompany the physician into the examination room
- Transcribe physician orders for diagnostic tests or medications
- Document procedures performed by the physician
- Research pertinent past medical records
- Enter documentation on patient progress into the medical record
- Document discharge and/or follow-up instructions, as dictated by the physician
- Prepare referral letters as directed by the physician
- Fax or transmit medical information as instructed by the physician
- Collect, organize, format, and catalog data for quality reporting initiatives
- Support workflow and documentation for medical record coding
- Be available for physician concerns and questions and ready to assist at all times.

Medical students often act as scribes in the Emergency Department (ED) or other hospital outpatient settings. This role is not to be confused with the medical student's participation in a specific service as part of their training. According to the Centers for Medicare & Medicaid Services (CMS) in the Medicare Claims Processing Manual:[5]

E/M Service Documentation Provided By Students. *Any contribution and participation of a student to the performance of a billable service (other than the review of systems and/or past family/social history which are not separately billable, but are taken as part of an E/M service) must be performed in the physical presence of a teaching physician or physical presence of a resident in a service meeting the requirements set forth in this section for teaching physician billing.*

Students may document services in the medical record. However, the documentation of an E/M service by a student that may be referred to by the teaching physician is limited to documentation related to the review of systems and/or past family/social history. The teaching physician may not refer to a student's documentation of physical exam findings or medical decision making in his or her personal notes. If the medical student documents E/M services, the teaching physician must verify and re-document the history of present illness as well as perform and re-document the physical exam and medical decision making activities of the service.

While this policy does not prohibit using medical students as scribes, it is important to distinguish between scribed services and patient care performed and documented by the medical student to support a service rendered by the attending physician.

Salary & Certification

The Joint Commission states if an organization chooses to allow the use of scribes, surveyors will expect to see:

- A formal job description that clearly defines the qualifications and extent of responsibilities
- Documentation of orientation and training, competency assessment, and performance evaluations
- Documentation that all information management, confidentiality, and patient rights standards are met by the medical scribe.

Make certain that the range of duties to be performed by the scribe has been carefully considered before hiring an individual for this position. For example, will the scribe only make notes in the medical record, or will he or she also provide patient education materials, distribute the physician's prescriptions, and answer relevant questions? Establishing job functions in advance will help determine if a non-clinical staff person, medical assistant, nurse, or nonphysician practitioner is best suited for the practice setting.

According to *Medical Scribe*, a scribe can attain certification through vocational schools and through community colleges or state universities.[6] These degree programs average nine months to two years and typically result in either a certificate of completion or an associate degree. Bachelor degrees are available for human resource or hospital administration programs, which may be a career path for medical scribes.

Although salaries for scribes may vary regionally and based on the practice setting, beginning scribes generally receive $12 to $18 an hour while certified medical scribes can make up to $28 an hour with benefits. In contrast, the Medical Group Management Association (MGMA) *Physician Compensation and Production Survey 2013* lists the average annual nurse practitioner salary at $93,977 and the average annual physician assistant salary at $92,635.[7] According to the American College of Emergency Physicians (ACEP):[8]

A scribe records the findings of a physician. If the NPP independently obtains the history and performs a physical exam, many third party payers might not consider this as a scribe function but rather an independent service component by a healthcare provider, hence subject to the payer's relevant payment policies.

Most payers do not anticipate that midlevel providers will be hired to scribe for a physician practice or in the outpatient hospital setting.

Documentation

Make certain to review local payer information with respect to documentation for scribed services. For example, the Texas Medical Association states:[9]

For Medicare to cover a service for which you use a scribe, the documentation must clearly indicate:

- *Who performed the service*
- *Who recorded the service*
- *The qualifications (e.g., professional degree, medical title) of each.*

Example: "Leslie Smith, RN, recording E&M service performed by Jay B. Jones, MD."

Further, both the physician and scribe must sign the documentation.

According to WPS Medicare, the J5 MAC Part B Contractor:[10]

Hospital or nursing facility E/M services documented by a Non Physician Practitioner (NPP) for work that is independently performed by that NPP, with the physician later making rounds and reviewing and/or co-signing the notes, is not an example of a "scribe" situation. Such a service cannot be billed under the physician's National Provider Identifier (NPI), since it would not qualify as a split/shared visit. Neither would it qualify as "incident to," which is not applicable in a facility setting. In this case, the service should be billed under the NPP's name and NPI.

In the office setting, the physician's staff member may independently record the Past, Family, and Social History (PFSH) and the Review of Systems (ROS), and may act as the physician's "scribe," simply documenting the physician's words and activities during the visit. The physician may count that work toward the final level of service billed. However, in the same setting, an NPP accomplishing not only the PFSH and ROS, *but the entire visit*, should report those services under his or her own PTAN (Provider Transaction Access Number), unless "incident to" guidelines have been met. Only when the "incident to" guidelines have been met, should the physician's name and NPI be used to bill Medicare for that service.

Under the above circumstances, "scribe" situations are appropriate and can be a part of the physician's billing of services to Medicare. It is important, however, to be certain that the "scribe's" services are used and documented appropriately, and that the documentation is present in the medical record to support that the *physician* actually performed the E/M service at the level billed.

As stated above, scribed documentation must clearly support the name of the individual acting as a scribe, which means that the scribe must use their own security rights when logging into the EHR. Key to scribed documentation is the ability of an EHR to capture *both* the signature of the scribe and the separate signature of the physician. The performing physician remains responsible for all documentation in the patient medical record and must verify that

the scribed notes accurately reflect the service provided.

In addition, a scribe may be able to enter documentation of physician services, but depending on local regulations or provider policy, may not be able to scribe physician orders (e.g., orders for imaging studies, laboratory tests, nutrition services, etc.). Last, TJC guidelines state that verbal orders may not be given by scribes or to scribes.

Return on Investment

Each healthcare organization needs to perform its own return on investment (ROI) summary, but here is a general formula to use when deciding if employing medical scribes will be cost effective.

First, establish the scribe salary and benefits package (if a full-time employee). For the purposes of this example, a salary of $18 per hour ($144 per day) will be used. If benefits are 20 percent of salary (about $28 per day), then the total per diem cost for the scribe will be approximately $172.

Next, determine the increased physician productivity that will result from employing a medical scribe. For example, if the physician spends two hours of the workday performing medical record documentation, and these duties are assumed by the medical scribe, then the physician can potentially see an additional four to six patients during that time period. Physician revenue is therefore increased by approximately $292 to $438 per day.

In this example, the ROI is $120 to $266 per day (the amount of increased physician income minus the salary of the medical scribe). Assuming 220 workdays a year, this represents and annual revenue increase of $26,400 to $58,520 (not to mention more satisfied physicians who can focus on patient care).

The potential downside of a scribe arrangement was recently detailed in an article at www.newsobserver.com:[11]

Dr. Donald Gehrig, a St. Paul physician in private practice, said doctors working with scribes likely feel pressure to see more patients in order to cover the cost of a scribe. Patients might be reluctant to talk about issues ranging from sexual health issues and marital problems to abuse in the home when there's a scribe in the room, Gehrig said.

Therefore, even if the numbers make sense, it is essential that the cancer program survey patients and provide physicians with an opportunity to voice concerns related to the employment of medical scribes.

Closing Thoughts

Scribes are responsible for capturing medical information at point-of-care, which allows the physician to deliver hands-on patient treatment. Organizations that employ medical scribes or anticipate hiring for this position should:

- Set goals for the scribe program
- Define the scribe role and responsibilities
- Ensure appropriate examination room setup to maximize scribe use
- Communicate with patients and maintain physician engagement.

A scribe's responsibilities are ultimately controlled by the regulatory requirements and guidance that impact the written policies established by their healthcare setting and the level of risk the employer is willing to accept.[12] Last, healthcare organizations should continue to monitor federal, state, and other regulatory changes to ensure compliance is maintained in this area. OI

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tools

Approved Drugs

• The Food and Drug Administration (FDA) has approved **Beleodaq® (belinostat)** (Spectrum Pharmaceuticals, Inc., www.sppirx.com) for the treatment of patients with peripheral T-cell lymphoma (PTCL). It is intended for patients whose disease returned after treatment or who did not respond to previous treatment.

• Genentech (www.gene.com) announced that the FDA has approved **Avastin® (bevacizumab solution for intravenous infusion)** for the treatment of persistent, recurrent, or metastatic cervical cancer, in combination with paclitaxel and cisplatin or paclitaxel and topotecan.

• The FDA has approved a new indication for Bayer HealthCare's (www.bayer.com) **Gadavist® (gadobutrol) injection** for intravenous use with MRI of the breast to assess the presence and extent of malignant breast disease.

• The FDA expanded the approved use of **Imbruvica® (ibrutinib)** (Janssen Biotech, www.janssenbiotech.com) to treat patients with chronic lymphocytic leukemia (CLL) who carry a deletion in chromosome 17 (17p deletion), which is associated with poor responses to standard treatment for CLL.

• **Lymphoseek (technetium Tc 99m tilmanocept) Injection** (Navidea Biopharmaceuticals, www.navidea.com) has received FDA approval as an agent to guide sentinel lymph node biopsy procedures, specifically in head and neck cancer patients with squamous cell carcinoma of the oral cavity.

• The FDA approved **Zydelig™ (idelalisib)** (Gilead Sciences, Inc., www.gilead.com) to treat patients with three types of blood cancers. Zydelig is being granted traditional approval to treat patients whose CLL has returned. Used in combination with Rituxan (rituximab), Zydelig is to be used in patients for whom Rituxan alone would be considered appropriate therapy due to other existing medical conditions. The FDA is also granting Zydelig accelerated approval to treat patients with relapsed follicular B-cell non-Hodgkin lymphoma (FL) and relapsed small lymphocytic lymphoma (SLL), another type of non-Hodgkin lymphoma. Zydelig is intended to be used in patients who have received at least two prior systemic therapies.

Drugs in the News

• AbbVie, Inc. (www.abbvie.com) announced that the FDA has granted orphan drug designation to **ABT-414**, an anti-epidermal growth factor receptor antibody drug conjugate, which is being evaluated for safety and efficacy in patients with glioblastoma multiforme.

• Mirati Therapeutics, Inc. (www.mirati.com) announced that **mocetinostat**, a spectrum selective HDAC inhibitor, has been granted orphan drug designation by the FDA as a treatment for myelodysplastic syndrome (MDS).

Approved Devices

• Varian Medical Systems (www.varian.com) announced that it has received FDA 510(k) clearance for the **Calypso® soft tissue Beacon® transponder**, which can help enhance the precision of radiotherapy and radiosurgery treatments for cancer.

• IBA (Ion Beam Applications SA, www.iba-worldwide.com) announced that it has received FDA 510(k) clearance for its **Compact Gantry Beam Line**. **Proteus® ONE** is a single-room proton therapy system, which is smaller, less expensive, faster to install, and encompasses the latest in targeted proton therapy technologies.

• **ProctiGard™** (Access Pharmaceuticals, Inc., www.accesspharma.com), a novel treatment for symptomatic management of rectal mucositis, has received FDA 510(k) clearance.

Genetic Tests and Assays in the News

• Exact Sciences Corp. (www.exactsciences.com) announced that the FDA has approved **Cologuard**, the first stool-based colorectal screening test that detects the presence of red blood cells and DNA mutations that may indicate the presence of certain kinds of abnormal growths that may be cancers such as colon cancer or precursors to cancer.

spotlight

The Patricia D. and M. Scot Kaufman Cancer Center

Bel Air, Maryland

The Patricia D. and M. Scot Kaufman Cancer Center at Upper Chesapeake Health is part of a comprehensive cancer center in partnership with the University of Maryland Medical System, serving the residents of northeastern Maryland. In September 2012, University of Maryland Upper Chesapeake Health (UM UCH) and the University of Maryland Marlene and Stewart Greenebaum Cancer Center (UMGCC) signed an affiliation agreement to enhance cancer care services for patients in and around Harford County. This partnership both strengthened UM UCH's multidisciplinary cancer services and expanded patient access to clinical trials. Affiliation between UMGCC and the Patricia D. and M. Scot Kaufman Cancer Center brings the most advanced cancer therapies, state-of-the-art technology, enhanced supportive care services, and clinical research trials into one centralized location in Harford County.

The cancer programs at both of UM UCH's hospitals—UM Harford Memorial Hospital and UM Upper Chesapeake Medical Center—have received accreditation from the American College of Surgeons' Commission on Cancer (CoC).

The Kaufman Cancer Center officially opened its doors in October 2013. The cancer center is named after two visionary philanthropists who reside in Harford County and are strong advocates of improving cancer care in their community. As leaders of the "Hope and Healing Close to Home, Campaign for the Cancer Center," Pat and Scot Kaufman raised a total of $17.5 million for the new facility.

Radiation Oncology

At the Kaufman Cancer Center, radiation therapy is directed by a highly trained team of experts from the University of Maryland department of radiation oncology who helped develop the Varian TrueBeam System and Trilogy™ System with Rapid Arc, which allows the team to handle even the most advanced or complex cases. Radiation oncologists also have access to Flexitron afterloading platform technology, which helps improve safety and efficiency of brachytherapy treatment delivery.

Medical Oncology

Upper Chesapeake Hematology/Oncology is a hospital-employed medical oncology group with five board-certified medical oncologists and has been a mainstay in the community since 1984. Phil Nivatpumin, MD, is the medical director for the Kaufman Cancer Center and serves as the lead in all program development. In addition, all medical oncologists in the practice have taken on leadership roles in specific areas, such as research, infusion, breast cancer, and tumor conferences. The oncologists also serve as volunteer faculty with the University of Maryland, ensuring our patients have access to the most advanced treatments.

Infusion Center

The Kaufman Cancer Center's infusion area was designed to provide maximum comfort for patients and allow for maximum visual oversight by infusion nursing staff. The infusion area has 27 treatment bays, two private rooms, and one procedure room. There are on-site lab services, Fast Track chairs for injections, and an in-house pharmacy. The infusion center is staffed by seven ONS chemo-certified nurses, four of whom hold OCN certification. Directly adjacent to the treatment bays is a rooftop garden.

Multidisciplinary Cancer Clinics

The Kaufman Cancer Center offers multidisciplinary cancer clinics for patients with lung and breast cancers and their families, as well as clinics for gynecologic oncology, palliative care, and a survivorship clinic in a modified format. These clinics allow an interdisciplinary team of specialists to coordinate with each other and patients and their families to create a comprehensive treatment plan in a timely fashion. The patients can leave the clinic with a consensus opinion on their cancer treatment plan, as well as with a wealth of information enhancing their decision-making capabilities, and information on accessing clinical trials available in partnership with UMGCC.

In addition, through an agreement with the University of Maryland, the cancer center offers on-site genetic counseling.

Breast Center

The UM UCH Breast Center, which is located within the Kaufman Cancer Center, is staffed with a fellowship-trained breast surgeon, a reconstructive and general surgery expert, and specialists in oncology, radiology, pathology, and radiation therapy, providing patients with comprehensive, high-quality services in one convenient location.

With advanced diagnostic imaging technology, including digital screening, diagnostic and 3D mammograms, breast

ultrasound, breast MRI, surgical and nonsurgical biopsies, and DEXA bone density screenings, Kaufman Cancer Center and the Upper Chesapeake Health Imaging Center, in partnership with Advanced Radiology Services, provide cutting-edge screening and diagnostic services.

Under the direction of the medical director of breast surgery, the High-Risk Breast Cancer Clinic at the UM UCH Breast Center focuses on prevention and early detection of breast cancer through risk-factor modification and screening recommendations tailored to each individual patient. The surgeon, nurse practitioner, and nurse navigator work together to provide a comprehensive network of services to ensure every patient has breast care resources available in one location.

Dresher Family Healing Garden

The Dresher Family Healing Garden, located in the center of the Kaufman Cancer Center, was designed for meditation and integrative health. The garden includes seasonal flowers, benches, a labyrinth, reflecting ball, and waterfall. The garden theme continues throughout the cancer center in the natural landscape and artwork. A rooftop garden beside the infusion center continues to emphasize the healing aspects of nature where individuals can take a break from the medical environment for outside calm and reflection.

Cancer LifeNet & Support Services

Since the program first started in 2006, the Cancer LifeNet (CLN) team has helped patients cope with their cancer from diagnosis, through treatment, and well into recovery. Centrally located on the first floor of the cancer center, CLN includes oncology nurse navigators and oncology-certified social workers who provide critical health education and support to residents of Harford and Cecil counties at no cost, regardless of their cancer diagnosis or where they are receiving medical treatment. The nurse navigators are supported by a network of specially trained volunteers who have firsthand experience with cancer and provide telephone outreach to patients.

The Cancer LifeNet team provides free navigator and supportive care services to individuals and their families helping them balance work, family, and cancer treatment.

Financial counseling services are available to assist oncology patients and their families with understanding out-of-pocket medical expenses and helping them locate options and programs that might be of assistance in managing these costs.

An oncology-certified dietitian is available to monitor the nutritional effects of cancer and treatment in an effort to assist individuals with regaining optimal health.

All support groups in the Cancer LifeNet program are led by experienced healthcare professionals who strive to create a nurturing and safe environment for patients and families. Whether newly diagnosed, in treatment, remission, or experiencing recurrence, individuals are invited to share common experiences and receive education, information, and support.

Numerous disease-site-specific support groups are available, as well as:

- Just for Me (for patients with advanced cancer)
- Look Good, Feel Better
- CLIMB™ *Children's Lives Include Moments of Bravery* (for children who have a family member with cancer).

Integrated Therapy

CLN offers a variety of complementary therapies as part of an integrative approach to the care of those experiencing and recovering from cancer. Complementary therapies are used to reduce symptoms and adverse effects of anti-cancer therapies and to promote overall health and wellness of the mind, body, and spirit. In 2014 the cancer center began working closely with Maryland University of Integrated Health in an effort to bring student interns on site and offer a wider range of services such as acupuncture, individual and group yoga, life coaches, nutritional management, massage therapy, mindful meditation, and Reiki and healing touch.

Cancer LifeNet is entirely funded by donations and fundraising by The Upper Chesapeake Health Foundation, Cancer Care Alliance, and a Dresher Foundation grant. OI

Select Support Services

- Integrative therapies
- Oncology nutrition
- Spiritual care
- Financial counseling
- Speech & physical therapy

Number of analytic cases in 2013: 1,042

BY DAN SHERMAN, MA, LPC

Oncology Financial Navigators

Integral members of the multidisciplinary cancer care team

The lights were dim when I entered the room of a newly-diagnosed cancer patient. As an oncology social worker, I had walked into rooms like this hundreds of times before. Little did I know that this encounter was going to change lives—not only the patient's, but mine as well. In fact, this one visit with "Cathy" would affect thousands of other patients diagnosed with cancer in the future.

Having been a medical social worker for well over 10 years, I had all too often observed the financial devastation that a major medical issue could bring down on an individual and/or family. In fact, just six months before my meeting with Cathy, I'd had discussions with the leadership team at Lacks Cancer Center about the need to have a skilled individual on staff who could address the financial distress that our patients were experiencing, and to address it *differently* than we had in the past.

Far too many of my patients were anxious about their ability to pay for their cancer treatments. Too many were confused about options for reducing their out-of-pocket financial responsibilities; some were turning down care altogether. Not that charity care wasn't available. In fact, our hospital wrote off millions of dollars in charity care every year. But when I spoke with the leadership team, I communicated that our current healthcare system was complicated, and our solutions to reduce the financial distress of our cancer patients were too simplistic.

But let's return to the patient encounter that changed everything. Cathy had been admitted to our hospital with newly-diagnosed acute myeloid leukemia (AML). I recognized immediately that she would need extensive treatments for the next six months and close follow-up for several more years. Cathy had turned 65 a few months earlier; therefore, Medicare was her primary insurance. Although she did not have secondary insurance, Cathy did have a Medicaid spend-down (deductible) of about $800 a month.

When I entered the room to talk to her about coverage options, I found Cathy sitting alone in a corner of the room with various papers and forms in front of her. I introduced myself and asked if I could spend some time with her to talk about her health insurance status and her options for reducing her out-of-pocket responsibility.

For the next 45 minutes we talked through Cathy's options. One option was to enroll in a Medicare plan that would provide 100 percent coverage for radiation treatments, chemotherapy, and hospitalizations. This policy (at that time) would cost Cathy $25 a month. Obviously this was a much-improved scenario over the $800 a month Medicaid spend-down deductible. Cathy expressed her wish to enroll in this plan, and I walked her through the enrollment process.

Having completed the work of getting the appropriate coverage for her care, I was ready to leave for my next patient visit. As I started to leave the room, Cathy said, "*Thank you.*" I stopped and acknowledged her kindness and turned once again to leave. Again she called out, "*Thank you*," so I turned and acknowledged her again. Finally, she said it again, "*Thank you*!" but this time with more force. I turned around and saw tears forming in her eyes, so I walked over to Cathy and gave her a hug. As I turned to leave for the fourth time, she grabbed my arm and said, "*You just don't get it! Before you walked into my room, I was planning my funeral. I knew I couldn't afford the care I needed, so I was writing down what I wanted my funeral to look like. Now, I will plan to live.*"

Cathy was right of course—I didn't get it. At the time I didn't fully understand the significance of the financial distress Cathy was experiencing. For this patient, the financial cost of her cancer care had implications far beyond something as basic as putting food on the table.

When I left her room that day, I had a new appreciation for the role of the financial navigator and a newfound passion that compelled me to step away from medical social work to become an expert in the field of financial navigation services.

