ONCOLOGY ISSUES

This publication is a benefit of membership
Association of Community Cancer Centers

July | August 2017

A Cognitive Approach to Cancer Treatment

ACCC
Association of Community Cancer Centers

TAGRISSO® (osimertinib): BREAK THROUGH THE T790M RESISTANCE BARRIER

in patients with metastatic EGFR T790M mutation-positive NSCLC, as detected by an FDA-approved test, at progression on or after EGFR TKI therapy

A targeted therapy researched in two clinical trials

- Effective in two separate global, Phase II, single-arm, open-label clinical trials in patients with metastatic EGFR T790M mutation-positive NSCLC who had progressed on or after EGFR TKI therapy[1]
  - A 59% objective response rate (95% CI: 54–64) in patients who progressed with previous EGFR TKI therapy
- In a separate dose-finding part of AURA, 63 patients with centrally confirmed EGFR T790M-positive NSCLC who progressed on prior systemic therapy, including an EGFR TKI, were administered TAGRISSO 80 mg[1]:
  - 51% (32/63) of patients in the 80-mg cohort had a confirmed response by BICR
  - The median DoR was 12.4 months
- Grade 3/4 adverse events occurred at <3.5%[1]
- <6% of patients in a pooled analysis (N=411) had either dose reductions or discontinuations due to adverse events[1]
- Interstitial Lung Disease (ILD)/Pneumonitis occurred in 3.3% and was fatal in 0.5% of 813 TAGRISSO patients. Withhold TAGRISSO and promptly investigate for ILD in any patient presenting with worsening of respiratory symptoms indicative of ILD (e.g., dyspnea, cough and fever). Permanently discontinue TAGRISSO if ILD is confirmed[1]
- The most common adverse events in a pooled analysis of TAGRISSO patients (N=411) were diarrhea (42%), rash (41%), dry skin (31%) and nail toxicity (25%)[1]

IMPORTANT SAFETY INFORMATION

- There are no contraindications for TAGRISSO
- Interstitial Lung Disease (ILD)/Pneumonitis occurred in 3.3% and was fatal in 0.5% of 813 TAGRISSO patients. Withhold TAGRISSO and promptly investigate for ILD in any patient presenting with worsening of respiratory symptoms indicative of ILD (e.g., dyspnea, cough and fever). Permanently discontinue TAGRISSO if ILD is confirmed
- QTc interval prolongation occurred in TAGRISSO patients. Of the 411 patients in two Phase II studies, 0.2% were found to have a QTc greater than 500 msec, and 2.7% had an increase from baseline QTc greater than 60 msec. Conduct periodic monitoring with ECGs and electrolytes in patients with congenital long QTc syndrome, congestive heart failure, electrolyte abnormalities, or those who are taking medications known to prolong the QTc interval. Permanently discontinue TAGRISSO in patients who develop QTc interval prolongation with signs/symptoms of life threatening arrhythmia

Visit **TAGRISSOhcp.com** for more information

IMPORTANT SAFETY INFORMATION (cont.)

- Cardiomyopathy occurred in 1.4% and was fatal in 0.2% of 813 TAGRISSO patients. Left Ventricular Ejection Fraction (LVEF) decline >10% and a drop to <50% occurred in 2.4% of (9/375) TAGRISSO patients. Assess LVEF before initiation and then at 3 month intervals of TAGRISSO treatment. Withhold TAGRISSO if ejection fraction decreases by 10% from pretreatment values and is less than 50%. For symptomatic congestive heart failure or persistent asymptomatic LV dysfunction that does not resolve within 4 weeks, permanently discontinue TAGRISSO
- Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during TAGRISSO treatment and for 6 weeks after the final dose. Advise males with female partners of reproductive potential to use effective contraception for 4 months after the final dose
- The most common adverse reactions (>20%) observed in TAGRISSO patients were diarrhea (42%), rash (41%), dry skin (31%) and nail toxicity (25%)

INDICATION

TAGRISSO is indicated for the treatment of patients with metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive non-small cell lung cancer (NSCLC), as detected by an FDA-approved test, who have progressed on or after EGFR tyrosine kinase inhibitor therapy.

This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Please see Brief Summary of complete Prescribing Information.

Reference: 1. TAGRISSO [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2015.

AstraZeneca

TAGRISSO®
osimertinib

TAGRISSO™ (osimertinib) tablets, for oral use

Brief Summary of Prescribing Information.

For complete prescribing information consult official package insert.

INDICATIONS AND USAGE

TAGRISSO is indicated for the treatment of patients with metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive non-small cell lung cancer (NSCLC), as detected by an FDA-approved test, who have progressed on or after EGFR tyrosine kinase inhibitor (TKI) therapy.

This indication is approved under accelerated approval based on tumor response rate and duration of response *[see Clinical Studies (14) in full Prescribing Information]*. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

DOSAGE AND ADMINISTRATION

Patient Selection

Confirm the presence of a T790M EGFR mutation in tumor specimens prior to initiation of treatment with TAGRISSO *[see Indications and Usage (1) and Clinical Studies (14) in full Prescribing Information]*. Information on FDA-approved tests for the detection of T790M mutations is available at http://www.fda.gov/companiondiagnostics.

Recommended Dosage Regimen

The recommended dose of TAGRISSO is 80 mg tablet once a day until disease progression or unacceptable toxicity. TAGRISSO can be taken with or without food.

If a dose of TAGRISSO is missed, do not make up the missed dose and take the next dose as scheduled.

Administration to Patients Who Have Difficulty Swallowing Solids

Disperse tablet in 60 mL (2 ounces) of non-carbonated water only. Stir until tablet is dispersed into small pieces (the tablet will not completely dissolve) and swallow immediately. Do not crush, heat, or ultrasonicate during preparation. Rinse the container with 120 mL to 240 mL (4 to 8 ounces of) water and immediately drink.

If administration via naso-gastric tube is required, disperse the tablet as above in 15 mL of noncarbonated water, and then use an additional 15 mL of water to transfer any residues to the syringe. The resulting 30 mL liquid should be administered as per the nasogastric tube instructions with appropriate water flushes (approximately 30 mL).

Dosage Modification

Adverse Reactions

Table 1 Recommended Dose Modifications for TAGRISSO

Target Organ	Adverse Reaction[a]	Dose Modification
Pulmonary	Interstitial lung disease (ILD)/Pneumonitis	Permanently discontinue TAGRISSO.
Cardiac	QTc[†] interval greater than 500 msec on at least 2 separate ECGs[b]	Withhold TAGRISSO until QTc interval is less than 481 msec or recovery to baseline if baseline QTc is greater than or equal to 481 msec, then resume at 40 mg dose.
	QTc interval prolongation with signs/symptoms of life-threatening arrhythmia	Permanently discontinue TAGRISSO.
	Asymptomatic, absolute decrease in LVEF[c] of 10% from baseline and below 50%	Withhold TAGRISSO for up to 4 weeks. • If improved to baseline LVEF, resume. • If not improved to baseline, permanently discontinue.
	Symptomatic congestive heart failure	Permanently discontinue TAGRISSO.
Other	Grade 3 or higher adverse reaction	Withhold TAGRISSO for up to 3 weeks.
	If improvement to Grade 0-2 within 3 weeks	Resume at 80 mg or 40 mg daily.
	If no improvement within 3 weeks	Permanently discontinue TAGRISSO.

[a] Adverse reactions graded by the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0 (NCI CTCAE v4.0).
[b] ECGs = Electrocardiograms
[c] LVEF = Left Ventricular Ejection Fraction
[†] QTc = QT interval corrected for heart rate

Drug Interactions

Strong CYP3A4 Inducers

If concurrent use is unavoidable, increase TAGRISSO dosage to 160 mg daily when coadministering with a strong CYP3A inducer. Resume TAGRISSO at 80 mg 3 weeks after discontinuation of the strong CYP3A4 inducer *[see Drug Interactions (7), and Clinical Pharmacology (12.3) in full Prescribing Information]*.

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

Interstitial Lung Disease/Pneumonitis

Across clinical trials, interstitial lung disease (ILD)/pneumonitis occurred in 3.3% (n=27) of TAGRISSO treated patients (n=813); 0.5% (n=4) were fatal.

Withhold TAGRISSO and promptly investigate for ILD in any patient who presents with worsening of respiratory symptoms which may be indicative of ILD (e.g., dyspnea, cough and fever). Permanently discontinue TAGRISSO if ILD is confirmed *[see Dosage and Administration (2.4) and Adverse Reactions (6) in full Prescribing Information]*.

QTc Interval Prolongation

The heart rate-corrected QT (QTc) interval prolongation occurs in patients treated with TAGRISSO. Of the 411 patients in Study 1 and Study 2, one patient (0.2%) was found to have a QTc greater than 500 msec, and 11 patients (2.7%) had an increase from baseline QTc greater than 60 msec *[see Clinical Pharmacology (12.2) in full Prescribing Information]*.