I knew then that the status quo had to change. I thought to myself, "If we're truly going to be a cancer center of excellence, we cannot allow our patients to go through what this patient just experienced." Cathy needed help to understand *all* of her coverage options—not just the simplest and/or partial options that had been offered to her prior to my visit. Without my intervention that day, the "status quo" method of delivering financial navigation services would likely have put Cathy on a path to her premature death. Since that fateful visit, I have worked each day to make sure that all of my patients are given the best, most practical, and comprehensive options for paying for their cancer care.

Today's cancer programs must accept that their old, band-aid approaches to discussing financial issues with patients are inadequate for solving a complex, systemic problem.

For social workers, financial advocates, patient navigators, and others who wish to offer a similar level of service at their own cancer programs, here is why we need to step up for change.

Challenging the Status Quo

Simply put, the standard of financial intervention in most cancer programs is inferior. When patients are underinsured with their Medicare plan, most cancer programs automatically try to get patients qualified for Medicaid benefits. Cathy qualified for that program—but with an $800-a-month cost-sharing responsibility. Obviously, the rote "business as usual" option did not solve Cathy's problem. Today's cancer programs must accept that their old, band-aid approaches to discussing financial issues with patients are inadequate for solving a complex, systemic problem.

Mercy Health Saint Mary's health system has provided financial advocacy services at its hospital for many years. In fact, most U.S. hospitals have financial advocates to assist cancer patients. But as Cathy's example illustrates—we need to ask ourselves if our current services are truly meeting the needs of our patients.

When we read the work of Zafar[1] and Ramsey[2] and reports about financial distress among cancer patients provided by the Kaiser Family Foundation,[3] the Oncology Roundtable,[4] the Community Oncology Alliance,[5] and the American Society of Clinical Oncology,[6] we must acknowledge that, as a whole, the oncology community is not alleviating the financial distress of a significant portion of the oncology population. And we must be ready to ask some difficult questions. For example, if the financial counseling services we provide are effective:

- Why do more cancer patients fear the financial obligation more than dying from the disease itself?[5]
- Why are oncology patients twice as likely to file for bankruptcy compared to the general public?[2]
- Why does 29 percent of this same population avoid or delay filling prescriptions due to the cost?[1]
- Why do 24 percent of oncology patients suffer relationship problems due to the financial pressures of the cost of care?[1]
- Finally, why are patients making treatment decisions based on cost rather than factors such as survivorship or ability to tolerate treatments?

These grim statistics clearly show that the oncology community has done an inadequate job of addressing the financial burden of this country's oncology patients.

When patients receive a cancer diagnosis, they trust that the care they will receive will be the best available. Most cancer programs promote their use of the latest available technology; I contend that financial navigation services need to match this same high level of care.

In 2009 the Advisory Board's Oncology Roundtable released a statement that succinctly captured the issue:[4]

At present, few cancer programs have a systematic process in place to identify patients in need and to develop a plan to meet their cost of care. Rather, financial counseling services are typically fragmented, with responsibility for various aspects of the process divided among registration staff, social workers, business office staff and clinicians. As a result, many miss opportunities to assist patients and improve revenue capture."

Unfortunately, this "siloed" approach to financial navigation services plays out daily in cancer programs across the country. But it's time to get serious about change. Our patients desperately need the oncology community to provide these services at a level that truly meets their needs.

Understanding the Problem

Over the last few years, researchers have paid increased attention to this issue, resulting in a newly coined term—financial toxicity.

"Financial toxicity" is defined as both an objective financial burden and subjective financial distress. Recent research by Yousuf Zafar, MD, MHS, found the following:[1]

- 42 percent of individuals applying for co-pay assistance reported a significant or catastrophic subjective financial burden
- 68 percent cut back on leisure activities
- 46 percent reduced spending on food and clothing
- 46 percent used savings to defray out-of-pocket expenses
- 20 percent took less than the prescribed amount of medications
- 19 partially filled prescriptions
- 24 percent avoided filling prescriptions altogether.

Zafar's conclusion: having health insurance does *not* eliminate financial distress or health disparities among cancer patients.[1]

A recent ASCO report found similar results among insured cancer patients, with more than 47 percent of the patients in the study reporting concerns about healthcare costs.[6]

At the same time, financial navigation services face a number of hurdles, including lack of resources, a lack of motivation to change, internal system failures, and/or a shortage of informed, qualified personnel. And certainly the complexity of available coverage options and the time required to fully understand how to apply these options to meet the unique needs of each patient are also important factors.

It's Complicated

Let's face it, financial navigation is complex. Patients and providers alike get lost in a maze of health insurance policies and assistance programs, all requiring different information for successful enrollment. For example, the rules governing Medicare Part D, with the initial coverage, coverage gap, catastrophic coverage levels, co-pay assistance guidelines, and steps to qualify for extra assistance programs are overwhelming for most individuals. With up to 35 percent of new oncology products being oral medications[7] and 11 out of 12 of these medications costing more than $100,000 a year,[8] it is essential that we help patients apply for programs that are the most appropriate and readily available to meet their specific needs.

All too often I have seen patients refuse oral treatment recommendations due to cost; only to find out that if these patients had received comprehensive financial navigation, they would have had access to these medications without significant cost-sharing responsibilities. In fact, a recent report published by the Community Oncology Alliance stated that Medicare beneficiaries abandoned their oral prescriptions almost twice as frequently as commercially insured beneficiaries; data showed that 16 percent of Medicare beneficiaries abandoned oral oncolytic treatments due to cost-sharing responsibilities.[9]

The complexity of Medicare coverage choices, for example, understanding the coverage differences of Medicare Advantage plans vs. Medigap vs. employer-based plans vs. Medicaid, frequently results in patients making uninformed decisions, often at the advice of well-meaning family members or friends. The fact is that Medicare beneficiaries who must choose from a list of 30 to 60 different coverage options—many of which have significant cost-sharing responsibilities—need advice from someone with more experience. More importantly, the uninformed consumer often is not aware of national open-enrollment and special-enrollment periods for Medicare plans. Patients who are unaware of the "fine print" details of their insurance plans often experience problems accessing care. At times, patients find themselves having to change doctors as a result of selecting a plan that puts their current providers out-of-network. Other patients choose plans that put them outside networks that are vital to their recovery needs.

This confusion harms not only the patient, but also the financial stability of the cancer program treating the patient.

While patients sometimes have questions about open enrollment and if, or when, they should apply, most often I see patients who are confused about the high out-of-pocket responsibilities that come with the Medicare plan they have enrolled in. The reasons for this confusion over cost-sharing responsibilities are multifaceted, but one major reason to consider is the host of Medicare options available to the general public. A recent publication from the Kaiser Family Foundation reported that the leading contributor to medical debt for the individuals surveyed was cost-sharing responsibilities incurred for in-network services.[3] Studies have also found that non-elderly Medicare beneficiaries experience more problems with cost-sharing responsibilities compared to elderly Medicare beneficiaries.[1]

In most states, access to supplemental policies for non-elderly Medicare beneficiaries is more restrictive, thus increasing the odds that these patients will enroll in a high cost-sharing Medicare plan. A well-trained financial navigator can help educate patients so that they enroll in the most advantageous plan for their specific medical needs.

The oncology community is seeing similar trends with the roll out of the health insurance exchanges under the Affordable Care Act (ACA). Again, patients are overwhelmed and confused about the enrollment process and the choices of coverage policies available to them. As an example, I recently worked with a patient who was facing medical costs exceeding $150,000 after being diagnosed with ALL (acute lymphoblastic leukemia). He had not enrolled in a healthcare-reform-based insurance plan. Feeling overwhelmed and confused about that process, he was now

outside the ACA's open enrollment period. Just prior to being admitted to our cancer center, the patient had been seen at two other hospital systems—neither of which provided financial navigation services. On his admission to our program, I assessed his situation and was able to assist the patient with enrollment into an ACA health exchange plan under special enrollment guidelines. As a result this patient will now avoid medical bankruptcy and the hospital will be reimbursed for services provided.

When patients are left on their own to wade through the 50+ Medicare options; the extra help program for Part D; co-pay assistance programs; premium assistance programs; ACA enrollment guidelines; the choices of bronze, silver, gold, or platinum plans; and available out-of-pocket subsidies, they will likely experience financial toxicity as they journey through cancer treatment. The key to successful financial navigation is presenting patients with all the available choices in the context of their medical condition. Each patient is unique and, in most cases, the "status quo" approaches used by many hospitals and cancer programs of enrolling patients in Medicaid, charity, or patient assistance programs are simply inadequate in today's market.

So How Can We Help?

I am proud to work for an organization that sees its mission as serving the poor and underserved. My hospital system often provides charity to those in financial distress. But charity programs can only manage a certain amount of debt load before program sustainability starts to be impacted. A better approach to financial navigation services is to educate patients on the programs that can help reduce their out-of-pocket responsibility. This education results in savings for the hospital's charity program and reduces the number of patients who fall into collection services. Furthermore, this process helps preserve the dignity of our patients, as most would prefer to avoid applying for charity altogether.

In 2009, following my experience with Cathy, I asked to head up a six-month pilot program (on a .5 FTE basis) where I would provide financial navigation services to the hospital's oncology population. My responsibilities during the pilot period were to reduce financial barriers, improve access to care, and measure the financial benefit for patients and the cancer program. For the pilot, I targeted patients who were uninsured and underinsured and for whom Medicaid was not their best option. Specifically, I targeted patients who were:

- In health insurance plans with out-of-pocket responsibilities of more than $5,000 a year
- Medicare Part D patients in the coverage gap due to high-cost oral oncology medications
- Medicaid patients with a spend down
- Patients with Medicare A/B only
- Patients without health insurance coverage
- COBRA recipients who could not afford the COBRA premiums
- Patients receiving off-label treatments
- Any patients expressing financial distress due to cost of care.

The pilot had two governing goals: 1) to improve access to care by reducing the financial barriers experienced by oncology patients and 2) to reduce charity and bad debt by $70,000 within the pilot program's six-month time period. Everyone agreed that the first goal would always take precedence over the second goal. The decision to prioritize these goals in this way was not only the right one to make, but it also created an atmosphere of trust that contributed to the success of the pilot program.

To put this in perspective, medical providers see patients at quite possibly the most vulnerable time in their lives, a time when they are being asked to make long-term, deeply life-impacting decisions. When a patient is considering their future financial security, they need to trust that the providers advising them truly have their best interests in mind. If patients do not have that level of trust, they will not be open to education about better solutions for their health coverage needs.

Our Approach

I would first interview patients to get to know them and understand their medical and financial situation. Next, I would introduce patients to coverage options that improved their out-of-pocket responsibilities.

In most cases, I sought out patients myself, but I also educated the social work, case management, and nursing departments to refer patients to the pilot program who met the specific patient types described above. I also worked closely with the billing department to identify patients with significant write-offs on their accounts. I made a concerted effort to communicate with each patient's oncologist so that I would have a more informed under-

standing of his or her medical needs. This improved understanding allowed me to better educate patients about coverage options that would complement their upcoming treatment regimen. This communication also helped me to build trust with oncologists, who then referred more patients for consultation.

The pilot program had great success. I reached the $70,000 goal in savings to the hospital by the second month. By the end of month five, I had saved the hospital system $265,000 and decreased out-of-pocket expenses for the patient by more than $700,000. In all, 78 patients were navigated. Based on these results, the hospital hired one FTE for the financial navigator position. Since then, the program has achieved the following outcomes:

- ***Year two of the program:*** 218 patients received navigation services, reducing out-of-pocket responsibility for patients by more than $2.6 million and saving the hospital system over $1 million in reduced charity and bad debt.
- ***Year three of the program:*** 168 patients received navigation services, and The Lacks Cancer Center added a second .8 FTE. Out-of-pocket responsibility for patients was reduced by more than $4 million and saved the hospital system $2.5 million in reduced charity and bad debt.
- ***Year four of the program:*** 211 patients received navigation services, reducing out-of-pocket responsibility for patients by more than $5 million and saving the hospital system $3.7 million in reduced bad debt and charity.

The decrease in the number of patients receiving financial navigation over the program's four years is due to a large backlog of patients needing these services during the program's first two years. However, the program's benefits have increased significantly every year—even when fewer patients received services. This is attributable to the roll out of the federally funded Pre-Existing Condition Insurance Plan (PCIP) program during year two of our financial navigation program. PCIP utilization significantly increased savings to both our patients and our cancer program.

Today, we offer financial navigation services to the following patient types:

- Uninsured
- Underinsured (relative to the patient's income status; we allow patients to self-describe as being underinsured)
- Patients on high-dollar oral medications who need assistance with their co-pays
- COBRA recipients
- Medicaid patients with a spend-down
- Patients with Medicare A/B only
- Patients who are entering into the Medicare system
- Every patient with advanced-stage disease.

Financial navigators may self-refer patients or receive referrals from the multidisciplinary cancer care team. Financial navigators then interview patients to see if they want to discuss their financial obligation for the medical care they are seeking, and if they'd like to discuss options for finding coverage systems that may reduce their out-of-pocket responsibilities.

Anecdotally, our team has found that patients and families who address their initial fears of financial obligations early on tend to be more at peace with the disease and more compliant with care.

For individuals with advanced-stage disease, we educate patients on the available options (STD, LTD, SSDI, SSI, COBRA, and Medicare) and answer any other questions they may have about how their disease may affect their long-term financial health. Anecdotally, our team has found that patients and families who address their initial fears of financial obligations early on tend to be more at peace with the disease and more compliant with care.

Financial Toxicity & Patient Satisfaction

A recent study by the Duke Cancer Institute found a correlation between high financial burden and patients' dissatisfaction with their healthcare services, concluding that:[10]

Understanding the connection between financial burden and patient satisfaction may help identify the extent to which modification of burden can improve this important metric of quality patient-centered care and improve the downstream results of an enhanced patient experience.

Anecdotal evidence from our cancer program suggests that successful financial navigation programs can improve patient satisfaction scores. Successful financial navigation can also reduce distress among oncology patients. It is rare that a day goes by without a patient approaching me or my colleague with heartfelt gratitude for the services we've provided to them. Some of the comments we've received:

- *Because of you, we were able to keep our house.*
- *Thank you for helping us access the medication we needed but could not afford.*
- *I would never have understood my insurance options without your guidance.*

I suspect that financial navigators from other cancer programs have heard similar sentiments from patients. At The Lacks Cancer Center, we have focused attention on the issue of financial toxicity, reducing the problem with solutions tailored to meet the needs of individual patients.

The Right Person for the Job

The financial navigation program has now been successfully replicated at 12 different cancer programs. I've learned that successful replication requires that financial navigators have a singular focus on the task, comprehensive training, one-on-one education, and peer support as solutions and programs constantly change and evolve. Successful financial navigation programs also require support from different departments, including billing, patient access, and pharmacy.

Successful financial navigators require multiple skill sets. The ideal candidate should possess clinical, financial, and mental health skills. It's essential that financial navigators are able to build trust within the first few minutes of meeting with the patient—otherwise the ability to fully assist the patient becomes very difficult. Financial navigators must be prepared to have treatment-planning conversations with the ordering physician and understand how different coverage policies can complement the treatment regimen. Financial navigators need to have empathy and the skills to have difficult conversations with patients; this is why good mental health skills are critical to the role. Finally, the person you hire for this unique position must exhibit utmost professionalism, balanced with a clear passion for the role.

Financial navigators play a critical role on the multidisciplinary cancer care team. Unfortunately, in many cancer programs, financial navigation services are relegated to secondary status, resulting in less than optimal solutions being offered to patients. Focused, educated, and passionate financial navigators are motivated to improve their skills and continually identify better solutions for their patients.

In the end, financial navigators with a clear understanding of the patient's medical diagnosis and treatment needs and who build trust with the patient can reduce or even alleviate patient financial toxicity. In some cases, a small delay in treatment may be an option as the financial navigator waits for new or added coverage to take effect. However, a comprehensive financial navigation program should never get in the way of providing optimal care for the patient. With the onset of the Affordable Care Act and considering some of the more complex solutions mentioned above, I believe that we are entering a new chapter of financial navigation services. This new era requires new wisdom and new processes so that our patients suffer less and our cancer programs remain financially stable.

Six Years Later. . .

I saw Cathy again this spring—six years after our first meeting. A little more frail and now in a wheelchair, her body is showing signs of aging. But one aspect of her personality has not changed—her smile. When I saw her in our cancer center, she yelled out "*Hi Dan*!" with a grin that defies description. Our first meeting changed the trajectory of my vocation and my life. I hope that Cathy realizes how her emphatic words of "*You just don't get it!*" have gone on to impact the lives of thousands of other cancer patients being treated in our health-care system.

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1 Carlson JJ, et al. *Breast Cancer Res Treat.* 2013 Aug;141(1): 13–22.
2 Data on file.

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BY STEVEN CASTLE, JOHN TURNER, MD, AND TRICIA COX, ANP

Skin Cancer Screening

A creative business model to offer an important community service

Skin cancer is the most common cancer in the U.S., accounting for more than half of all cancers in this country.[1, 2] More than 3.5 million cases of basal and squamous cell skin cancer are diagnosed in the U.S. each year; melanoma, the most serious type of skin cancer, will account for more than 76,000 cases of skin cancer in 2014.[2] Once diagnosed with skin cancer, a person's likelihood of developing a non-skin primary cancer at some point in his or her lifetime significantly increases. Many patients with skin cancer are treated by a dermatologist or primary care physician; patients with more advanced cancer are usually treated by an oncologist.

The Richmond, Virginia metropolitan service area has a long history of excessive demand and inadequate supply of available dermatology appointments—with some patients having to wait six months for an available appointment. To help better meet the needs of these patients and its community, one Virginia hospital developed a skin cancer clinic model that:

- Addressed long wait times for a basic skin examination
- Expanded the hospital's scope of services, differentiating the hospital from other providers
- Increased community awareness about the risk of skin cancer
- Expanded the hospital's brand in the marketplace.

The first challenge: identifying skilled personnel with the core competencies necessary to develop and implement a Skin Cancer Screening Clinic and doing so in a financially viable and compliant manner.

In this article, the authors share information about their initial feasibility study, a clinic description, a case study, implementation tips, and possible next steps with the hope that this information will help other programs looking to implement a skin cancer screening program.

The ultimate goal of the new Skin Cancer Screening Clinic: to generate volume, community awareness, and new revenue for the hospital.

Getting Started

In 2010 the cancer program's medical director and oncology service line administrator spearheaded a Strengths, Weakness, Opportunities, and Threats (SWOT) analysis (Table 1, page 28). Initially, the hospital approached private practice dermatology groups about the possibility of developing a partnership clinic. While these groups were unable to or not interested in participating, they were supportive of the hospital's efforts to launch its own Skin Cancer Screening Clinic and agreed to expedite appointments of screened patients needing higher-level care.

Next, the hospital established a new department cost center (Cancer Clinics—720) to support the Skin Cancer Screening Clinic and its associated services. Fortunately, costs were minimal as the hospital had access to an available skilled physician and office space. (The physical space used by the clinic also supports the hospital's Cancer Survivorship Clinic and outpatient palliative care.) The ultimate goal of the new Skin Cancer Screening Clinic: to generate volume, community awareness, and new revenue for the hospital.

The hospital found a physician leader for its Skin Cancer Screening Clinic in John Turner, MD, a physician accredited by

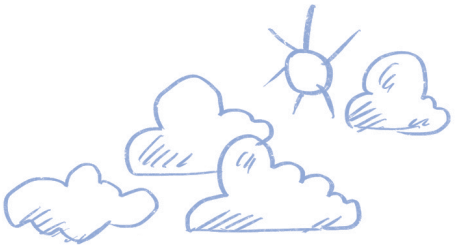

Table 1. SWOT Analysis

STRENGTHS	OPPORTUNITY
• A visible and respected oncology program with the skilled personnel to offer skin cancer screening • Great unmet demand for this service • Dermatology providers and surgical groups supportive of the hospital entering the market • Primary Care Physician support that is in line with hospital recruitment strategy • The ability to market service direct to consumer • Pathology services in place • Newly-built clinic space available • Minimal start-up costs • The ability to use existing 1-800 "Consult-a-Nurse" system for scheduling	• The potential for high patient volume • Underserved market as patients currently have 6–7 month wait for available dermatology appointments, leading to public demand for early access • The potential to increase traffic and awareness of the hospital's cancer program • Service differentiator • The opportunity to establish patient relationships within the healthcare system • The ability to generate patient volume for support services, such as pathology • The resources to take this service "on the road" and do off-site skin cancer screening • A replicable service model that could be extended to other network facilities • The ability to refer to a Mohs surgeon (once recruited) able to perform microscopically controlled surgery to treat skin cancer
WEAKNESSES	**THREATS**
• Limited physician capacity (addressed through training a nurse practitioner) • Allocation of the necessary marketing funds to grow awareness in the community • A process for gaining support from dermatology groups to ensure timely consultations for suspicious lesions	• Potential backlash from dermatologists • Managing expectations and relationships within the pathology practice

the American Board of Pathology (ABP) and the American Board of Dermatology (ABD), who joined the pathology practice affiliated with the hospital in 2009. The hospital contracted with Dr. Turner to serve as the medical director of Skin Cancer Services, reimbursing him fair market value for his time. Soon after, Commonwealth Laboratory Consultants, Inc., renewed its contract with the healthcare system, adding a provision to offer skin cancer screening services.

To test market demand, the hospital piloted four American Dermatology Association (ADA)-sponsored Skin Cancer Screening Days. Although marketing was limited, the hospital saw 46 patients—more than the allotted number of appointments. Of these 46 patients, 41 percent received recommendations for biopsy. A secondary review of this high biopsy rate conducted by Dr. Turner proved it was appropriate.

The next challenges the hospital faced were financial. Payers had different policies for skin cancer screening. For instance, some payers said that screening could only be conducted with primary care physician (PCP) orders and authorizations; other payers refused to pay for the screening service at all. To address this challenge, the hospital elected to charge patients a flat $30 out-of-pocket fee. This dollar amount was determined to be about equal to a patient co-payment and was within the hospital's *pro forma* (pages 30-31), ensuring that the Skin Cancer Screening Clinic would be financially viable.

To meet high patient demand, Dr. Turner trained (and now supervises) a hospital-employed advanced nurse practitioner (ANP) to serve in a physician extender capacity. Today, the ANP is able

to work independently, thus minimizing the demand on Dr. Turner's time. This staffing model strengthened the financial outlook of the Skin Cancer Screening Clinic as Dr. Turner was then able to allocate fewer clinic hours. Also, as both providers were on staff, the hospital was able to "float" hours to the Skin Cancer Screening Clinic when there was demand; thus, minimizing sunk costs. The Skin Cancer Screening Clinic is "bloodless and non-treating," so patients are referred to specialists for additional care when warranted. The hospital developed patient materials that identify qualified physicians who have requested to be listed. The list includes general surgeons, plastics surgeons, and dermatologists.

Clinic Model

The Skin Cancer Screening Clinic operates on a regular schedule within the hospital's cancer program—every Tuesday afternoon

(continued on page 32)

Figure 1. Flowchart of Skin Cancer Screening Clinic Process

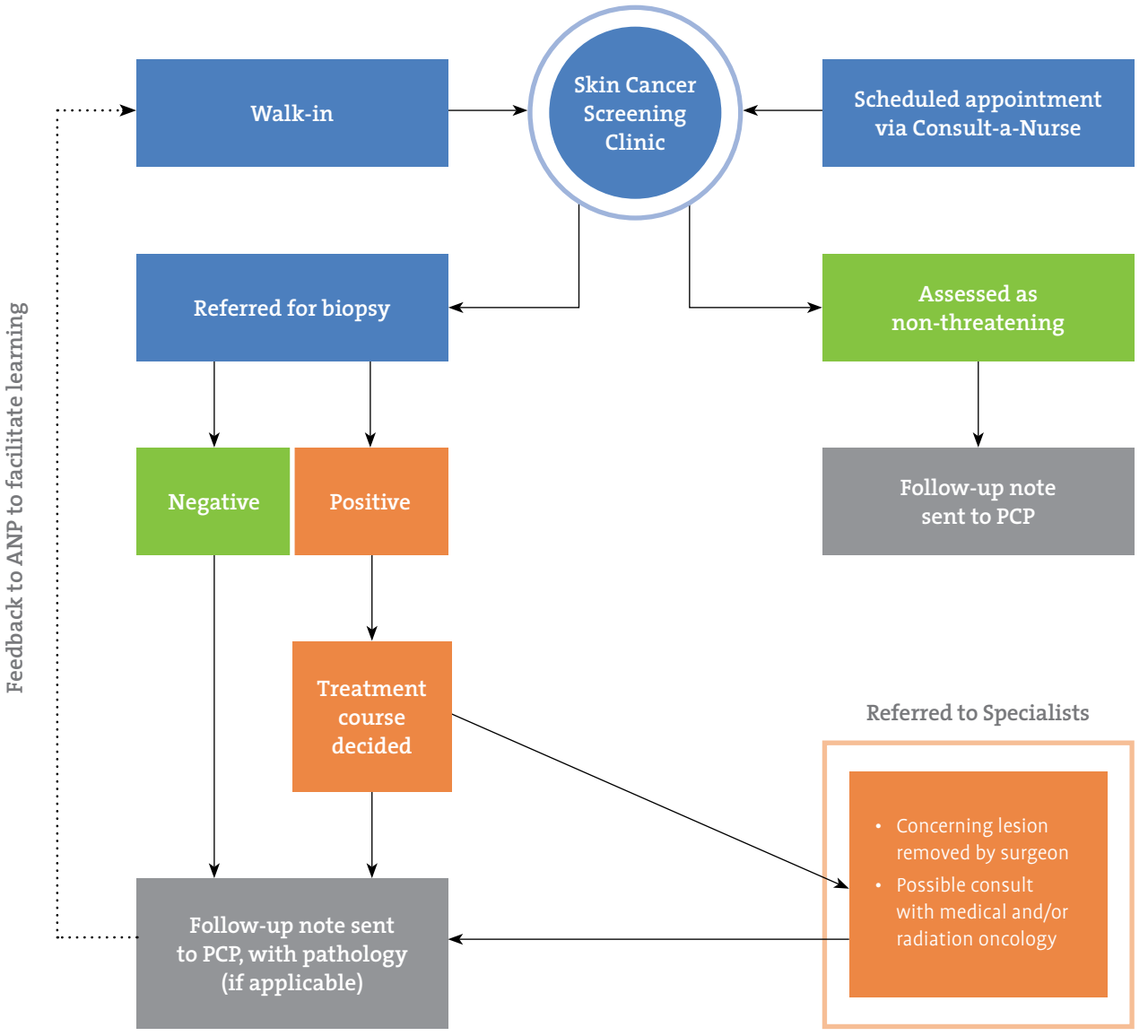

Figure 2. *Pro forma* for Skin Cancer Screening Clinic

SCENARIO	DESCRIPTION	%	PROCEDURE CODE	CODE DESCRIPTION	PAYMENT
1	Screening only	100%	Out-of-pocket	Clinic	$ 30.00
2	Screening with biopsy	41%	99201	Clinic	$ 53.43
			11301	Same as above 0.6 to 1.0 cm	$ 76.45
			88305		$ 32.75
3	Screening with biopsy and removal	20%	99201	Clinic	$ 53.43
			11301	Same as above 0.6 to 1.0 cm	$ 76.45
			88305	Biopsy	$ 32.75
			8505	Surgery	$ 32.75
			88305	Pathology	$ 247.00
4	Screening, biopsy, and surgery	1%		Basal, back	$ 13,815.00
				Basal, face, neck, scalp	$ 13,920.00
				Basal, lower extremity	$ 13,859.80
				Basal, upper extremity	$ 11,607.60
				Anesthesia, other OR fees	Unknown
5	Screening, biopsy, and radiation	0.25%		ICD-9 Code 171.0, 32 treatments	$ 48,761.00
				ICD-9 Code 174.9, 30 treatments	$ 38,687.00
				ICD-9 Code 173.3, 20 treatments	$ 28,784.00
				DESCRIPTION	RATE/HOUR
				Medical Directorship Fee	$ 150.00
				ANP Salary	$ 50.00
				Materials	
				Marketing	

Usually the Skin Cancer Screening Clinic is able to see a new patient consultation within three weeks, significantly improving the six-month wait patients experienced in the past.

CASE/100	CHARGES/ CASE	CHARGES/ 100 CASES	CHARGES/ 200 CASES	CHARGES/ 300 CASES	CHARGES/ 500 CASES	CHARGES/ 800 CASES
100	$ 30.00	$ 3,000.00	$ 6,000.00	$ 9,000.00	$ 15,000.00	$ 24,000.00
41	$ 162.63	$ 6,667.83	$ 13,335.66	$ 26,671.32	$ 40,006.98	$ 66,678.30
20	$ 442.38	$ 8,847.60	$ 17,695.20	$ 26,542.80	$ 44,238.00	$ 70,780.80
1	$ 13,300.60	$ 13,300.60	$ 26,601.20	$ 39,901.80	$ 79,803.60	$ 119,705.40
0.25	$ 38,744.00	$ 9,686.00	$ 19,372.00	$ 29,058.00	$ 48,430.00	$ 77,488.00
	TOTAL	$ 41,502.03	$ 83,004.06	$ 131,173.92	$ 227,478.58	$ 358,652.50
	20% DISCOUNT	$ 8,300.41	$ 16,600.81	$ 26,234.78	$ 45,495.72	$ 71,730.50
	HOURS	2	4	6	10	16
		$ 300.00	$ 600.00	$ 900.00	$ 1,500.00	$ 2,400.00
		$ 1,250.00	$ 2,500.00	$ 3,750.00	$ 6,250.00	$ 10,000.00
		$ 100.00	$ 200.00	$ 300.00	$ 500.00	$ 800.00
		$ 500.00	$ 500.00	$ 500.00	$ 500.00	$ 500.00
		$ 2,150.00	$ 3,800.00	$ 5,450.00	$ 8,750.00	$ 13,700.00
	RETURN	**$ 6,150.41**	**$ 12,800.81**	**$ 20,874.78**	**$ 36,745.72**	**$ 58,030.50**

(continued from page 29)
in the busy spring, summer, and fall months and alternating Tuesdays in winter months when demand is lower. The clinic is able to quickly add days if there is increased demand. In addition, skin cancer screening is also held off-site at sister hospitals, employer-sponsored events, and community events and/or health fairs.

The hospital uses a third-party service center, Consult-a-Nurse, to schedule appointments via a 1-800 number. Tuesday afternoon clinics are scheduled for 4 hours, with 10 minutes per appointment, yielding a capacity of 912 available appointment slots in a 38-week year. Walk-in appointments are welcome, based on capacity. (During program launch, the hospital initially marketed the program internally and allocated 20 minutes per patient.) As stated previously, patients are charged $30 for the clinic visit; the Skin Cancer Screening Clinic does not accept (or require) insurance.

Clinic staff triages and performs whole body screening. If additional care is recommended, staff provides patients with a "Patient Choice Letter," a comprehensive listing of qualified providers to ensure fairness and compliancy. (At their request, qualified physicians can be added.)

Skin lesions requiring medical management are generally referred to dermatology. Usually, the Skin Cancer Screening Clinic is able to see a new patient consultation within three weeks; thus, significantly improving the six-month wait patients experienced in the past. Patients with a clinically suspicious lesion are triaged as follows:

- Lesions on the hands or face are generally referred to a plastic surgeon (if the patient desires); this sometimes occurs the same day.
- Large or especially deep-seated lesions are generally referred to a surgical oncologist for biopsy and excision; patients are generally seen within a week.

Clinic staff generates and sends letters to the patient's PCP. Figure 1, page 29 illustrates the clinical process.

By implementing a weekly Skin Cancer Screening Clinic, the hospital created an avenue to provide quick and easy access to an important service for a large patient population. This increase in patient traffic improved market awareness of the hospital's cancer program. Another programmatic benefit was the ability to enroll melanoma patients into the hospital's award-winning Cancer Survivorship Program, which helps to ensure adherence to evidence-based surveillance follow-up.

Dollars & Sense

The Skin Cancer Screening Clinic had the support of the Oncology Executive Committee and was part of the hospital's strategic business plan. As the pilot clinic demonstrated, skin cancer screening carried high demand with little associated risk. No capital was required to implement this service. Instead, to support the new Skin Cancer Screening Clinic, the hospital "floated" existing staff from other areas of the cancer program. Thus, the service required minimal cost and supply is derived only by demand, leaving no fixed costs.

Under this "demand-induced supply model," the financial goal was to cover expenses on the screening portion, and make any return downstream. The $30 cash payment slightly exceeded the clinic expenses once the clinic went to a 10-minute-per-patient schedule, and the hospital eventually realized a positive financial return generated by downstream revenue. Figure 2, pages 30-31, illustrates a prospective sample *pro forma*, outlining initial expenditure based on variable volumes with expected return.

P&L Realized

After one year of service, the hospital conducted a retrospective review of cases seen in the Skin Cancer Screening Clinic to assess the projected financial return versus actual return. This review included data on the 383 patients screened onsite. (Due to registration and tracking challenges, these data do not include the nearly 400 patients screened offsite at health fairs, employee-sponsored events, community events, or quarterly clinics offered at a sister hospital.) Data showed that 47 patients received services at the hospital following the initial screening, resulting in a net revenue gain.

The hospital also experienced an unforeseen benefit: the Skin Cancer Screening Clinic helped to build and solidify relationships with PCPs in the community. Specifically, the visit notes mailed to each PCP after the screening established a clinical connection between the hospital and the practices of the primary care providers. After seeing an increase in lab volume, hospital data showed this uptick was patients from primary care practices who had not previously used the facility. The only identifiable factor: these patients had been seen at the Skin Cancer Screening Clinic.

On the qualitative side, the hospital believed that the new Skin Cancer Screening Clinic increased community awareness of its facilities and services. When surveyed, clinic participants expressed overwhelmingly positive feedback and appreciation. Therefore, it is reasonable to assume that these positive experiences may influence patients to choose to receive additional services at the hospital.

Next Steps: A Possible Melanoma Clinic?

The hospital is considering adding a Melanoma Screening and Surveillance Clinic. With 172 total melanoma cases seen at the hospital during one year, the hospital has the resources to manage its existing patient volumes and grow the clinic with new referrals. Currently, there is no competition for melanoma screening and surveillance in the hospital's marketplace. With support from the Cancer Survivorship Clinic, the hospital can incorporate melanoma-specific services into the existing Skin Cancer Screening Clinic; thus, leveraging the services together.

As patients with melanoma are at a high risk of recurrence, NCCN guidelines currently recommend following these patients every 3 to 12 months, depending on the stage of disease at the initial diagnosis. The hospital can use its Varian ARIA®-Equicare Cancer Survivorship (ECS) tool to manage cases using evidence-based guidelines. ARIA-ECS can generate reminders, provide education, and offer a patient portal. The hospital would also send letters to PCPs to engage the referral base and market the Melanoma Screening and Surveillance Clinic. Patients would then be seen in clinic as a follow-up surveillance visit. Patients with no suspicious lesions would be scheduled for their next follow-up appointment. For patients found to have a suspicious lesion, a multidisciplinary virtual "fast track" system would result in an expedited review by a team of multidisciplinary physicians. The initial goal of the Melanoma Screening and Surveillance Clinic would be to deliver definitive treatment within one week of a suspicious finding.

Last Words

In the first two years of operation, the Skin Cancer Screening Clinic saw more than 2,000 patients. Melanoma cases have increased from 63 (prior to clinic launch) to 130 cases the first year of operation to 172 cases the second year of operation. An increase of 109 cases in any single disease site is noteworthy. For the hospital's cancer program, melanoma case mix increased from 4.2 percent to 7.8 percent of its total case mix.

As healthcare becomes more and more competitive, finding opportunities to gain a competitive advantage is growing more challenging for cancer programs. And while the new Skin Cancer Screening Clinic may not necessarily be a "home run" for the hospital's cancer program, as the book and movie "Money Ball" proved, baseball teams win games by getting on base, and adding this service line certainly achieved that outcome.

Cancer programs looking to develop and implement a similar Skin Cancer Screening Clinic should remember that this article reflects the experience of a single hospital. Variables, such as facility volumes and patient mix, will affect clinic performance. Other markets may not have a similar demand for services or may not have the access to the providers necessary to establish a Skin Cancer Screening Clinic. Further, before cancer programs invest too much time and resources in this type of endeavor they should first engage their legal department and Ethics Compliance Officer. That said, cancer program leaders may find this model applicable to other service lines beyond skin cancer screening. OI

Steven Castle has 24 years of oncology experience in clinic, research, academics, and service line. John Turner, MD, is medical director of Skin Cancer Services, and Tricia Cox, ANP, is advanced nurse practitioner, Skin Cancer Services for a community-based cancer program.

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A Patient Story

A nurse at a nearby hospital visited a friend who had recently been diagnosed with melanoma. After this visit, she noted a flyer for the Skin Cancer Screening Clinic. She made an appointment and was seen the very next week.

During her examination, the woman reported that she was healthy and had no specific skin complaints. She enjoyed the outdoors, and ran regularly. During the full-body scan, a 5-mm, ink-dark, slightly raised lesion was noted. Otherwise, the woman had only moderate sun damage. Clinic staff considered the lesion "serious," and the patient agreed to meet with a surgical oncologist listed in the patient choice letter.

On biopsy, the lesion was diagnosed as melanoma *in situ*, and the surgeon conducted a complete excision. The patient had her sutures removed weeks later, and has had no recurrences and/or additional malignancies. Impressed by the Skin Cancer Screening Clinic, this nurse soon scheduled her daughter and a family friend for a screening.

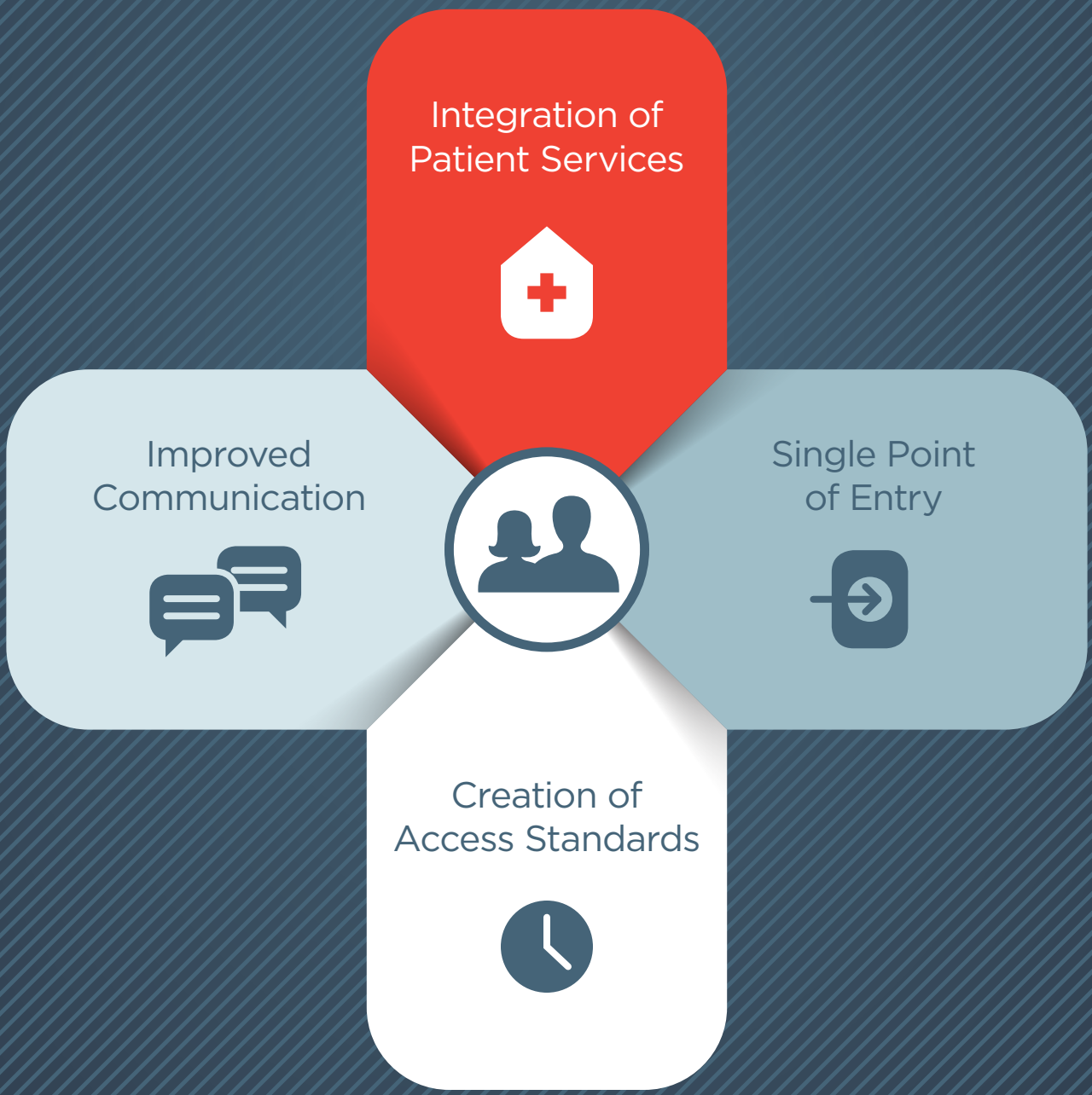
More Online!

Visit www.accc-cancer.org/oncology_issues/SO2014.asp for additional tools including:

- A template letter for PCPs recommending additional care after skin cancer screening
- A template letter for PCPs saying additional care after skin cancer screening is not needed
- A skin cancer clinic screening form
- A melanoma screening and surveillance clinic "fast track" form.

The Hub Model of Care

Two new coordinator roles streamline care at one cancer program



BY KATE SWEENEY, RN, MS, ACNS-BC, AOCN

The U.S. healthcare system is often looked at as difficult to navigate and understand. It can seem even more so for someone with a cancer diagnosis, as this complex disease requires treatment from multiple specialties. Patients and families navigating the healthcare system during a cancer diagnosis may find the task overwhelming. With this understanding, Froedtert & the Medical College of Wisconsin, an academic medical center in Milwaukee, Wisconsin, wanted to make the process of seeking cancer care easier for patients, caregivers, families, referring providers, and cancer physicians who provide care within the healthcare organization.

In the Beginning...

The genesis to improve care processes and the patient experience started back in the 1990s. Leadership within the Froedtert & the Medical College Cancer Center sought a better way for patients and families to first enter and then successfully navigate the complex world of cancer treatment. The resulting vision: a cancer center that would be centered around patients—with a single entry point for all components of care. The second part of the vision is that truly exceptional multidisciplinary care could not happen without a comprehensive upfront process for getting patients into the system (with all of their records) and then connecting patients to the appropriate provider(s) to start their care as quickly as possible.

Getting Started

In late 2003 and early 2004 Froedtert & the Medical College began to flesh out the vision and plan for a new cancer center facility. Recognizing the importance of the patient voice, hospital leadership actively engaged the people who would use the space. Patients, families, and caregivers were asked what they liked about the existing clinics, and what they might like to see improved or changed in the design of the new cancer center. They shared that 1) they wanted simple, understandable directions to help them find various services and 2) they would like care areas and providers to be consolidated in a single location and efficiently coordinated.