In Study 1 and 2, patients with baseline QTc of 470 msec or greater were excluded. Conduct periodic monitoring with ECGs and electrolytes in patients with congenital long QTc syndrome, congestive heart failure, electrolyte abnormalities, or those who are taking medications known to prolong the QTc interval. Permanently discontinue TAGRISSO in patients who develop QTc interval prolongation with signs/symptoms of life-threatening arrhythmia *[see Dosage and Administration (2.4) in full Prescribing Information]*.

Cardiomyopathy

Across clinical trials, cardiomyopathy (defined as cardiac failure, pulmonary edema, ejection fraction decreased or stress cardiomyopathy) occurred in 1.4% (n=11) of TAGRISSO treated patients (n=813); 0.2% (n=2) were fatal.

In Study 1 and Study 2, Left Ventricular Ejection Fraction (LVEF) decline >10% and a drop to <50% occurred in 2.4% (9/375) of patients who had baseline and at least one follow-up LVEF assessment.

Assess LVEF by echocardiogram or multigated acquisition (MUGA) scan before initiation of TAGRISSO and then at 3 month intervals while on treatment. Withhold treatment with TAGRISSO if ejection fraction decreases by 10% from pretreatment values and is less than 50%. For symptomatic congestive heart failure or persistent, asymptomatic LV dysfunction that does not resolve within 4 weeks, permanently discontinue TAGRISSO *[see Dosage and Administration (2.4) in full Prescribing Information]*.

Embryo-Fetal Toxicity

Based on data from animal studies and its mechanism of action, TAGRISSO can cause fetal harm when administered to a pregnant woman. In animal reproduction studies, osimertinib caused post-implantation fetal loss when administered during early development at a dose exposure 1.5 times the exposure at the recommended human dose. When males were treated prior to mating with untreated females, there was an increase in preimplantation embryonic loss at plasma exposures of approximately 0.5-times those observed in patients at the 80 mg dose level.

Advise pregnant women of the potential risk to a fetus.

Advise females of reproductive potential to use effective contraception during treatment with TAGRISSO and for 6 weeks after the final dose. Advise males with female partners of reproductive potential to use effective contraception for 4 months after the final dose *[see Use in Specific Populations (8.1), (8.3) and Clinical Pharmacology (12.3) in full Prescribing Information]*.

ADVERSE REACTIONS

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

Interstitial Lung Disease/Pneumonitis *[see Warnings and Precautions (5.1) in full Prescribing Information]*

QTc Interval Prolongation *[see Warnings and Precautions (5.2) in full Prescribing Information]*

Clinical Trials Experience

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

The data described below reflect exposure to TAGRISSO (80 mg daily) in 411 patients with EGFR T790M mutation-positive non-small cell lung cancer who received prior EGFR TKI therapy, in two single-arm studies, Study 1 and Study 2. Patients with a past medical history of ILD or radiation pneumonitis that required steroid treatment, serious arrhythmia or baseline QTc interval greater than 470 ms were excluded from Study 1 and Study 2. Baseline patient and disease characteristics were: median age 63 years, 13% of patients were ≥75 years old, female (68%), White (36%), Asian (60%), metastatic (96%), sites of brain metastases (39%), World Health Organization (WHO) performance status of 0 (37%) or 1 (63%), 1 prior line of therapy [EGFR-TKI treatment only, second line, chemotherapy-naïve (31%)], 2 or more prior lines of therapy (69%). Of the 411 patients, 333 patients were exposed to TAGRISSO for at least 6 months; 97 patients were exposed for at least 9 months; however, no patient was exposed to TAGRISSO for 12 months.

In Studies 1 and 2, the most common (>20%) adverse reactions (all grades) observed in TAGRISSO-treated patients were diarrhea (42%), rash (41%), dry skin (31%), and nail toxicity (25%). Dose reductions occurred in 4.4% of patients treated with TAGRISSO. The most frequent adverse reactions that led to dose reductions or interruptions were: electrocardiogram QTc prolonged (2.2%) and neutropenia (1.9%). Serious adverse reactions reported in 2% or more patients were pneumonia and pulmonary embolus. There were 4 patients (1%) treated with TAGRISSO who developed fatal adverse reactions of ILD/pneumonitis. Other fatal adverse reactions occurring in more than 1 patient included pneumonia (4 patients) and CVA/cerebral hemorrhage (2 patients). Discontinuation of therapy due to adverse reactions occurred in 5.6% of patients treated with TAGRISSO. The most frequent adverse reactions that led to discontinuation were ILD/pneumonitis and cerebrovascular accidents/infarctions.

Tables 2 and 3 summarize the common adverse reactions and laboratory abnormalities observed in TAGRISSO-treated patients.