Next, physicians were surveyed to learn what changes or processes would make their jobs easier so that they could provide better care to patients. Physicians shared a need for reliable mechanisms to support care coordination, collaboration, and research. Hospital leadership also reached out to referring physicians who wanted simplified access to cancer services for their patients and timely communication during and after their care.

Hospital leadership then made site visits to other large U.S. cancer programs to learn from their best practices, as well as their challenges.

All of this input contributed to the decision to build a new facility where cancer patients could see all of their providers in one building and—more importantly—in one clinic. Care would be centered around patients, their needs, and their cancer type. The new facility's design would create an optimal healing environment built around a new model of care—the Hub (Figure 1, page 36).

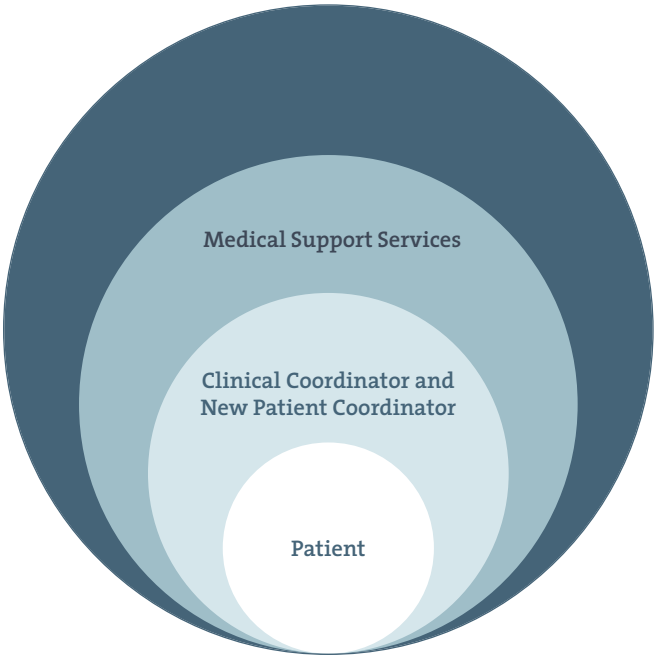
The Hub Model

In this model, patients are at the center, or "hub," with all the services they need surrounding them. Providers are grouped into disease-site specific clinics—rather than by specialty. For example, the Breast Program includes breast experts in medical oncology, radiation oncology, surgical oncology, plastic surgery, radiology, pathology, pharmacy, and more—all working in one clinic at Froedtert & the Medical College Cancer Center. The same is true for all of the 13 disease-site-specific teams. Providers are also disease-site specific, specializing in one or two types of cancer. This specialization is a marketplace differentiator; patients cannot receive this level of expertise at every cancer treatment facility. Under the hub model, patients always visit the same clinic—regardless of the provider they are seeing. Patients see the same staff each time they visit the program, reducing anxiety and improving communication and care coordination.

The hub model brought together access and coordination services for patients with four objectives:

1. Integration of disease-site-specific services in one area
2. Establishment of a single point of entry for all cancer patients
3. Creation of access standards from time of referral to evaluation and time from evaluation to treatment
4. Improved communication with patients and referring providers.

Figure 1. Froedtert and the Medical College of Wisconsin Hub Model of Care



To fulfill those objectives, the Froedtert & the Medical College Cancer Center created two new positions: the new patient coordinator and the RN clinical coordinator. These coordinators are responsible for:

- Streamlining patient entry into the healthcare system
- Facilitating establishment of consensus-driven, evidence-based standards of care for each disease
- Ensuring consistency across programs
- Facilitating timely patient access to the appropriate provider
- Ensuring that all relevant records, imaging, and pathology slides are available prior to the evaluation
- Facilitating physician communication by capturing information about primary, referring, and consulting providers
- Managing data for reporting and quality and outcomes initiatives.

These two new staff members work together with the multidisciplinary care team in each disease-site-specific program. The end goal of the hub model of care is to create, measure, improve, and maintain an infrastructure to support patients and providers in the provision of high-quality cancer care.

New Patient Coordinators

The new patient coordinator is the first line of contact for new patients who need to be seen in the cancer center; they are the "voice" of the cancer center. New patient coordinators are primarily responsible for managing the intake and triage of new cancer patients within one or two specific multidisciplinary programs. They work behind the scenes, gathering all the necessary information, including records, imaging, and pathology slides so that patients can be seen with all of the necessary medical information in a timely manner. This facilitation helps ensure that a treatment plan is developed and initiated as quickly as possible. New patient coordinators set up all the initial consults with surgery, radiation oncology, medical oncology, and other relevant specialists, as well as coordinating additional tests and referrals between providers.

New patient coordinators also begin entering patient information into the cancer center's database, which is used as a tool to help measure outcomes and efficiency.

New patient coordinators handle all of the legwork so patients do not need to worry about issues like *"What kinds of information will my doctor need to look at?"* or *"I forgot to bring my CT scan from two years ago. Will my doctor need to see that?"* Patients only need to be concerned with coming to the appointment and taking care of themselves. This intake process is just as beneficial to providers, as they have all the information they need to make treatment decisions—not dealing with incomplete records that may require bringing the patient back in one or two weeks. Cancer treatment can start sooner because all of the information is available at the first appointment.

The job description for the new patient coordinator was written to identify staff with a slightly higher level of education compared to most scheduling positions within the healthcare system. An associate's degree is required for the position, but a bachelor's degree is preferred. New patient coordinators do not need to have a medical background. The most important qualities are excellent customer service skills, exceptional communication skills, and the ability to multitask. New patient coordinators are expected to call every new patient back by the end of the day—so no one is waiting overnight to start the intake process. There is also a very quick turnaround time for getting patients into the cancer center. The goal is that each new patient is seen within five business days of their initial contact with the cancer center. To meet this goal, new patient coordinators must work quickly and efficiently to talk with patients, gather their records and imaging, make sure no information is missing, and then assemble information for the provider who will be seeing the patient.

New patient coordinators receive training tailored to their disease-specific clinic. They spend two weeks with the lead new patient coordinator going through an extensive orientation and

shadowing opportunities so that they understand the general workflow for the position. After those two weeks, new staff are then transitioned into their disease-specific program where they:

- Observe the clinic's intake process
- Familiarize themselves with the clinic flow
- Get to know the staff and providers
- Gain additional understanding and knowledge of the disease process.

New patient coordinators shadow all of the different disciplines, including medical oncology, radiation oncology, surgery, and any other providers that work with their disease-specific clinic. New patient coordinators are able to observe surgeries, procedures, radiation treatments, chemotherapy infusions, radiology exams, and consult and follow-up appointments. They are also expected to attend tumor boards or cancer conferences. These opportunities increase the new patient coordinators' knowledge of the disease and clinic processes so that they can share that information with patients coming into the cancer center.

Since new patient coordinators are not nurses, each one is paired with a clinical coordinator who is a registered nurse that can address any medical questions or concerns the patient may have prior to coming to the cancer center. This pairing is a unique way of helping new patients prior to their arrival at the cancer center, as well as helping ensure that patients have a great experience once they begin treatment.

Clinical Coordinators

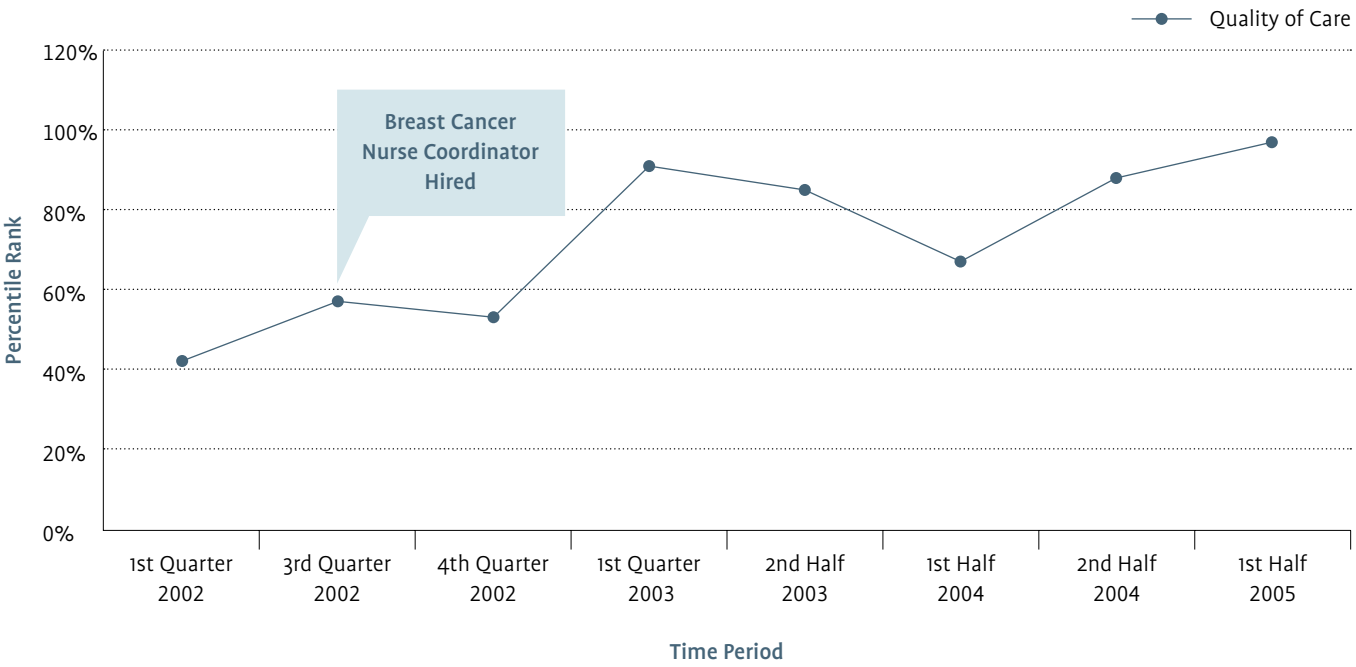
These staff members are nurses (RNs) who partner with new patient coordinators. Clinical coordinators facilitate the development of a multidisciplinary care process with new patient coordinators. This new staff role works to:

- Improve and enhance communication among the multidisciplinary team
- Continually improve quality by working with the team to define the standard of care for every situation based on evidence
- Consistently measure results and improve outcomes.

As part of this process clinical coordinators work with physicians and other clinicians to establish evidence-based protocols for each type of cancer.

Clinical coordinators also organize, participate in, monitor, and report on quality improvement activities to ensure cost-effective, timely, and high-quality cancer care. They work with new patient coordinators to ensure that new patients coming to the cancer center are seen in a timely manner, by the appropriate providers, and with as much medical information available as possible.

Figure 2. Breast Program, "Quality of Care" Ranking



Clinical coordinators provide the cancer patient and their family support and education to help them navigate the healthcare system. Often they work with patients before their first appointment to answer questions and ease some of their fears.

Clinical coordinators are either bachelor's or master's prepared nurses who have expertise in an area of oncology, chronic disease, case management, and/or quality care. They are experienced nurses who are able to communicate well with patients, families, and providers. The clinical nurse coordinator role is different from the typical nursing role, as they are not in clinic face-to-face with patients. Instead, they work behind the scenes, ensuring care coordination for each patient and the delivery of care at the highest possible level.

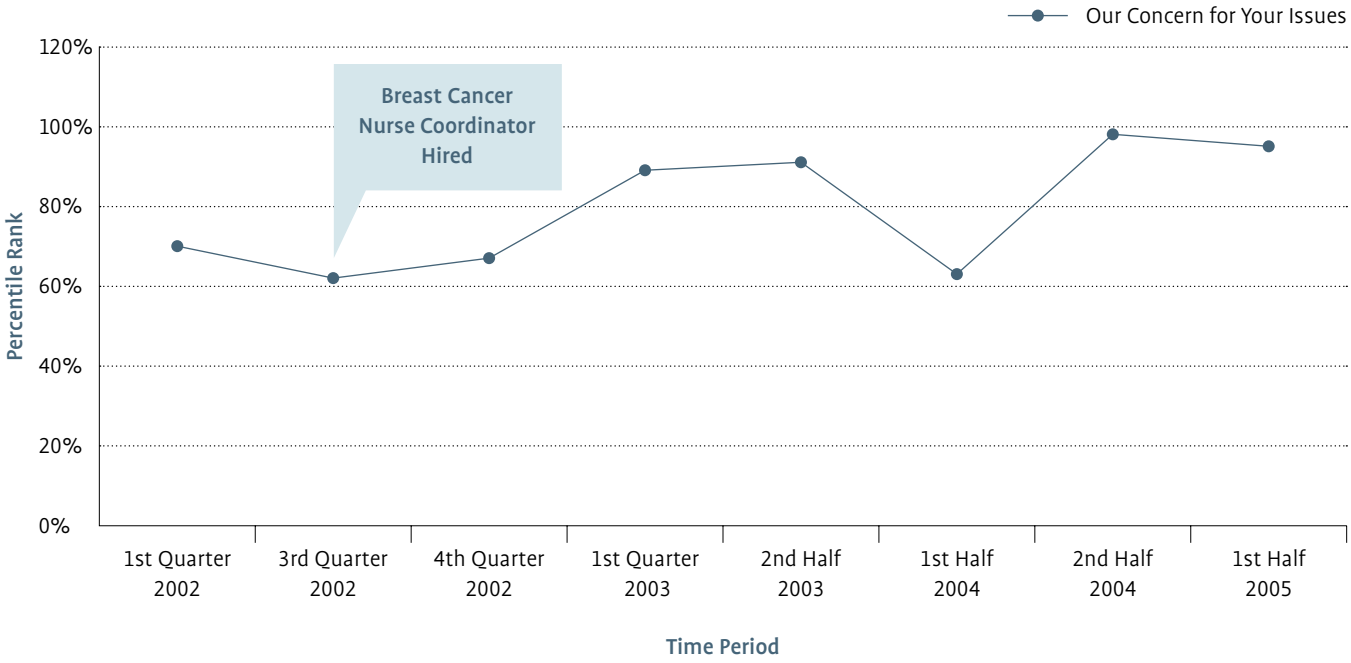
Clinical coordinators are not typical navigators. Froedtert & the Medical College Cancer Center is set up so that the coordinators do not "hold the hand" of every new patient that moves through the system. Instead, disease-site-specific clinics are arranged to help move patients through without gaps in care and everyone has a part to play in navigating patients at the cancer center. New patient coordinators and clinical coordinators get new patients into the healthcare system quickly, with all of the correct information, and seen by the appropriate provider. Once the patient has been seen in consult, the clinic nurses—who are also disease-site specific—navigate patients through that phase of their treatment.

When a patient needs to see a new provider in consult, the new patient coordinator gets involved again, scheduling the consult and ensuring that all of the necessary information is available for the new specialist. Then, the clinic nurses step back in to navigate the patients through the next phase of treatment. Treatment transitions can be stressful for patients, so their new patient coordinator and clinical coordinator are always available, especially at those transition points so patients can contact them for assistance. Both coordinators' job—at any point in the process—is to get the patient to the right providers, at the right time, with all of the correct information.

A Single Point of Entry

A key element of the hub model was one phone number for patients and referring providers—no matter what type of service was needed in the cancer center. To implement a single point of entry into the healthcare system, Froedtert & the Medical College Cancer Center established an 800 number that is answered by specially trained staff. These staff members triage all incoming calls to the appropriate new patient coordinator based on the type of cancer the patient has or is suspected of having. Since new patient coordinators and clinical coordinators are disease-site specific, call center staff must gather some information to ensure that patients are connected to the appropriate program.

Figure 3. Breast Program, "Our Concern for Your Issues" Ranking



The expertise of the new patient coordinators has allowed specialization of the intake process for each disease-site-specific program...

Early in the process, call center staff learned that many patients do not fully understand metastatic disease and the fact that cancers can move to other areas of the body. Now, calls from patients with certain types of cancer trigger call center staff to ask additional questions to make sure patients are connected to the correct new patient coordinator. For example, if a patient mentions bone cancer, liver cancer, brain cancer, or lung cancer, call center staff ask additional questions to fully understand that patient's situation. Figure 8, page 43, is a flowchart that illustrates how call staff responds to each new patient call. In the unlikely event that patients are inadvertently put through to the wrong hub program, staff work together behind the scenes so that the patient is not inconvenienced or impacted by having to talk to numerous staff.

Once call center staff connects the patient to the new patient coordinator, this disease-site-specific expert knows exactly what questions to ask, what history is critical for the treating provider to know, and which records and imaging scans are most important to gather for the patient's initial consult. Every cancer is different, just like every patient with cancer is different, so new patient coordinators know the diseases they work with, as well as the providers on that team and their preferences. The expertise of the new patient coordinators has allowed specialization of the intake process for each disease-site-specific program versus using a call center approach in which staff just pick up the next call in queue—no matter the diagnosis.

Piloting the Hub Model

The Froedtert & the Medical College Cancer Center made the decision to pilot its hub model in the breast program. In mid-2002 a breast clinical coordinator was hired, quickly resulting in a significant increase in the breast program's Press Ganey patient satisfaction scores. In 2004 the breast program hired a new patient coordinator, and patient satisfaction scores continued to soar. These data supported the value and benefit of the two new staffing positions.

Specifically, the breast program's percentile rank for "overall score" increased from the low 30th percentile in 2002 (prior to the hiring of the clinical coordinator) to the high 50th percentile by mid-2003, and then to 93 percent by 2005.

The "quality of care" percentile ranking went from 57 percent in the 3rd quarter of 2002 to 91 percent in the first quarter of 2003, and then to 97 percent in the first half of 2005 (Figure 2, page 37). The breast program's "our concern for your issues"

Figure 4. Breast Program, "Ease of Making Appointments" Ranking

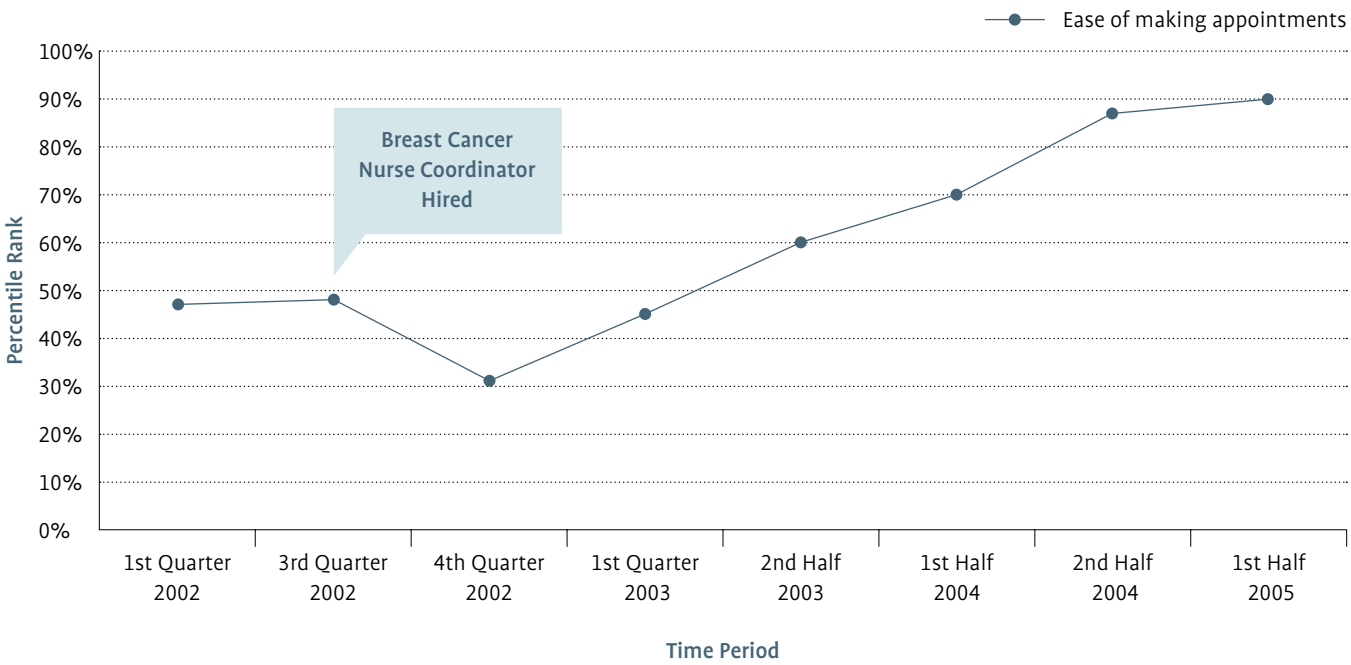


Figure 5. Breast Program, "Calendar Days from MRI Ordered to Performed" Ranking

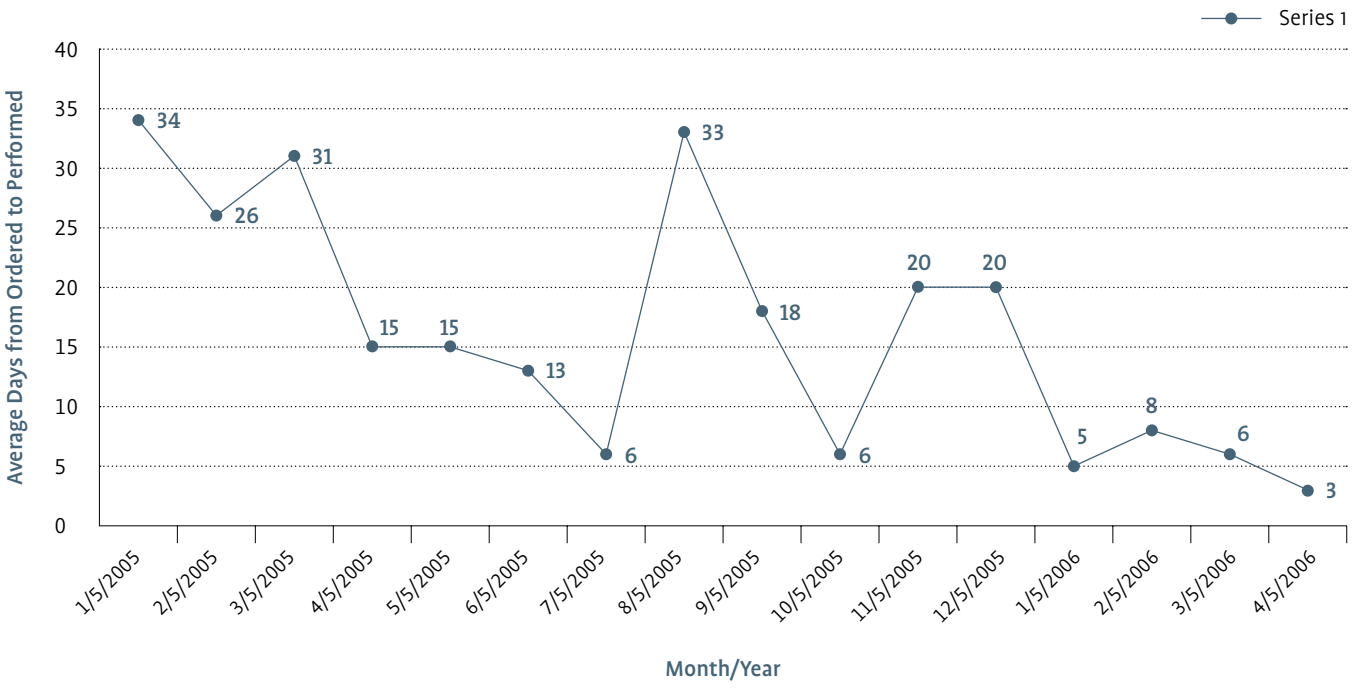
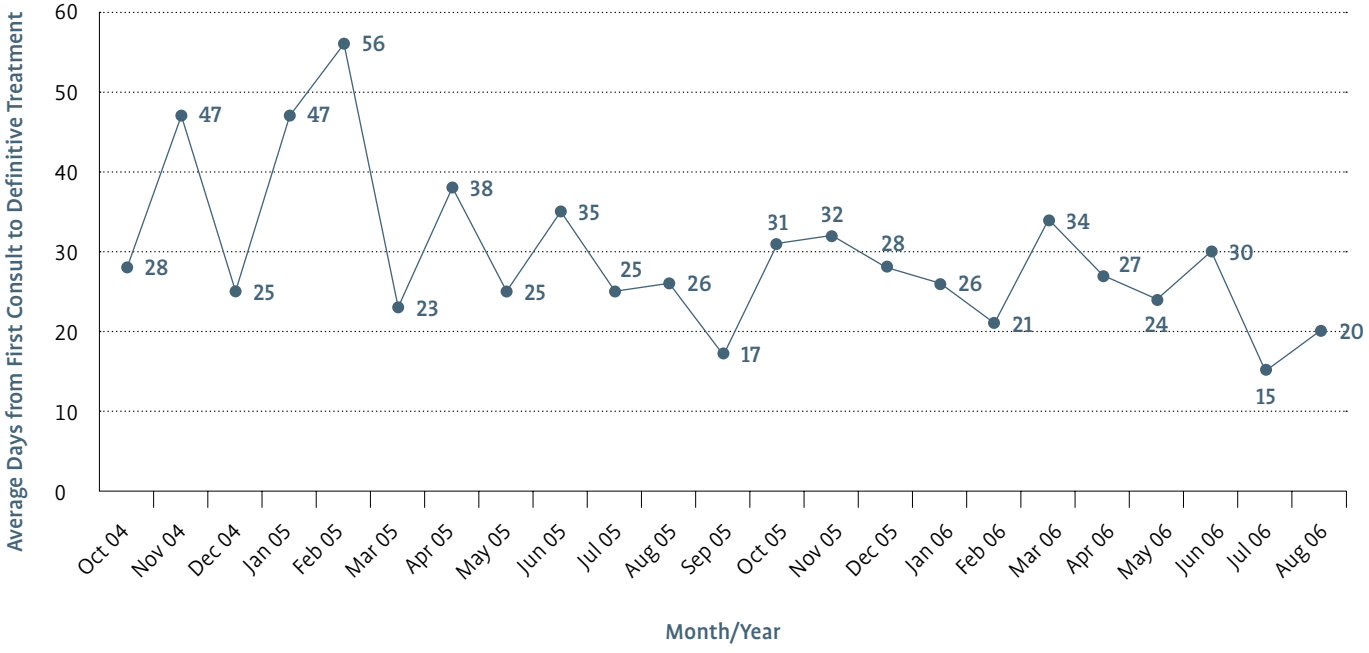


Figure 6. Breast Program, "Calendar Days from Consult to Start of Treatment" Ranking



ranking was 62 percent in the 3rd quarter of 2003, increasing to the high 80s in the first quarter of 2003, and then to the mid-90s in the 2nd half of 2004 (Figure 3, page 38). The "ease of making appointments" was in the high 40th percentile in the third quarter of 2002; by the 2nd half of 2003 it rose to 60 percent, and was at 90 percent by the first half of 2005 (Figure 4, page 39).

The breast program also saw significant improvements in other key rankings: the number of calendar days from an MRI being ordered to MRI being performed (Figure 5, above) and calendar days from consult to the start of first treatment (Figure 6, above). Although Froedtert & the Medical College Cancer Center now uses Avatar to measure patient satisfaction,

Figure 7. Thoracic Oncology Quality Study of the Thoracic Oncology Program at Froedtert Hospital and the Medical College of Wisconsin

Study Topic: Adherence to National Comprehensive Cancer Network (NCCN) Guidelines for Non-Small Cell Lung Cancer (NSCLC), American Society of Clinical Oncology (ASCO) Guidelines, and Froedtert Hospital and the Medical College of WI Thoracic Oncology (FMLH) HUB Program Standards.

Objective: To ensure patient treatment plans meet key standards established for quality patient care.

Measurement: Random sample of 30 of the 2007 analytic NSCLC cases who received their initial treatment at FMLH and had a hematology/oncology (H/O) consult as part of their care.

Method: Retrospective chart review. A total of 30 cases will be reviewed for 2007.

NSCLC Cases with Initial Thearpy at Froedtert Hospital and the Medical College of Wisconsin

STANDARD	SOURCE	TOTAL	% COMPLIANT
Initial consult within 5 working days of first contact	FMLH		
Reviewed at tumor board	FMLH		
Initial consult note to include performance status and weight loss	NCCN		
CT of chest pre-treatment	NCCN		
PET scan pre-treatment	NCCN		
Imaging of brain (MRI preferred) for clinical Stage II and higher pre-treatment	NCCN		
Smoking cessation counseling	NCCN		
Lymph node sampling during surgery or pre-surgery	NCCN		
PFTs (pulmonary function tests) performed pre-surgery	NCCN		
Chemotherapy recommended for patients with curative resection for NSCLC with T3 or T4 tumor size or lymph node involvement (%)	ASCO		
Chemotherapy received by patients with NSCLC after, curative resection with T3 or T4 tumor size or lymph node involvement	ASCO		
Prior to H/O consult, CT of chest within 2 months (either performed or ordered)	FMLH-H/O		
If patient is post-surgical, new CT prior to H/O consult (either performed or ordered)	FMLH-H/O		
Prior to H/O consult, brain imaging (MRI preferred) within 3 months (either performed or ordered)	FMLH-H/O		
Prior to H/O consult, PET within 3 months (either performed or ordered)	FMLH-H/O		

scores have remained high since the implementation of these staffing positions.

In 2005—based on the success of the breast program pilot—Froedtert & the Medical College Cancer Center approved clinical coordinators and new patient coordinator positions for both the thoracic and prostate programs. Since then, the hub model has grown to 11 clinical coordinators and 17 new patient coordinators across all 4 sites in the Froedtert & the Medical College of Wisconsin Cancer Network—although 14 of the new patient coordinators remain at the cancer center location on the academic medical center campus.

Quality Metrics & Reporting

Each disease-site-specific program monitors basic metrics that are measured across the entire cancer center, including:

- Turnaround time from first call or referral to initial consult
- Time from referral to subsequent specialist consult
- Patient satisfaction
- Retention of second opinions.

The goal of the Froedtert & the Medical College Cancer Center is to see patients within five business days. This goal is challenging—with patients coming from other healthcare systems, other states, and sometimes even other countries. If there are no openings in a five-day period, new patient coordinators and clinical coordinators work with providers to ensure patients are seen as soon as possible. "As soon as possible" sometimes means extending clinic times or opening up clinics on non-clinic days. This flexibility has been a huge satisfier for patients, as well as referring providers.

This metric has improved considerably since the addition of the new patient coordinator role. For example, many disease-site-specific programs had waits of 10 to 15 days. Today, some programs have appointment turnaround times of 2 to 3 days for new patients, while others are closer to the 5 day goal.

Each disease-site-specific program is then responsible for defining unique metrics or outcomes within its program. Clinical coordinators work with the multidisciplinary team to define those metrics and then report these back to the team throughout the year. Quality reports look at national standards and guidelines, as well as Froedtert & the Medical College Cancer Center standards. These quality reports are often one of the first places where the cancer care team can identify problems or an issue to work on for the following year.

For example, an early quality report in the head and neck program revealed that many patients did not have documentation of dental evaluation or referrals in their charts. When this issue was brought to the team's attention, providers said that evaluations and referrals were a regular part of practice. Unfortunately, this information was not being documented in the patient chart. The clinical coordinator worked with the Epic team to add this line to the EMR templates so that providers would not miss this documentation going forward.

There was a similar example in the 2007 quality report from the lung cancer clinic. Specifically, looking at patient records, it appeared that providers had conducted smoking cessation discussions with only 11 percent of patients who were current smokers. However, the lung cancer team reported that almost all patients received education about smoking cessation; it was simply not being documented in the patient record. By the next year, that documentation glitch had been fixed and the 2008 lung cancer quality report revealed that 85 percent of patients had documentation in their medical that they had discussed smoking cessation with their provider.

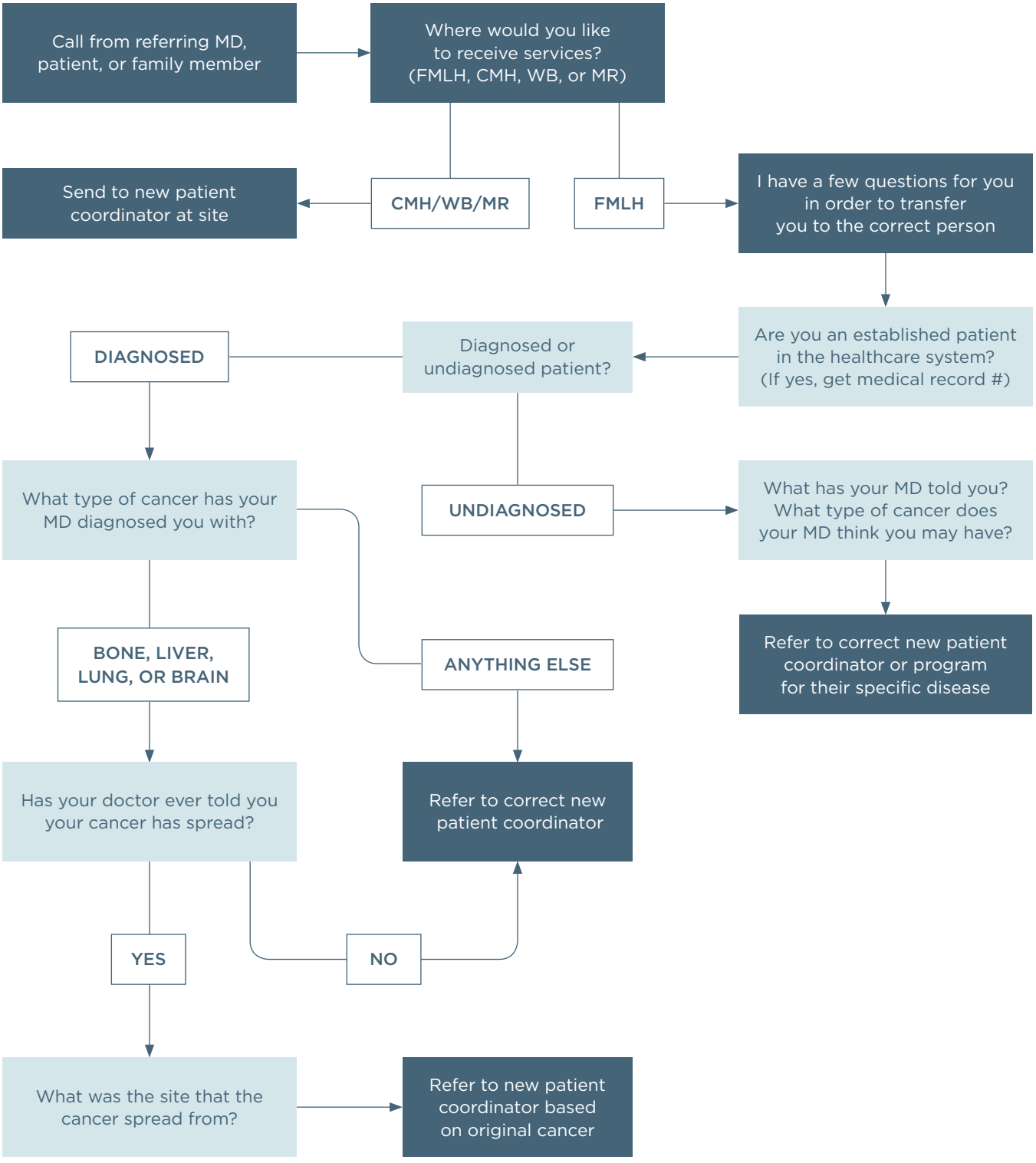
These examples are very basic, but serve to illustrate the importance of good documentation and the monitoring of standards to quality patient care. Figure 7, page 41, is an example of the template used for an early thoracic oncology quality study. Quality studies at Froedtert & the Medical College Cancer Center continue to evolve as new evidence and changes to national guidelines occur.

The Cancer Center Today

Froedtert & the Medical College of Wisconsin Cancer Center broke ground on its new building in 2006; construction was completed in 2008. Today the Froedtert & the Medical College Cancer Center building includes:

- 6 disease-site-specific clinics that house 13 disease-site-specific teams
- Day Hospital for chemotherapy and other infusions, open 365-days-a-year
- Education center for tumor boards/cancer conferences, support groups, and other education opportunities
- Outpatient pharmacy for prescription and OTC medications
- Laboratory with full hematology and chemistry capabilities
- Diagnostic imaging
- Breast Care Center
- Radiation oncology
- Procedure rooms
- Translational research unit specifically for cancer clinical trial patients
- Skin Cancer Center
- Small Stones Wellness Center, which offers resources for restoring and maintaining appearance
- Quality of Life Center, which houses support services for patients and their families
- Patient and Family Resource Library
- Walking track
- Bistro with healthy food choices and wireless access
- Meditation room
- Free underground or valet parking
- Three affiliated community sites that also house disease specialists as part of our Cancer Network.

Figure 8. Decision Tree for New Cancer Patients or Undiagnosed Patients with Suspicion of Cancer



Lessons Learned

The hub model and the new patient coordinator and clinical coordinator positions have been incredibly successful (as shown in the growth of the number of positions), improving both patient and provider satisfaction with the healthcare system. That said, there are some processes that Froedtert & Medical College Cancer Center planners might have done differently or changed along the way.

For example, new patient coordinators were initially called journey coordinators; however, this title gave patients the perception that a specific staff member would be assigned to the patient throughout their entire cancer journey. To correct that perception, the name was changed to new patient coordinator. It was a much better fit as these staff are only coordinating care for new patients.

A similar issue emerged with the clinical coordinators, which were initially called nurse navigators. Since the model of navigation at Froedtert & the Medical College Cancer Center emphasizes care coordination, with clinical coordinators most involved in the beginning of the patient's cancer journey—as well as coordination and quality of care behind the scenes—the name was changed to clinical coordinator very early on in the process.

The early success of the hub model of care, the new coordinator positions, the new building, and referring provider satisfaction, generated rapid growth in the volume of patients, leading to some space problems that the program had not anticipated so early on. When the facility was built, it was designed to accommodate growth through 2015. In 2012, cancer center leadership realized that more clinic and infusion space was needed quickly. In the fall of 2013, the fifth clinic quadrant opened and the disease-site-specific programs were able to spread out so there were more clinic rooms to see additional patients. The Day Hospital also expanded, adding more infusion spaces and opening its Translational Research Unit for patients participating in clinical trials including Phase I and II studies.

The specialization of the new patient coordinators created coverage challenges. When new patient coordinators are on vacation, sick, and/or move to a different position, their expertise is gone as well. To fix this issue, cancer center leaders created two coverage positions that would receive training on numerous disease-site programs. Coverage new patient coordinators work with their disease-site-specific programs on a regular basis and cover staff whenever necessary. Because coverage new patient coordinators have a broad level of expertise, they can also step in and help train new staff members. The new patient coordinator and clinical coordinator from the same disease-site specific team do not take vacation at the same time. This means there is always an expert coordinator available.

Measuring the benefits and return on investment (ROI) of the hub model of care and the coordinator positions is increasingly important. Quantifying the effectiveness of the program to show patient and referring provider satisfaction and creating metrics for each disease-site-specific program are needed to demonstrate the programmatic benefits. This ROI has been somewhat difficult as the coordinator positions do not directly generate revenue. Instead, the benefits are downstream and have to do with patient, family, and referring provider satisfaction, which drives more patients to the organization, as well as the quality improvement efforts that lead to higher quality care and better patient outcomes. Executive leadership had to buy into the hub model of care and the coordinator positions for them to succeed; senior leaders needed to see the value in it as well and support requests for new positions when needed. Froedtert & the Medical College Cancer Center has been fortunate as the organization and senior leadership realized very early on how important the hub model of care and the coordinator roles are to the success of the cancer program. Indeed, they are the "secret sauce" that makes the whole program work. OI

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A special thanks to Sue Derus, Executive Director of Cancer Services at Froedtert & the Medical College of Wisconsin. Without her vision, this new building and model of care at Froedtert & the Medical College of Wisconsin Cancer Center would not be where it is today.

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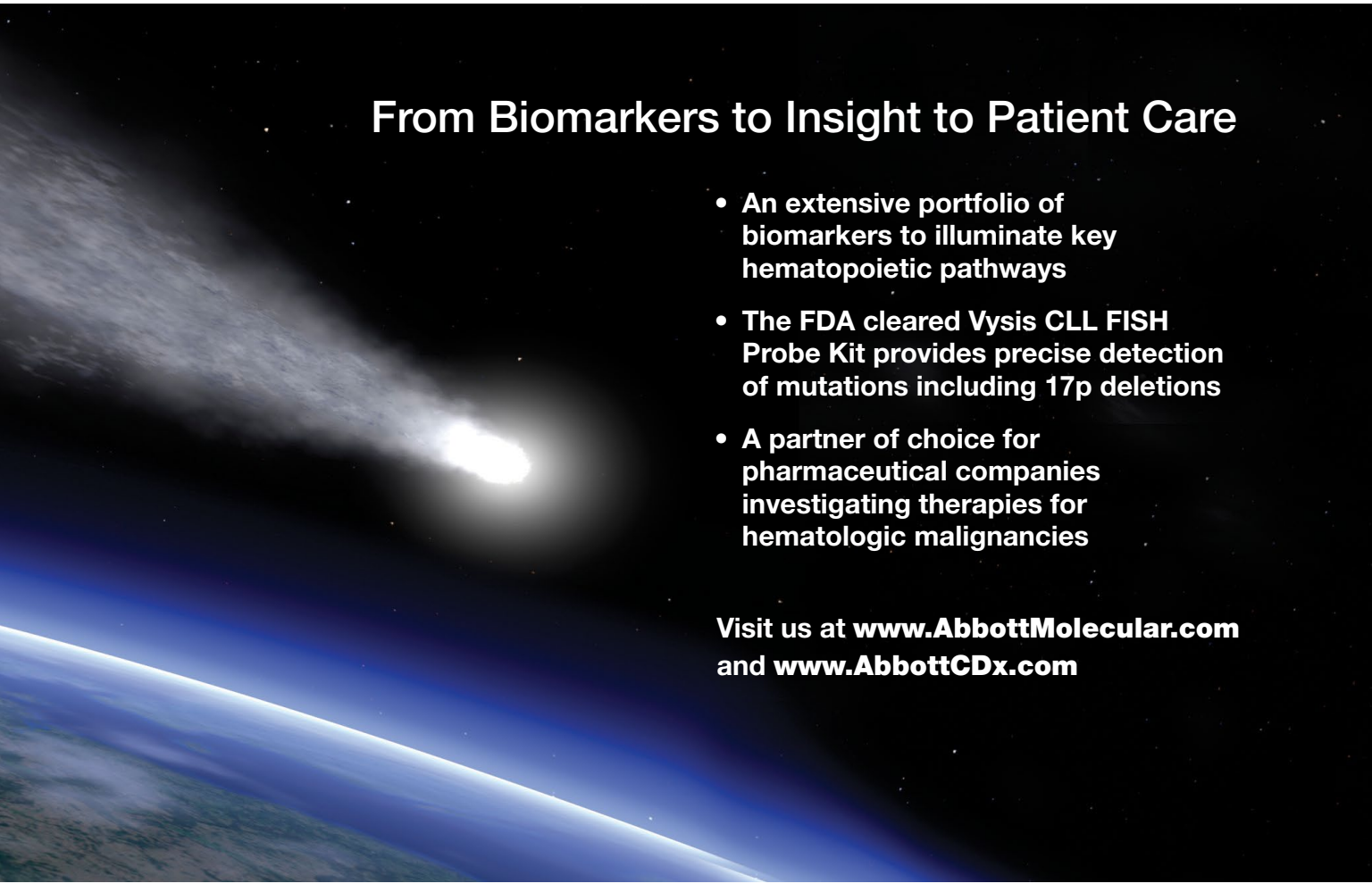

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BY ANDREW S. KENNEDY, MD, FACRO

^{90}Y Radioembolization

Success in Colorectal Cancer Liver Metastases

Colorectal cancer does not discriminate; it is the third leading type of cancer among men and women in the United States.[1] While the disease is largely preventable through early detection, the Centers for Disease Control and Prevention (CDC) reports that more than 20 million adults in this country have not had the recommended screening for colorectal cancer.[2] Early detection is essential because often when a patient becomes aware of symptoms, the disease has spread to other organs, resulting in a diagnosis of metastatic colorectal cancer (mCRC). In fact, of the nearly 140,000 Americans diagnosed with colorectal cancer every year, at least 60 percent will see their cancer spread to the liver and will die of the disease.[3,4] While surgical resection of liver tumors is the preferred treatment, factors such as size, distribution, and accessibility of tumors often preclude a patient from this treatment path.