Table 2 Adverse Reactions (>10% for all NCI CTCAE* Grades or >2% for Grades 3-4) in Study 1 and Study 2

Adverse Reaction	TAGRISSO N=411	
	All Grades	Grade 3-4[f]
	%	%
Gastrointestinal disorders		
Diarrhea	42	1.0
Nausea	17	0.5
Decreased appetite	16	0.7
Constipation	15	0.2
Stomatitis	12	0
Skin disorders		
Rash[a]	41	0.5
Dry skin[b]	31	0
Nail toxicity[c]	25	0
Pruritus	14	0
Eye Disorders[d]	18	0.2
Respiratory		
Cough	14	0.2
General		
Fatigue	14	0.5
Musculoskeletal		
Back pain	13	0.7
Central Nervous System		
Headache	10	0.2
Infections		
Pneumonia	4	2.2
Vascular events		
Venous thromboembolism[e]	7	2.4

* NCI CTCAE v4.0.
[a] Includes cases reported within the clustered terms for rash adverse events: Rash, rash generalized, rash erythematous, rash macular, rash maculo-papular, rash papular, rash pustular, erythema, folliculitis, acne, dermatitis and acneform dermatitis.
[b] Includes dry skin, eczema, skin fissures, xerosis.
[c] Includes nail disorders, nail bed disorders, nail bed inflammation, nail bed tenderness, nail discoloration, nail disorder, nail dystrophy, nail infection, nail ridging, onychoclasis, onycholysis, onychomadesis, paronychia.
[d] Includes dry eye, vision blurred, keratitis, cataract, eye irritation, blepharitis, eye pain, lacrimation increased, vitreous floaters. Other ocular toxicities occurred in <1% of patients.
[e] Includes deep vein thrombosis, jugular venous thrombosis, and pulmonary embolism.
[f] No grade 4 events have been reported.

Additional clinically significant adverse reactions occurring in 2% or more of patients treated with TAGRISSO included cerebrovascular accident (2.7%).

Table 3 Laboratory Abnormalities (≥20% for all NCI CTCAE Grades) in Study 1 and Study 2

Laboratory Abnormality	TAGRISSO N=411	
	Change from Baseline All Grades (%)	Change from Baseline to Grade 3 or Grade 4 (%)[a]
Clinical Chemistry		
Hyponatremia	26	3.4
Hypermagnesemia	20	0.7
Hematologic		
Lymphopenia	63	3.3
Thrombocytopenia	54	1.2[a]
Anemia	44	0.2
Neutropenia	33	3.4

[a] The only grade 4 laboratory abnormality was 1 patient with grade 4 thrombocytopenia.

DRUG INTERACTIONS

Effect of Other Drugs on Osimertinib

Strong CYP3A Inducers

Coadministering TAGRISSO with a strong CYP3A4 inducer decreased the exposure of osimertinib compared to administering TAGRISSO alone *[see Clinical Pharmacology (12.3) in full Prescribing Information]*. Decreased osimertinib exposure may lead to reduced efficacy.

Avoid coadministering TAGRISSO with strong CYP3A inducers (e.g., phenytoin, rifampin, carbamazepine, St. John's Wort) [note: effect of St. John's Wort varies widely and is preparation-dependent]. Increase the TAGRISSO dosage when coadministering with a strong CYP3A4 inducer if concurrent use is unavoidable *[see Dosage and Administration (2.4) in full Prescribing Information]*. No dose adjustments are required when TAGRISSO is used with moderate and/or weak CYP3A inducers.

Effect of Osimertinib on Other Drugs

Coadministering TAGRISSO with a BCRP substrate increased the exposure of the BCRP substrate compared to administering the BCRP substrate alone *[see Clinical Pharmacology (12.3) in full Prescribing Information]*. Increased BCRP substrate exposure may increase the risk of exposure-related toxicity.

Monitor for adverse reactions of the BCRP substrate (e.g., rosuvastatin, sulfasalazine, topotecan), unless otherwise instructed in its approved labeling, when coadministered with TAGRISSO.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

Based on data from animal studies and its mechanism of action, TAGRISSO can cause fetal harm when administered to a pregnant woman. There are no available data on TAGRISSO use in pregnant women. Administration of osimertinib to pregnant rats was associated with embryolethality and reduced fetal growth at plasma exposures 1.5 times the exposure at the recommended human dose *[see Data]*. Advise pregnant women of the potential risk to a fetus.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically-recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data