An Alternative Treatment Option

More than 30 years ago, selective internal radiation therapy (SIRT) or radioembolization via microsphere therapy began to gain momentum as an option to target challenging liver tumors. With the development of a ^{90}Y bound microsphere that could be carried easily in the bloodstream to the capillary bed of the liver tumor, targeted internal liver radiation was achieved. In 2002 SIR-Spheres® microspheres received pre-market approval by the U.S. Food and Drug Administration (FDA) for colorectal cancer that has metastasized to the liver;[5] currently, they are the only microspheres approved for this indication. Today, the therapy continues to gain acceptance through ongoing trial results supporting the survival, tumor response, safety, and quality of life among patients who were challenged in finding an effective treatment option after heavy pre-treatment, including multiple lines of systemic chemotherapy and biological agents.

SIR-Spheres microspheres and SIRT are considered a safe and effective method of using radiation to treat colorectal liver metastases and are often used concurrently with chemotherapy or as monotherapy.

How SIRT Works

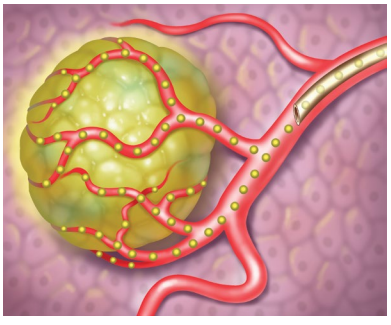
The microspheres are microscopic polymer beads that contain the radioactive isotope ^{90}Y and emit beta radiation to kill cancer cells. Due to their small size—the average size is approximately 32.5 microns—the microspheres travel easily through the bloodstream directly to the tumor. The microspheres become lodged in the tumor vasculature and kill the cancer cells by emitting beta radiation to the tumors, while the surrounding healthy liver tissue remains unaffected. SIR-Spheres microspheres and SIRT are considered a safe and effective method of using radiation to treat colorectal liver metastases and are often used concurrently with chemotherapy or as monotherapy.

SIRT is performed as an outpatient procedure by a team that includes an interventional radiologist who places a transfemoral microcatheter into the hepatic arteries. Other team members include radiation oncology, nuclear medicine, and medical oncology. Using the liver's unique vascular supply, millions of tiny resin microspheres charged with ^{90}Y are released into the hepatic artery leading to multiple tumors. The radioactive microspheres selectively implant in the microvascular supply of the tumor where they become trapped and emit beta radiation for a period of about two weeks. Concurrent chemotherapy has been safely given via the typical agents proven to be effective in colorectal cancers.

SIRT treatment normally takes about 60 to 90 minutes. After careful monitoring, most patients return home four to six hours after the procedure. The reported side effects are few; most patients experience only mild temporary abdominal pain, minimal nausea, and fatigue, (Grade 3 toxicity is <10 percent, CTCAE [Common Terminology Criteria for Adverse Events] 3.0) for a period of one to three weeks.

In prospective clinical studies of mCRC patients who were heavily pre-treated with multi-agent chemotherapy, SIRT with ^{90}Y resin microspheres delivered as monotherapy or combined with modern chemotherapy has been proven to:

- Decrease the tumor burden in the liver [6-13]
- Increase time-to-disease progression[7-8]
- Increase survival time[14]
- Potentially downsize tumors to liver resection or ablation[7,9,12-13]
- Provide palliation of symptoms.



Tumor with microspheres. Here yttrium-90 kills tumor cells while preserving healthy liver tissue.

The MORE Study

The **M**etastatic colorectal cancer liver metastases **O**utcomes after **R**adio **E**mbolization (**MORE**) retrospective study (clinicaltrials.gov identifier: NCT01815879) was designed to evaluate the safety and overall survival associated with ^{90}Y therapy in patients with mCRC, based on the collective experience of SIRT centers of excellence in the United States. The multi-center retrospective review includes eight years of clinical and radiographic outcomes after ^{90}Y resin microsphere radioembolization treatment (SIR-Spheres microspheres) in patients with metastatic colorectal liver metastases. Below are highlights of the MORE's study safety and efficacy findings.

Safety and Efficacy: Overview. Patients in the MORE study had a history of heavy pre-treatment, including multiple lines of systemic chemotherapy and biological agents, and were challenged in finding an effective treatment option. The primary purpose of the study was to further define the role of SIRT in treating mCRC

The key finding of this study—with SIRT, patients have an opportunity to live longer and live well.

patients. This retrospective study provided "real world" patient experience to confirm results from initial prospective studies used to gain regulatory approval of the microsphere therapy, initially granted in 2002. It is well accepted that the highest response rate and tumor control indices are accomplished when the intervention is applied earliest in the course of therapy. Despite the fact that most patients presenting for SIRT received more than one year of multi-agent chemotherapy and biologic agents, liver-directed radiotherapy was shown to be both safe and well tolerated, and for some patients likely improved survival with no negative impact on quality of life.

Safety and Efficacy: Methods. A total of 606 patients were included in the overarching MORE study that lasted from July 2002 to December 2011 and included 11 U.S. institutions.[15] Centers invited to participate included those that had more than 50 cases of mCRC patients treated with SIR-Spheres microspheres. The investigator-initiated study was a retrospective analysis that involved the collection of data by independent clinical researchers who compiled all the data from the source documents and submitted them to a central data bank. Original pre- and post-treatment CT, MRI, and PET scans were included in this data collection process and were sent to commercial clinical research organizations (CROs) outside the U.S. specializing in liver-directed radiology reviews. A stringent reading protocol was instituted for all the data to ensure that the retrospective data was handled as close to the manner in which prospective study data would be handled. Finally, independent groups completed audits of data. This method helped to provide the truest picture of SIR-Spheres microspheres/mCRC outcomes in the U.S.

In order to ensure efficient assessment of the data and the ability to identify trends, the principal investigator partnered with an independent medical statistics company to develop a specially-designed database for this project. The CROs at each center used source data and a toxicity grade assigned to ensure consistent reporting. Pre- and post-treatment (CT, MRI, PET) imaging data were sent via CD or DVD to an independent central radiology review center outside the U.S. that is experienced in radioembolization. RECIST and WHO criteria were used for objective grading of response at 12 weeks, and for later time points if scans were available for a large number of patients. All data were analyzed by the independent medical statistics company, which has significant experience in clinical oncology trials, specifically in radioembolization protocols.

Key Findings from the MORE Study

The MORE study's design yielded a great amount of data, and the findings may be considered as valuable or more valuable than prospective study results. Further, the results validate every previous study conducted on microspheres over the past 20 years—in many cases within a percentage point. As time progresses, researchers continue to dissect the data from the MORE study. The areas to be discussed here include the following:

- Overall safety and efficacy findings from a multi-institutional U.S. study
- An independent imaging study confirming the efficacy of SIRT
- Safety and efficacy in patients over the age of 70
- Pre-^{90}Y hepatic radiotherapy; diagnostic values help to predict overall survival in mCRC patients.

A Safety and Efficacy Study. One study of the safety and efficacy of resin ^{90}Y-microspheres examined the outcomes in 548 patients with metastatic colorectal cancer treated with microspheres therapy.[17] All patients in this subset of data had received prior chemotherapy, with more than 30 percent having also received prior liver surgery or ablation. Survivals of 13.0, 9.0, and 8.1 months, respectively, were reported in patients who had received 1, 2, or 3+ prior lines of chemotherapy. There were no significant differences in the adverse event profiles between the three groups. Most patients (97.8 percent) spent less than 24 hours in the hospital with the most common grade 3 side effects being abdominal pain (7 percent) and fatigue (6 percent). Data indicated that SIRT with microspheres appears to have a favorable risk/benefit ratio in patients with metastatic colorectal cancer who failed chemotherapy. These data show a clinically relevant survival benefit in patients not responding to chemotherapy, including those who have been heavily pre-treated.

While SIRT treatment is not a silver bullet, it does offer a potential gift of time for patients to spend with loved ones while maintaining a good quality of life. The key finding of this study—with SIRT, patients have an opportunity to live longer and live well. Specifically, recent studies in chemo-refractory patients with colorectal liver metastases reported a median survival range of 10.5 to 13 months compared to 3.5 months for untreated patients.[6,14,16]

An Independent Imaging Study. The response to SIRT therapy from an imaging perspective was assessed using further results from the MORE study.[17] Findings from the independent central review by a board-certified radiologist evaluated 195 patients with metastatic colorectal cancer that were treated with microspheres therapy and had measureable lesions at baseline and follow-up imaging. Patients who showed a partial response using

RECIST 1.0 and 1.1 criteria—with tumors shrinking at least 30 percent—had triple the survival rate compared to the expected historical rate in chemo-refractory disease studies. The patients who showed stable disease actually demonstrated doubled survival rate. Even in patients with progressive disease, SIRT therapy offered additional time, coupled with the improved quality of life that all patients were afforded.

Overall, the results show that hepatic radiological response to SIRT appears to predict longer-term prognosis. It is important to note that response to SIRT by RECIST 1.0 and 1.1 criteria at three months must be interpreted with caution due to the significant proportions of peri-tumoral edema and necrosis encountered. Imaging findings may lead to either the underestimation of partial response/stable disease or the overestimation of progressive disease, respectively.

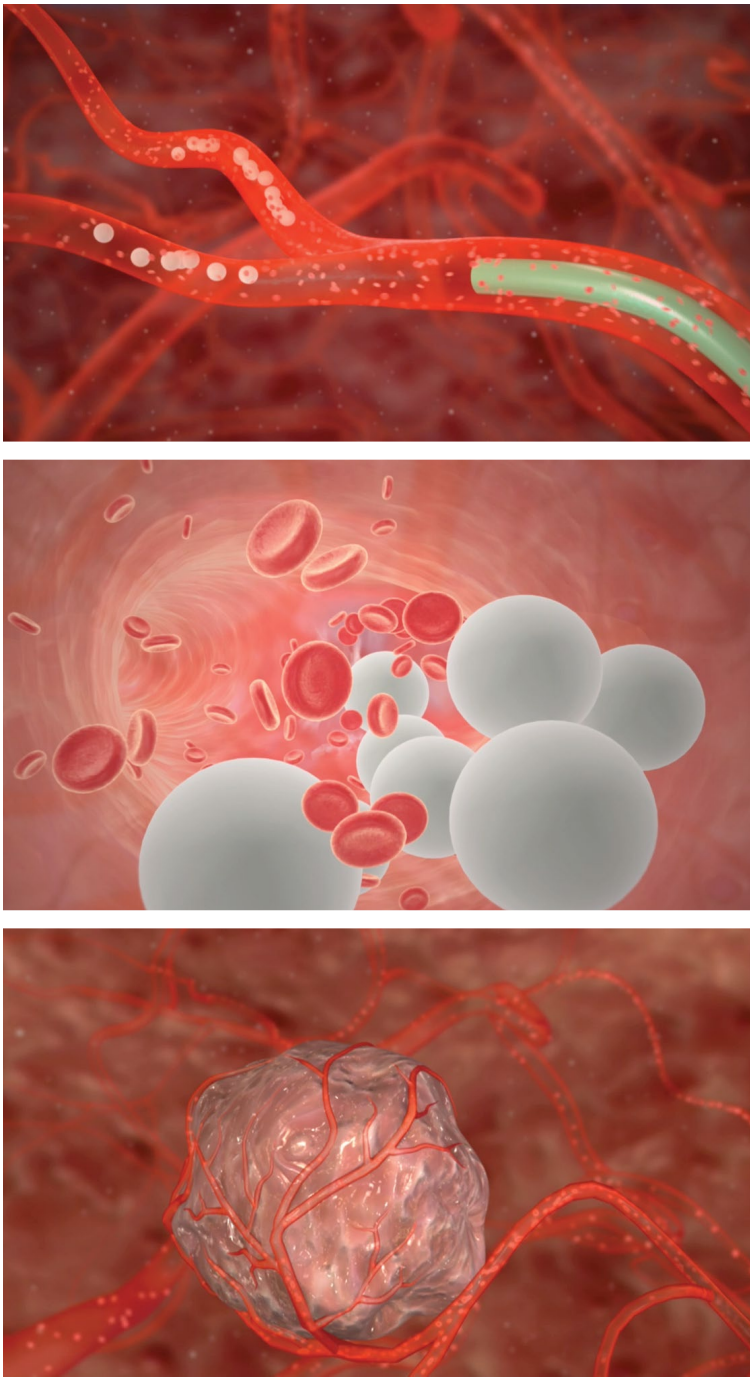
Safety and Efficacy of ^{90}Y Resin Microspheres in the Elderly. Many standard chemotherapy regimens are either not offered to elderly patients (≥ 70 years of age) or are given at lower, potentially less effective, levels due to the perception or existence of data indicating that elderly patients cannot tolerate these drugs. As a result, this population of patients has been left without effective treatment options. Due to the minimally invasive nature of ^{90}Y microsphere therapy, researchers hypothesized that SIRT may provide an effective treatment option for older patients without the concerns of side effects often seen with chemotherapy.

One retrospective analysis, which also was part of the MORE study, evaluated clinical outcomes among 160 elderly (≥70 years) and 446 younger (<70 years) patients with unresectable mCRC consecutively treated using resin ^{90}Y microspheres.[18] Regardless of age, patients were similar in terms of sex, race, performance status, and other characteristics.

Outcomes between both cohorts were similar following treatment with resin ^{90}Y microspheres. Median overall survival in elderly patients was 9.3 months compared to 9.7 in the younger group. The treatment was equally well-tolerated in both age groups, with no significant increase in grade 3+ adverse events in elderly patients. The most common grade 3+ adverse events were abdominal pain and fatigue. Investigators also noted that a sub-analysis of the oldest patients in the study (98 patients ≥75 years) compared to younger patients also confirmed equivalent outcomes for survival and toxicity.

These outcomes are significant since the oncology community has long struggled to understand the best approach for treating older patients with inoperable liver tumors. The main contribution of this particular subset analysis is important, namely SIRT is equally as effective in all patient ages. Too many times clinicians undertreat this patient population or these patients often choose to forgo treatment due to concerns about quality of life.

Images, top to bottom:
Mode of Action 1. SIR-Spheres microspheres are released into the arterial blood supply. **Mode of Action 2.** SIR-Spheres microspheres being carried through the hepatic arteries to the tumor. **Mode of Action 3.** Tumors can be selectively irradiated leaving normal tissue unaffected.



Pre-^{90}Y Hepatic Radiotherapy Hemoglobin and Liver Functions Help Predict Overall Survival in mCRC Patients.[19] The MORE study findings continue to unveil additional insights of importance to SIRT therapy for mCRC patients. New trends and opportunities to improve patient outcomes using SIR-Spheres microspheres cannot be overlooked. For example, researchers have learned that diagnostic results reflecting organ function are valuable predictors of the patient's survival after resin ^{90}Y microsphere radioembolization. Among the data collected in retrospective review 10 days prior to treatment: hemoglobin, albumin, alkaline phosphatase, AST, ALT, total bilirubin, and creatinine. A CTCAE v3.0 Grade was assigned to each parameter and analyzed for impact on survival by line of chemotherapy. Where applicable, consensus guidelines[20] were used to establish the abnormal limits of these parameters prior to radioembolization. While some parameters might be challenging to improve prior to radioembolization, hemoglobin <10 g/dL, which is a well-known negative factor in radiation response in external beam therapy, can be easily corrected before the procedure. These data suggest hemoglobin correction prior to radioembolization will enable maximal tumor response.

This retrospective MORE study analysis to establish predictive survival results evaluated clinical data values, including medical histories and pre-treatment laboratory values, obtained from 606 mCRC patients.[19] The patients (370 male; 236 female) were studied with a median follow-up of 8.5 months after radioembolization. Fewer than 11 percent of patients were treated outside recommended guidelines, with grade 2 albumin (<3–2.0 g/dL) being the most common (10.5 percent) at time of radioembolization. Abnormal parameters (grade >0) were associated with statistically significantly decreased median survivals ($p<0.05$) and this was consistent across most lines of prior chemotherapy. Compared to patients with grade 0, those with grade 2 albumin decreased median survival by 67 percent; for grade 2, total bilirubin by 63 percent; and grade 1, hemoglobin by 66 percent.

The team concluded that review of pre-radioembolization laboratory parameters may aid in improving median survival if correctable grade >0 values are addressed prior to radiation delivery. These efforts are important in optimizing treatment response to liver radiotherapy.

MORE Study Conclusions

The MORE study findings and other research studies to date have helped to improve understanding and acceptance of SIRT using SIR-Spheres microspheres and the results have further validated the treatment's safety and efficacy. Researchers look to continue the study of SIR-Spheres microspheres in various patient populations, with the goal of adding this treatment to conventional chemotherapy even earlier in the treatment algorithm. Separately, the SIRFLOX study, which completed enrollment in 2013, will test this hypothesis with the hope that controlling liver tumors will allow patients to live longer and experience an improved quality of life. Researchers look forward to those results.

Researchers look to continue the study of SIR-Spheres microspheres in various patient populations, with the goal of adding this treatment to conventional chemotherapy even earlier in the treatment algorithm.

As scientific developments continue to enhance treatment options for patients, it is the role of the medical provider to understand the various treatment avenues to identify the proper fit for a patient based on his or her comprehensive medical history and needs. With any procedure there are risks. In the case of SIRT, those risks have been presented earlier. Additionally, radiation damage (radioembolization-induced liver disease, REILD) to normal liver reserve is always a concern and guides careful ^{90}Y activity selection and catheter placement. Fortunately, the incidence of REILD in the MORE study is the lowest of any study of mCRC patients to date (all grades 1.7 percent; grade ≥3, 0.5 percent), compared with 2 to 10.3 percent in key series.[14,17,20,21]

Going Forward

These insights show that even among patients who were heavily pre-treated, ^{90}Y-radioembolization appears to have a favorable risk/benefit profile. A clinically meaningful survival benefit was evident, even among patients who had received three or more prior chemotherapy regimens.

Going forward, the cancer research community continues to uncover new technologies and advancements in treatment. Researchers have said a lot about the MORE study and have even alluded to alternate treatment modalities. So what is next for delivery of SIRT for mCRC patients?

Further analysis of results shows promise to expand and improve treatment outcomes by identifying potentially correctable pre-radiation abnormalities prior to delivery of radioembolization. A new method is being proposed to enable complex modeling of the hepatic arterial route, and the tumor microvascular bed in which the radioactive particles will become permanently embedded to enhance treatment delivery.[25] I have begun to explore, with another talented team of physicians, predictive modeling in order to understand a patient's personal anatomy and the microspheres' final position in a tumor end arteriole.[25]

In January 2014 the findings surrounding research into the predictive modeling of the hepatic arterial tree and tumor microvasculature were announced. These findings, like earlier data discussed, were aimed at further advancing the SIRT treatment approach. Fractal methods were used to develop a software tool

that can represent the microvasculature of the human liver and different organs and can account for disease states, such as liver tumors. Normal liver and tumor artery trees were created, with malignant vessels employing a random generator at each node resulting in corkscrew, bifurcation, and/or trifurcation daughter-vessel pattern.

The team concluded that predictive modeling may now be possible for radioactive or non-radioactive microspheres exiting from a catheter into the hepatic artery to its final position in a tumor end arteriole, or for systemic therapies. In a nutshell, researchers learned that having access to predictive modeling software in the individualized pre-treatment mapping process will help to more accurately outline the final stop for radioactive particles in the tumor end arteriole, thereby helping to improve success rates.

It Takes a Multidisciplinary Team

With all of the data at the hands of treating physicians and patients, it is important for the oncology team to focus on each patient's individual medical history. Tumor board discussions play an essential role in encouraging dialogue among specialists to identify the best treatment course of action for a patient. It is during these valuable discussions that clinicians essentially put their heads together and discuss the patient's previous treatments. The interventional radiologist's seat at the table is relatively new in the area of oncology, but a valuable one. Many of the treatments offered through interventional radiology or interventional oncology actually help to enhance the body's acceptance of later treatments.

All treatment options, including newer agents such as aflibercept and regorafenib, must be considered, and the pros and cons for each patient should be weighed on balance.

There is a great deal of engaging work underway that is making great strides to improve patient outcomes in the area of SIRT delivery for mCRC patients. The MORE study research adds to the growing body of scientific data further supporting the role of SIRT in treating metastatic colorectal cancer. In this specific patient population, the results compare favorably to many recently-approved chemotherapy and biologic agents, and provide another option to patients who may have stopped responding to systemic therapy.

At the end of the day, the best action clinicians can take for their patients is to collaborate; through dialogue, clinicians are able to arrive at the best possible treatment path for a patient. Many cancer programs are enhancing their multidisciplinary approach to care, which is good news for patients. Tumor board discussions are another valuable strategy for cancer programs wishing to enhance their holistic approach to cancer care.

OTHER TREATMENT OPTIONS

Two other treatments are now being used with mCRC patients:

1. Regorafenib, a newly-approved oral multikinase inhibitor used in mCRC patients previously treated with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, with an anti-VEGF therapy, and, if *KRAS* wild type, with an anti-EGFR therapy.
2. Aflibercept, a dual vascular endothelial growth factor-A (VEGF-A) and placental growth factor (PIGF) inhibitor approved to treat mCRC when given in combination with the FOLFIRI (leucovorin calcium, fluorouracil, irinotecan hydrochloride) chemotherapy regimen.

Based on results from the recently published pivotal CORRECT trial,[22] the acute and delayed toxicities of regorafenib appear to be higher than ^{90}Y- radioembolization. Comparison of all toxicity grades, regorafenib vs. ^{90}Y-radioembolization revealed:

- Fatigue, 63 percent vs. 54 percent
- Anorexia, 47 percent vs. 8 percent
- Weight loss, 32 percent vs. 0 percent
- Fever, 28 percent vs. 8 percent
- Rash, 29 percent vs. <1 percent
- Hypertension, 30 percent vs. <1 percent
- Hand-foot syndrome, 47 percent vs. 0 percent
- Equal rates of hyperbilirubinemia, 20 percent respectively.

That said, caution should always be exercised in direct comparisons of data from prospective vs. retrospective studies.

SIRT studies have shown a median survival range of 10.5 to 13 months, which compares well to similar second-line patients receiving aflibercept (median 13.5 months)[23] and bevacizumab beyond progression (median 11.2 months).[24] The median survival of 9.0 and 8.1 months following ^{90}Y-radioembolization in patients with 2 or ≥3 prior lines of chemotherapy, respectively, in this study compares favorably with patients treated in a similar setting using regorafenib or placebo (median 6.4 vs. 5.0 months).[23]

The findings detailed here are important as researchers continue to identify trends and opportunities to improve patient outcomes using SIR-Spheres microspheres. Further, if clinicians work collaboratively to improve a patient's less than favorable results prior to undergoing a SIRT procedure, researchers believe they may be able to enhance outcomes. OI

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careers

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Shreveport, Louisiana

The Feist-Weiller Cancer Center (FWCC) at LSU Health Sciences Center (LSUHSC) is seeking clinicians/scientists for tenure track positions in its Aerodigestive and GU Malignancy Programs. The positions—available at all academic levels—offer unique opportunities to lead or participate in active multidisciplinary teams of clinicians and scientists, allowing the opportunity to create and build clinical or translational cancer research programs.

FWCC is the most active tertiary cancer care and cancer research facility in Louisiana, serving over 80 percent of the state. FWCC has a state-of-the-art research facility, a new 60,000-square-foot multidisciplinary outpatient clinical building, and a faculty of over 50 clinicians and scientists.

FWCC's Division of Basic Cancer Research, Clinical Cancer Research, and Cancer Prevention and Control maintain active NCI-funded clinical research programs, multiple strongly funded programs in various aspects of the molecular biology of cancer, and innovative translational research projects. A new state-of-the-art cancer genome sequencing laboratory has been established. Generous start-up packages are available for translational and clinical research faculty. A mentored research development program is in place for junior faculty in both basic and clinical translational arenas.

Shreveport is a progressive modern city with excellent schools, numerous family activities, and a very low cost of living. LSU Health–Shreveport is an equal opportunity employer and all qualified applicants will receive consideration for employment without regard to race, color, religion, sex, national origin, disability status, protected veteran status, or any other characteristic protected by law.

Interested individuals should send a CV with a letter describing research or clinical interests and with three letters of reference to: Glenn Mills, MD, Professor of Medicine, Chief, Section of Hematology and Oncology, Director, Feist-Weiller Cancer Center, LSU Health Science Center, 1501 Kings Highway, Shreveport, LA 71130-3932 or email: gmills@lsuhsc.edu.

For more information, email: gmills@lsuhsc.edu.

DIRECTOR STEM CELL TRANSPLANT PROGRAM

Shreveport, Louisiana

The Feist-Weiller Cancer Center's (FWCC) Stem Cell Transplantation (SCT) program is seeking a Director. The position—available at associate or full professorship level—offers unique opportunities to participate in an active SCT and leukemia program, interacting with established multidisciplinary teams of clinicians and scientists, allowing the opportunity to create and build clinical or translational cancer research programs. FWCC's SCT program has an active autologous transplantation program. The new Director is expected to re-activate our allogeneic transplant program.

FWCC is the most active tertiary cancer care and cancer research facility in Louisiana, serving over 80 percent of the state. FWCC has a state-of-the-art research facility, a new 60,000-square-foot multidisciplinary outpatient clinical building, and a faculty of over 50 clinicians and scientists. FWCC's Division of Basic Cancer Research, Clinical Cancer Research, and Cancer Prevention and Control maintain active NCI-funded clinical research programs, multiple strongly funded programs in various aspects of the molecular biology of cancer, and innovative translational research projects. A new state-of-the-art cancer genome sequencing laboratory has been established. Generous start-up packages are available for translational and clinical research faculty. A mentored research development program is in place for junior faculty in both basic and clinical translational arenas.

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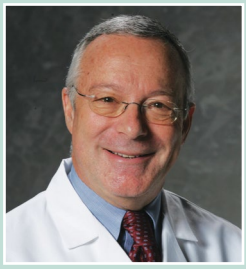


Highlights of ASCO 2014

Thoughts from a community oncologist

BY CARY A. PRESANT, MD, FACP, FASCO

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

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

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

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

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

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

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

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

And now for the science behind ASCO 2014.

Prevention & Epidemiology

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

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

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

> The meeting offers attendees important updates on scientific advances and the opportunity to get a feel for the state of the art in oncology.

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

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

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

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

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

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

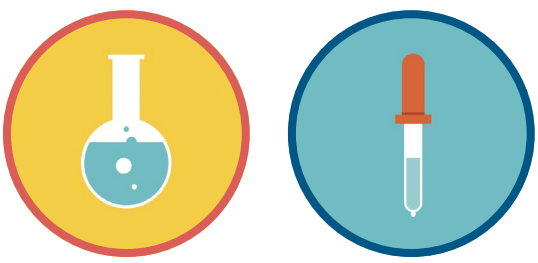
Ovarian Cancer

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

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

Pediatric Oncology

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



Breast Cancer

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

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

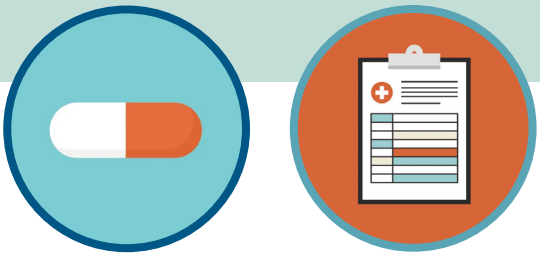
Abstract 511 (N. Turner et al.) looked at liquid biopsy. Plasma DNA was collected in 20 patients receiving neoadjuvant therapy, and circulating tumor DNA was positive in 90% of the patients who developed stage 4 disease. This marker may be important, and appeared to have a median eight-month lead time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

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

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

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

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



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

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

Multiple Myeloma

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

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

Non-Hodgkin Lymphoma

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

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

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

Prostate Cancer

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

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

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

Bladder Cancer

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

Renal Cell Cancer

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

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

Colon Cancer

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

Rectal Cancer

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

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

Gastric Cancer

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

Head and Neck Cancer

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

Central Nervous System

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

Non-Small Cell Lung Cancer

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

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

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

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

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

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

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

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

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

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

Small Cell Lung Cancer

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

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

Melanoma

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

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

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

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

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

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

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

Supportive Care

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

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

Chronic Lymphocytic Leukemia

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

General Oncology

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

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

Cary A. Presant, MD, FACP, FASCO, practices at City of Hope National Medical Center, Los Angeles, Calif. He is Past President, ACCC; Past President, American Cancer Society, California Division; Chairman of the Board, Medical Oncology Association of Southern California; and Professor of Clinical Medicine, University of Southern California KECK School of Medicine; and Chief Medical Officer, DiaTech Oncology, Nashville, Tenn.

Ask ACCC's Community Resource Centers: *Pancreatic Cancer*

Adenocarcinoma of the pancreas, commonly known as pancreatic cancer, continues to have a high mortality despite decades of research and modern chemotherapy. In 2014 there is estimated to be 46,420 new cases of pancreatic cancer, with 39,590 deaths.[1] The five-year survival rate for patients with advanced pancreatic cancer is estimated to be 2 percent; overall survival for all stages is 6 percent.[1] Erkut Borazanci, MD, MS, Virginia G. Piper Cancer Center Clinical Trials program, discusses current standard of care and future research directions for pancreatic cancer.

Treatment Options

Once a diagnosis of pancreatic cancer is made, options for treatment vary depending on whether the disease is resectable, borderline resectable, unresectable, or metastatic. If resectable, clinicians recommend that most patients proceed to surgery with consideration of adjuvant chemotherapy and/or radiation therapy, depending on pathologic findings. In cases of borderline resectable or locally advanced disease, neoadjuvant therapy is often indicated in the hope of getting a patient to surgery.

Surgical resection of pancreatic cancer remains the best chance for cure. However, even in the setting of an R0, node-negative resection, the five-year survival ranges from 25 to 30 percent. Many patients with resected pancreatic cancer ultimately experience recurrence and develop metastatic disease. Current front-line treatment options in advanced or metastatic pancreatic cancer involve the use of combination chemotherapy regimens, such as 5-FU, oxaliplatin, irinotecan, and leucovorin (FOLFIRINOX) or nab-paclitaxel plus gemcitabine.[2]

Once patients progress on initial chemotherapy, clinicians often suggest a clinical trial using a chemotherapy regimen consisting of a fluoropyrimidine-based or gemcitabine-based therapy, depending on what the patient received for initial therapy.[3]

One of our research institute's key foci has been treating pancreatic cancer. This focus led to the development of the nab-paclitaxel plus gemcitabine treatment regimen.[4] However, pancreatic cancer is very difficult to treat due to its effects on the digestive system, resulting in significant pain and pancreatic insufficiency, as well as the inherent resistance to drug delivery through the stroma of the pancreas.

A Multidisciplinary Approach

At Virginia G. Piper Cancer Center, Scottsdale, Ariz., we believe in a multidisciplinary approach in treating pancreatic cancer patients. This team includes dietitians, occupational and physical therapists, social workers, pharmacists, genetic counselors, nurses, nurse practitioners, and physicians. Each multidisciplinary team member plays a key role in treatment. For example, our dietitians help us to recommend a diet high in protein that tends to lower insulin levels, as we know that a patient's hemoglobin A1C impacts survival in pancreatic cancer.[5] One of the most common side effects of treatment involving agents such as oxaliplatin and nab-paclitaxel is peripheral neuropathy. Our occupational and physical therapists assist patients with a wide variety of exercises to help reduce the clinical impact of neuropathy and help patients attain maximal benefit from their chemotherapy. A dedicated social worker is vital in addressing patient's financial and social needs in addition to their stress of living with advanced pancreatic cancer.

Molecular Testing & Targeted Therapy

Once patients progress on initial therapy for pancreatic cancer, our next treatment decisions are based on available molecular profiling data on the individual's tumor. Data can be used from several sources:

- From commercial molecular profiling companies, such as Caris Life Sciences, Foundation One Medicine, or Paradigm
- From whole genomic sequencing through our partnership with Mayo Clinic Scottsdale and TGen (Translational Genomics Research Institute)
- Through the use of germline testing.

Tissue sources for this testing range from peripheral blood or cheek swabs for germline testing, to core needle biopsies obtained through interventional radiology (IR)-based procedures, to surgical specimens. Our clinicians and others have shown the benefit of molecular testing through improvements in progression-free survival (PFS) and overall survival (OS), particularly in patients who have progressed on several lines of therapy.[6,7]

More and more anti-cancer agents are coming to market each year, many of them targeted in nature. Examples include the agent Minnelide™, which targets heat shock protein 70 (HSP70) (ClinicalTrials.gov NCT01927965), which is up-regulated in times of cellular stress and explains resistance to HSP90 inhibitors.[2] Other agents designed to break down the pancreatic stroma, such as hyaluronidase, are being combined with nab-paclitaxel plus gemcitabine (ClinicalTrials.gov NCT01839487) and have shown promise in the pre-clinical setting.[2] A study using an agent targeting the JAK pathway, which has shown clinical utility in treating myelofibrosis and appears to be involved in the inflammation-driven mechanism of pancreatic cancer, is being studied in combination with nab-paclitaxel plus gemcitabine (ClinicalTrials.gov NCT01858883).

Researchers are also studying the use of older chemotherapies in combination. For example, thanks to Dr. Michael Barrett's profiling work through our partnership with TGen, our team noticed that there may be a BRCA-like phenotype in some patients with pancreatic cancer. This finding led to the development of a Phase IB/II study of patients with newly-diagnosed metastatic pancreatic cancer combining cisplatin plus nab-paclitaxel plus gemcitabine (ClinicalTrials.gov NCT01893801).

A recent clinical trial at Virginia G. Piper Cancer Center involved the use of the investigational agent, MM-398, a nanoliposomal encapsulation of irinotecan. This agent showed an improvement of OS when combined with 5-FU in patients with pancreatic cancer on second line therapy for patients who progressed on gemcitabine.[8]

Immunotherapy

In the past few decades, treatment of solid tumor malignancies has largely ignored the use of immunotherapies. Recently, the use of agents targeting proteins, such as CTLA-4, have been developed for the treatment of melanoma, showing—in a subset of patients—long lasting responses.[9] Other agents targeting the programmed death 1 (PD-1) receptor, which is also involved in dampening the immune system in response to cancer, have also shown efficacy in melanoma patients with prior CTLA-4 treatment.[10]

Not only have these treatments shown promise in other immune responsive malignancies, such as renal cell carcinoma, they are also being studied in solid tumor malignancies, such as pancreatic cancer. One such trial at Virginia G. Piper Cancer Center involves PD-1 blockade (ClinicalTrials.gov NCT02054806). Furthermore, a pancreatic cancer specific trial using a combination of low-dose cyclophosphamide and two pancreatic cancer vaccines called GVAX and CRS 207 has also been brought to the clinic (ClinicalTrials.gov NCT02004262). It is currently in Phase IIB and an early Phase IIA study and has shown great promise by using the body's own immune system to home in on pancreatic cancer.

Case Study

An otherwise healthy 65-year-old woman was diagnosed in September 2013 with pancreatic cancer with liver metastasis. She was initially treated with the chemotherapy combination FOLFIRINOX. Despite obtaining a significant partial radiographic response after 4 cycles, the patient subsequently developed febrile neutropenia, requiring ICU admission in November 2013. The patient developed multi-organ failure and eventually recovered but required physical therapy.

On initial consultation with our clinic at the end of December 2013, we found that the patient had a family history of ovarian cancer, along with a background of Eastern European Jewish ancestry. The patient's repeat imaging exams and CA 19-9 tumor marker showed minimal disease and the patient elected to undergo expectant observation. During this time, the patient underwent genetic counseling that revealed a BRCA1 germline mutation.

The patient subsequently developed disease progression and was placed on an oral PARP inhibitor targeting her germline BRCA mutation. The patient had initial stable disease that eventually progressed and, as of July 2014, is undergoing therapy with gemcitabine chemotherapy. If the patient were to progress on this current therapy, the patient might consider enrolling in a pancreatic cancer vaccine trial examining the benefit of the agent CRS 207, an attenuated *Listeria monocytogenes* vaccine that expresses the pancreatic-tumor-associated antigen mesothelin.

This case highlights several unique aspects of pancreatic cancer, including germline mutations that can lead to potential treatment options for a patient with pancreatic cancer and how clinical trials can help difficult-to-treat cancers, including pancreatic cancer. It must be noted that the median overall survival for patients with stage IV pancreatic cancer is around 6 months, and this patient is alive at 10 months and has an excellent performance status to consider a clinical trial.

Going Forward

The reason why clinicians focus on the possibility of germline mutations is that they can now exploit these mutations through the use of agents, such as poly ADP ribose polymerase (PARP) inhibitors, for patients that carry mutations in the BRCA genes, PALB2, or APC genes (ClinicalTrials.gov NCT01286987). Other ways to exploit these types of mutations are by treating patients with DNA-damaging agents, such as gemcitabine, irinotecan, platinum agents, and a less commonly used agent, such as mitomycin C. Furthermore, knowing if a patient is a carrier for known germline mutations for pancreatic cancer can allow his or her

family members to be more vigilant about symptoms for pancreatic cancer and perhaps consider closer monitoring.

Pancreatic cancer remains a difficult disease to manage and treat, but clinicians have seen some success against the disease. Through better management of the disease and its innate side effects and more research into the mechanisms of how pancreatic cancer grows, researchers are hopeful they can turn the tide of this disease and improve the lives of pancreatic cancer patients and their families. OI

Erkut Borazanci, MD, MS, is a medical oncologist and the Drug Development Scholar at the Virginia G. Piper Cancer Center Clinical Trials program at Scottsdale Healthcare. Dr. Borazanci's clinical and research focus is on gastrointestinal cancers, particularly pancreatic cancer. He is a Clinical Assistant Professor of Internal Medicine at the University of Arizona College of Medicine in Phoenix and has the same title at TGen (Translational Genomics Research Institute).

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ADVERTISER'S INDEX

Lighting a Candle

Grassroots efforts for oral chemotherapy access in Wisconsin

BY PARAMESWARAN HARI, MD, MRCP, MS

It is better to light a candle than curse the darkness — John F. Kennedy

It was in 2007 that a patient of mine (Jane) called my office requesting that we not reorder her chemotherapy—even though it was working very well for her relapsed myeloma. Often, when patients ask to stop effective treatment, it is because of worries about the side effects of long-term therapy or chronic side effects. So I called Jane back and confirmed that she was tolerating treatment very well and experiencing no negative side effects. Her husband (Roger) finally told me that they simply could not afford the co-pay each month for her oral medication (lenalidomide) and there was no way they could refill the script. So they decided to take a chance on the myeloma staying inactive. Roger had a good job and their employer-based insurance was generally characterized as "good" insurance by our clinic's financial coordinators.

The Elephant in the Room

That experience was the first time I understood the financial challenges that newer oral chemotherapy drugs created for patients. Lenalidomide was new to the market at the time and it was considered by Jane's insurance as a regular prescription medication just like routine anti-hypertensives, for example. After several phone calls and many conversations with payers, I had a grasp of this problem—which, in fact, was now starting to affect patients with hematological malignancies in a major way.

Oral chemotherapy medications are revolutionizing oncology and converting diseases like myeloma into chronic illnesses. In addition to effectiveness, oral medications are more convenient, generate fewer office visits, and are more suitable for people who can continue to stay productive and active in society. However, our payment models seemed stuck in a past era where infusional chemotherapy was considered a medical benefit and reimbursed fully by payers and oral drugs—chemotherapy or otherwise—were covered by prescription coverage and entailed a system of co-pays and out-of-pocket costs, sometimes with no annual cap.

Addressing the Issue through Oral Parity Legislation

Fortunately, patient support groups across the country were hearing the same complaint and a movement was taking shape across several states. The oral chemotherapy parity movement sought to establish equivalency in payment for anti-cancer medications whether they were administered in IV or in pill form.

I was privileged to be part of this movement in my home state of Wisconsin. Starting in 2008 to 2009, we mobilized a coalition of patient support groups, disease-specific charities, hospitals,

On April 2, 2014, Wisconsin Governor Scott Walker signed the Cancer Treatment Fairness Act into law at the Froedtert and Medical College of Wisconsin.

oncologists, and patients to educate our state legislature about the issue and support passage of an oral chemotherapy parity law.

Early on we made several phone calls to influential state legislators who raised awareness about the issue and brought SB300 (Senate Bill 300) to the floor of the Wisconsin legislature. We had committee hearings, followed by public hearings, and years passed before we could rejoice in the passage of the oral parity bill.

Although Wisconsin was one of the states to get an early start on this initiative, the passage of oral parity legislation took five years and a lot of struggle.

In 2014 Dr. Hari received a grassroots advocacy award at ACCC's Annual National Meeting in Arlington, Va. Pictured (left to right) are the 2014 Oncology Grassroots Champion for Patient Access Award recipients: James Thomas, MD, PhD, Medical College of Wisconsin; Seija Olivier, RN, Allegiance Health, Jackson, Mich.; Parameswaran Hari, MD, MRCP, MS, Medical College of Wisconsin; and Matt Sherer, MBA, MHA, Tallahassee Memorial Cancer Center, Tallahassee, Fla.

It Takes a Village

As with most physicians, politics and activism were new territories for me. I needed considerable help from my patients, various societies, such as the Leukemia & Lymphoma Society, the International Myeloma Foundation, and many others, to navigate these uncharted seas. While I did not believe we would run into opposition, in a democracy there are always opposing viewpoints and our state legislators needed convincing. I quickly learned that what seems obvious, ethical, and beneficial from one's own viewpoint is not always the perspective shared by others.

Our grassroots effort had some close misses; there was also turnover in the state legislature during this period. Groups opposed to the bill felt that its passage would bring forth a mandate and they opposed passage within the broader context of healthcare reform that was happening across the country at the same time.

Our strategy was to keep up the public pressure and continually point out the benefits of the legislation. We were able to do so with newspaper articles featuring patient testimony, op-ed pieces, stories on television news channels, and radio programs. Using all of these venues, we were able to keep our side of the argument in front of the public.

My role was to be available and to articulate the argument for oral chemotherapy parity. Several of my patients who were finding it difficult to afford oral chemotherapy prescriptions shared their stories in the media. Working in partnership, providers and patients participated in the public hearings at the state Capitol.

The sense of camaraderie between patients, caregivers, and healthcare professionals and the emotional high of being able to meaningfully impact lives was the greatest reward for all of us involved in this grassroots effort.

Thanks for the Support

I must thank a number of people for their support; individuals and organizations that allowed and encouraged my participation. My employer, the Medical College of Wisconsin and its office of Public Affairs were helpful each step of the way. Our hospital partner, Froedtert Hospital, formed a coalition of like-minded hospitals in Wisconsin to support our grassroots effort for oral party legislation.

The efforts of patient support groups—especially the Leukemia & Lymphoma Society and the International Myeloma Foundation—was crucial as they assumed a liaison function between the various stakeholders.

Parting Words

For colleagues who are engaged in similar efforts, I offer this advice: stay engaged and listen to your patients as to what can be done beyond medicine to help them through their cancer journey. Luckily, I believe that most hospitals and medical practices are open to their clinicians spending time on such efforts.

Media engagement is also critical. Although I will admit that it takes practice to learn how to put one's viewpoint across succinctly during media interviews. In the future, social media will also be important in generating buzz around causes.

For us, April 2, 2014, was the day that the Governor of Wisconsin, Scott Walker, finally signed the bill into law. The signing was held at my hospital and in the presence of numerous patients, families, hospital representatives, legislators, and representatives from patient support groups and hospital systems. The venue was chosen in recognition of the efforts we had put in and it made the victory even sweeter.

Looking back, I learned much about the inner workings of our democratic government and what it takes to get legislation passed—even when the issue has bipartisan support. I now have a deeper appreciation of the fight our cancer patients and their caregivers and supporters have to go through. I know that putting together a coalition of people committed to a cause needs time, emotional energy, and patience. But when the cause is right and when victory is won—there is no greater satisfaction. OI

Parameswaran Hari, MD, MRCP, MS, is the Armand Quick-William Stapp Professor of Hematology at the Medical College of Wisconsin, Milwaukee, Wisc. In 2014 Dr. Hari received a grassroots advocacy award at ACCC's Annual National Meeting in Arlington, Va.

Xtandi® (enzalutamide) capsules

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

BRIEF SUMMARY OF PRESCRIBING INFORMATION
The following is a brief summary: please see the package insert for full prescribing information.

---------- **INDICATIONS AND USAGE** ----------
XTANDI is indicated for the treatment of patients with metastatic castration-resistant prostate cancer who have previously received docetaxel.

---------- **CONTRAINDICATIONS** ----------
Pregnancy
XTANDI can cause fetal harm when administered to a pregnant woman based on its mechanism of action. XTANDI is not indicated for use in women. XTANDI is contraindicated in women who are or may become pregnant. 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 the fetus and the potential risk for pregnancy loss *[see Use in Specific Populations]*.

---------- **WARNINGS AND PRECAUTIONS** ----------
Seizure
In the randomized clinical trial, 7 of 800 (0.9%) patients treated with XTANDI 160 mg once daily experienced a seizure. No seizures occurred in patients treated with placebo. Seizures occurred from 31 to 603 days after initiation of XTANDI. Patients experiencing seizure were permanently discontinued from therapy and all seizures resolved. There is no clinical trial experience re-administering XTANDI to patients who experienced seizures.
The safety of XTANDI in patients with predisposing factors for seizure is not known because these patients were excluded from the trial. These exclusion criteria included a history of seizure, underlying brain injury with loss of consciousness, transient ischemic attack within the past 12 months, cerebral vascular accident, brain metastases, brain arteriovenous malformation or the use of concomitant medications that may lower the seizure threshold.
Because of the risk of seizure associated with XTANDI use, patients should be advised of the risk of engaging in any activity where sudden loss of consciousness could cause serious harm to themselves or others.

---------- **ADVERSE REACTIONS** ----------
Clinical Trial Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.
In the randomized clinical trial in patients with metastatic castration-resistant prostate cancer who had previously received docetaxel, patients received XTANDI 160 mg orally once daily (N = 800) or placebo (N = 399). The median duration of treatment was 8.3 months with XTANDI and 3.0 months with placebo. All patients continued androgen deprivation therapy. Patients were allowed, but not required, to take glucocorticoids. During the trial, 48% of patients on the XTANDI arm and 46% of patients on the placebo arm received glucocorticoids. All adverse events and laboratory abnormalities were graded using NCI CTCAE version 4.
The most common adverse drug reactions (≥ 5%) reported in patients receiving XTANDI in the randomized clinical trial were asthenia/fatigue, back pain, diarrhea, arthralgia, hot flush, peripheral edema, musculoskeletal pain, headache, upper respiratory infection, muscular weakness, dizziness, insomnia, lower respiratory infection, spinal cord compression and cauda equina syndrome, hematuria, paresthesia, anxiety, and hypertension. Grade 3 and higher adverse reactions were reported among 47% of XTANDI-treated patients and 53% of placebo-treated patients. Discontinuations due to adverse events were reported for 16% of XTANDI-treated patients and 18% of placebo-treated patients. The most common adverse reaction leading to treatment discontinuation was seizure, which occurred in 0.9% of the XTANDI-treated patients compared to none (0%) of the placebo-treated patients. Table 1 shows adverse reactions reported in the randomized clinical trial that occurred at a ≥ 2% absolute increase in frequency in the XTANDI arm compared to the placebo arm.

Table 1. Adverse Reactions in the Randomized Trial

	XTANDI N = 800		Placebo N = 399	
	Grade 1-4 (%)	Grade 3-4 (%)	Grade 1-4 (%)	Grade 3-4 (%)
General Disorders				
Asthenic Conditions[a]	50.6	9.0	44.4	9.3
Peripheral Edema	15.4	1.0	13.3	0.8
Musculoskeletal And Connective Tissue Disorders				
Back Pain	26.4	5.3	24.3	4.0
Arthralgia	20.5	2.5	17.3	1.8
Musculoskeletal Pain	15.0	1.3	11.5	0.3
Muscular Weakness	9.8	1.5	6.8	1.8
Musculoskeletal Stiffness	2.6	0.3	0.3	0.0

(continued) **Table 1. Adverse Reactions in the Randomized Trial**

	XTANDI N = 800		Placebo N = 399	
	Grade 1-4 (%)	Grade 3-4 (%)	Grade 1-4 (%)	Grade 3-4 (%)
Gastrointestinal Disorders				
Diarrhea	21.8	1.1	17.5	0.3
Vascular Disorders				
Hot Flush	20.3	0.0	10.3	0.0
Hypertension	6.4	2.1	2.8	1.3
Nervous System Disorders				
Headache	12.1	0.9	5.5	0.0
Dizziness[b]	9.5	0.5	7.5	0.5
Spinal Cord Compression and Cauda Equina Syndrome	7.4	6.6	4.5	3.8
Paresthesia	6.6	0.0	4.5	0.0
Mental Impairment Disorders[c]	4.3	0.3	1.8	0.0
Hypoesthesia	4.0	0.3	1.8	0.0
Infections And Infestations				
Upper Respiratory Tract Infection[d]	10.9	0.0	6.5	0.3
Lower Respiratory Tract And Lung Infection[e]	8.5	2.4	4.8	1.3
Psychiatric Disorders				
Insomnia	8.8	0.0	6.0	0.5
Anxiety	6.5	0.3	4.0	0.0
Renal And Urinary Disorders				
Hematuria	6.9	1.8	4.5	1.0
Pollakiuria	4.8	0.0	2.5	0.0
Injury, Poisoning And Procedural Complications				
Fall	4.6	0.3	1.3	0.0
Non-pathologic Fractures	4.0	1.4	0.8	0.3
Skin And Subcutaneous Tissue Disorders				
Pruritus	3.8	0.0	1.3	0.0
Dry Skin	3.5	0.0	1.3	0.0
Respiratory Disorders				
Epistaxis	3.3	0.1	1.3	0.3

a Includes asthenia and fatigue.
b Includes dizziness and vertigo.
c Includes amnesia, memory impairment, cognitive disorder, and disturbance in attention.
d Includes nasopharyngitis, upper respiratory tract infection, sinusitis, rhinitis, pharyngitis, and laryngitis.
e Includes pneumonia, lower respiratory tract infection, bronchitis, and lung infection.

Laboratory Abnormalities
In the randomized clinical trial, Grade 1-4 neutropenia occurred in 15% of patients on XTANDI (1% Grade 3-4) and in 6% of patients on placebo (no Grade 3-4). The incidence of Grade 1-4 thrombocytopenia was similar in both arms; 0.5% of patients on XTANDI and 1% on placebo experienced Grade 3-4 thrombocytopenia. Grade 1-4 elevations in ALT occurred in 10% of patients on XTANDI (0.3% Grade 3-4) and 18% of patients on placebo (0.5% Grade 3-4). Grade 1-4 elevations in bilirubin occurred in 3% of patients on XTANDI and 2% of patients on placebo.

Infections
In the randomized clinical trial, 1.0% of patients treated with XTANDI compared to 0.3% of patients on placebo died from infections or sepsis. Infection-related serious adverse events were reported in approximately 6% of the patients on both treatment arms.

Falls and Fall-related Injuries
In the randomized clinical trial, falls or injuries related to falls occurred in 4.6% of patients treated with XTANDI compared to 1.3% of patients on placebo. Falls were not associated with loss of consciousness or seizure. Fall-related injuries were more severe in patients treated with XTANDI and included non-pathologic fractures, joint injuries, and hematomas.

Hallucinations
In the randomized clinical trial, 1.6% of patients treated with XTANDI were reported to have Grade 1 or 2 hallucinations compared to 0.3% of patients on placebo. Of the patients with hallucinations, the majority were on opioid-containing medications at the time of the event. Hallucinations were visual, tactile, or undefined.

----------DRUG INTERACTIONS ----------

Drugs that Inhibit or Induce CYP2C8

Co-administration of a strong CYP2C8 inhibitor (gemfibrozil) increased the composite area under the plasma concentration-time curve (AUC) of enzalutamide plus N-desmethyl enzalutamide in healthy volunteers. Co-administration of XTANDI with strong CYP2C8 inhibitors should be avoided if possible. If co-administration of XTANDI with a strong CYP2C8 inhibitor cannot be avoided, reduce the dose of XTANDI *[see Dosage and Administration (2.2) and Clinical Pharmacology (12.3)]*.

The effects of CYP2C8 inducers on the pharmacokinetics of enzalutamide have not been evaluated *in vivo*. Co-administration of XTANDI with strong or moderate CYP2C8 inducers (e.g., rifampin) may alter the plasma exposure of XTANDI and should be avoided if possible. Selection of a concomitant medication with no or minimal CYP2C8 induction potential is recommended *[see Clinical Pharmacology]*.

Drugs that Inhibit or Induce CYP3A4

Co-administration of a strong CYP3A4 inhibitor (itraconazole) increased the composite AUC of enzalutamide plus N-desmethyl enzalutamide by 1.3 fold in healthy volunteers *[see Clinical Pharmacology (12.3)]*.

The effects of CYP3A4 inducers on the pharmacokinetics of enzalutamide have not been evaluated *in vivo*. Co-administration of XTANDI with strong CYP3A4 inducers (e.g., carbamazepine, phenobarbital, phenytoin, rifabutin, rifampin, rifapentine) may decrease the plasma exposure of XTANDI and should be avoided if possible. Selection of a concomitant medication with no or minimal CYP3A4 induction potential is recommended. Moderate CYP3A4 inducers (e.g., bosentan, efavirenz, etravirine, modafinil, nafcillin) and St. John's Wort may also reduce the plasma exposure of XTANDI and should be avoided if possible *[see Clinical Pharmacology]*.

Effect of XTANDI on Drug Metabolizing Enzymes

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

---------- USE IN SPECIFIC POPULATIONS ----------

Pregnancy- Pregnancy Category X *[see Contraindications]*.

XTANDI can cause fetal harm when administered to a pregnant woman based on its mechanism of action. While there are no human or animal data on the use of XTANDI in pregnancy and XTANDI is not indicated for use in women, it is important to know that maternal use of an androgen receptor inhibitor could affect development of the fetus. XTANDI is contraindicated in women who are or may become pregnant while receiving the drug. 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 the fetus and the potential risk for pregnancy loss. Advise females of reproductive potential to avoid becoming pregnant during treatment with XTANDI.

Nursing Mothers

XTANDI is not indicated for use in women. It is not known if enzalutamide is excreted in human milk. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from XTANDI, a decision should be made to either discontinue nursing, or discontinue the drug taking into account the importance of the drug to the mother.

Pediatric Use

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

Geriatric Use

Of 800 patients who received XTANDI in the randomized clinical trial, 71 percent were 65 and over, while 25 percent were 75 and over. No overall differences in safety or effectiveness were observed between these patients and younger patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Patients with Renal Impairment

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

Patients with Hepatic Impairment

A dedicated hepatic impairment trial compared the composite systemic exposure of enzalutamide plus N-desmethyl enzalutamide in volunteers with baseline mild or moderate hepatic impairment (Child-Pugh Class A and B, respectively) versus healthy controls with normal hepatic function. The composite AUC of enzalutamide plus N-desmethyl enzalutamide was similar in volunteers with mild or moderate baseline hepatic impairment compared to volunteers with normal hepatic function. No initial dosage adjustment is necessary for patients with baseline mild or moderate hepatic impairment. Baseline severe hepatic impairment (Child-Pugh Class C) has not been assessed *[see Clinical Pharmacology]*.

---------- OVERDOSAGE ----------

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

Carcinogenesis, Mutagenesis, Impairment of Fertility

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

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

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

PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (PATIENT INFORMATION).

- Instruct patients to take their dose at the same time each day (once daily). XTANDI can be taken with or without food. Each capsule should be swallowed whole. Do not chew, dissolve, or open the capsules.
- Inform patients receiving a GnRH analog that they need to maintain this treatment during the course of treatment with XTANDI.
- Inform patients that XTANDI has been associated with an increased risk of seizure. Discuss conditions that may predispose to seizures and medications that may lower the seizure threshold. Advise patients of the risk of engaging in any activity where sudden loss of consciousness could cause serious harm to themselves or others.
- Inform patients that XTANDI may cause dizziness, mental impairment, paresthesia, hypoesthesia, and falls.
- Inform patients that they should not interrupt, modify the dose, or stop XTANDI without first consulting their physician. Inform patients that if they miss a dose, then they should take it as soon as they remember. If they forget to take the dose for the whole day, then they should take their normal dose the next day. They should not take more than their prescribed dose per day.
- Apprise patients of the common side effects associated with XTANDI: asthenia/fatigue, back pain, diarrhea, arthralgia, hot flush, peripheral edema, musculoskeletal pain, headache, upper respiratory infection, muscular weakness, dizziness, insomnia, lower respiratory infection, spinal cord compression and cauda equina syndrome, hematuria, paresthesia, anxiety, and hypertension. Direct the patient to a complete list of adverse drug reactions in PATIENT INFORMATION.
- Inform patients that XTANDI may be harmful to a developing fetus. Patients should also be informed that they should use a condom if having sex with a pregnant woman. A condom and another effective method of birth control should be used if the patient is having sex with a woman of child-bearing potential. These measures are required during and for three months after treatment with XTANDI.

Manufactured by: Catalent Pharma Solutions, LLC, St. Petersburg, FL 33716
Manufactured for and Distributed by:
Astellas Pharma US, Inc., Northbrook, IL 60062
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MEDIVATION

FOR THE TREATMENT OF PATIENTS WITH METASTATIC CASTRATION-RESISTANT PROSTATE CANCER (mCRPC) WHO HAVE PREVIOUSLY RECEIVED DOCETAXEL

Xtandi® (enzalutamide) capsules

XTANDI (enzalutamide) capsules is indicated for the treatment of patients with metastatic castration-resistant prostate cancer (mCRPC) who have previously received docetaxel.

Important Safety Information

Contraindications XTANDI can cause fetal harm when administered to a pregnant woman based on its mechanism of action. XTANDI is not indicated for use in women. XTANDI is contraindicated in women who are or may become pregnant.

Warnings and Precautions In the randomized clinical trial, seizure occurred in 0.9% of patients on XTANDI. No patients on the placebo arm experienced seizure. Patients experiencing a seizure were permanently discontinued from therapy. All seizures resolved. Patients with a history of seizure, taking medications known to decrease the seizure threshold, or with other risk factors for seizure were excluded from the clinical trial. Because of the risk of seizure associated with XTANDI use, patients should be advised of the risk of engaging in any activity where sudden loss of consciousness could cause serious harm to themselves or others.

Adverse Reactions The most common adverse drug reactions (≥ 5%) reported in patients receiving XTANDI in the randomized clinical trial were asthenia/fatigue, back pain, diarrhea, arthralgia, hot flush, peripheral edema, musculoskeletal pain, headache, upper respiratory infection, muscular weakness, dizziness, insomnia, lower respiratory infection, spinal cord compression and cauda equina syndrome, hematuria, paresthesia, anxiety, and hypertension. Grade 1-4 neutropenia occurred in 15% of XTANDI patients (1% grade 3-4) and in 6% of patients on placebo (no grade 3-4). Grade 1-4 elevations in bilirubin occurred in 3% of XTANDI patients and 2% of patients on placebo. One percent of XTANDI patients compared to 0.3% of patients on placebo died from infections or sepsis. Falls or injuries related to falls occurred in 4.6% of XTANDI patients vs 1.3% of patients on placebo. Falls were not associated with loss of consciousness or seizure. Fall-related injuries were more severe in XTANDI patients and included non-pathologic fractures, joint injuries, and hematomas. Grade 1 or 2 hallucinations occurred in 1.6% of XTANDI patients and 0.3% of patients on placebo, with the majority on opioid-containing medications at the time of the event.

Drug Interactions: Effect of Other Drugs on XTANDI Administration of strong CYP2C8 inhibitors can increase the plasma exposure to XTANDI. Coadministration of XTANDI with strong CYP2C8 inhibitors should be avoided if possible. If coadministration of XTANDI cannot be avoided, reduce the dose of XTANDI. Coadministration of XTANDI with strong or moderate CYP3A4 and CYP2C8 inducers can alter the plasma exposure of XTANDI and should be avoided if possible. **Effect of XTANDI on Other Drugs** XTANDI is a strong CYP3A4 inducer and a moderate CYP2C9 and CYP2C19 inducer in humans. Avoid CYP3A4, CYP2C9, and CYP2C19 substrates with a narrow therapeutic index, as XTANDI may decrease the plasma exposures of these drugs. If XTANDI is coadministered with warfarin (CYP2C9 substrate), conduct additional INR monitoring.

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

References: 1. XTANDI [package insert]. Northbrook, IL: Astellas Pharma US, Inc; 2012. **2.** Scher HI, Fizazi K, Saad F, et al. Increased survival with enzalutamide in prostate cancer after chemotherapy. *N Engl J Med*. 2012;367:1187-1197. **3.** Referenced with permission from The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer V.2.2013. © National Comprehensive Cancer Network, Inc 2013. All rights reserved. Accessed March 11, 2013. To view the most recent and complete version of the guideline, go online to www.nccn.org. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, NCCN GUIDELINES®, and all other NCCN Content are trademarks owned by the National Comprehensive Cancer Network, Inc.

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MEDIVATION
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FOR THE TREATMENT OF PATIENTS WITH METASTATIC CASTRATION-RESISTANT PROSTATE CANCER (mCRPC) WHO HAVE PREVIOUSLY RECEIVED DOCETAXEL

Xtandi® (enzalutamide) capsules

18.4 MONTHS MEDIAN OVERALL SURVIVAL
VS **13.6 MONTHS** WITH PLACEBO[1]

18.4 AND MORE:

- **Convenient, oral, once-daily administration**
  - Dosed as four 40 mg capsules (160 mg) without food restrictions or steroid requirements. Each capsule should be swallowed whole. Patients should not chew, dissolve, or open the capsules[1,2]
- **Comparable overall rate of grade 3-4 adverse reactions**
  - No increased overall rate of grade 3-4 adverse reactions with XTANDI (enzalutamide) capsules vs placebo (47% vs 53%, respectively)[1]
- **37% reduced risk of death**
  - HR = 0.63 (95% CI, 0.53-0.75); $P < 0.0001$[1]

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) include enzalutamide (XTANDI) with a category 1 recommendation for use following docetaxel in patients with mCRPC.[3]

Select Important Safety Information

In the randomized clinical trial, seizure occurred in 0.9% of patients on XTANDI versus none on the placebo arm.

The most common adverse drug reactions (≥ 5%) were asthenia/fatigue, back pain, diarrhea, arthralgia, hot flush, peripheral edema, musculoskeletal pain, headache, upper respiratory infection, muscular weakness, dizziness, insomnia, lower respiratory infection, spinal cord compression and cauda equina syndrome, hematuria, paresthesia, anxiety, and hypertension. Grade 3 and higher adverse reactions were reported among 47% of XTANDI-treated patients and 53% of placebo-treated patients. Discontinuations due to adverse events were reported for 16% of XTANDI-treated patients and 18% of placebo-treated patients.

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