When administered to pregnant rats prior to embryonic implantation through the end of organogenesis (gestation days 2-20) at a dose of 20 mg/kg/day, which produced plasma exposures of approximately 1.5 times the clinical exposure, osimertinib caused post-implantation loss and early embryonic death. When administered to pregnant rats from implantation through the closure of the hard palate (gestation days 6 to 16) at doses of 1 mg/kg/day and above (0.1-times the AUC observed in patients at the recommended dose of 80 mg), an equivocal increase in the rate of fetal malformations and variations was observed in treated litters relative to those of concurrent controls. When administered to pregnant dams at doses of 30 mg/kg/day during organogenesis through lactation Day 6, osimertinib caused an increase in total litter loss and postnatal death. At a dose of 20 mg/kg/day, osimertinib administration during the same period resulted in increased postnatal death as well as a slight reduction in mean pup weight at birth that increased in magnitude between lactation days 4 and 6.

Lactation

Risk Summary

There are no data on the presence of osimertinib in human milk, the effects of osimertinib on the breastfed infant or on milk production. Administration to rats during gestation and early lactation was associated with adverse effects, including reduced growth rates and neonatal death *[see Use in Specific Populations (8.1) in full Prescribing Information]*. Because of the potential for serious adverse reactions in breastfed infants from osimertinib, advise a lactating woman not to breastfeed during treatment with TAGRISSO and for 2 weeks after the final dose.

Females and Males of Reproductive Potential

Contraception

Females

Advise females of reproductive potential to use effective contraception during treatment with TAGRISSO and for 6 weeks after the final dose *[see Use in Specific Populations (8.1) in full Prescribing Information]*.

Males

Advise male patients with female partners of reproductive potential to use effective contraception during and for 4 months following the final dose of TAGRISSO *[see Nonclinical Toxicology (13.1) in full Prescribing Information]*.

Infertility

Based on animal studies, TAGRISSO may impair fertility in females and males of reproductive potential. The effects on female fertility showed a trend toward reversibility. It is not known whether the effects on male fertility are reversible *[see Nonclinical Toxicology (13.1) in full Prescribing Information]*.

Pediatric Use

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

Geriatric Use

One hundred eighty-seven (45%) of the 411 patients in clinical trials of TAGRISSO were 65 years of age and older, and 54 patients (13%) were 75 years of age and older. No overall differences in effectiveness were observed based on age. Exploratory analysis suggests a higher incidence of Grade 3 and 4 adverse reactions (32% versus 25%) and more frequent dose modifications for adverse reactions (23% versus 17%) in patients 65 years or older as compared to those younger than 65 years.

Renal Impairment

No dose adjustment is recommended in patients with mild [creatinine clearance (CLcr) 60-89 mL/min, as estimated by the Cockcroft Gault method (C-G)] or moderate (CLcr 30-59 mL/min, as estimated by C-G) renal impairment. There is no recommended dose of TAGRISSO for patients with severe renal impairment (CLcr <30 mL/min) or end-stage renal disease *[see Clinical Pharmacology (12.3) in full Prescribing Information]*.

Hepatic Impairment

No dose adjustment is recommended in patients with mild hepatic impairment [total bilirubin less than or equal to upper limit of normal (ULN) and AST greater than ULN or total bilirubin between 1.0 to 1.5 times ULN and any AST]. There is no recommended dose for TAGRISSO for patients with moderate or severe hepatic impairment *[see Clinical Pharmacology (12.3) in full Prescribing Information]*.

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FROM THE EDITOR

Improving the Care Experience—It's Complicated

BY CHRISTIAN DOWNS, JD, MHA

As another edition of *Oncology Issues* rolls off the presses, I am struck by how the feature articles in this issue reflect the nuances of what "improving the care experience" means for our patients and their families, our cancer program staff members, and the wider oncology community.

For patients, improving the care experience must include addressing the emotional burdens that accompany cancer, author Marlena Ryba asserts in "A Cognitive Approach to Cancer Treatment." Her article describes research on cognitive behavioral therapy interventions that have helped patients with the psychological impact of living with cancer and reaffirms the important role such interventions can play in patient-centered care, supporting patients in developing the tools and the confidence to regain control of their lives—whether or not treatment is able to control their disease.

In "Normalizing Feelings of Grief & Loss in Oncology Nurses" authors Jennifer Collins and Sandra Tan explore how Sarah Cannon Cancer Institute at Johnston-Willis Hospital is addressing the emotional and spiritual impact of patient death through the bi-annual Service of Remembrance that offers both nursing staff and families the opportunity to reconnect and honor the lives of cancer patients. Further, to help oncology nurses "step out of their caregiver role," this ACCC member program developed a Reflection Service, exclusively to support oncology nurses.

From Stony Brook Cancer Center, Linda Bily describes "An Evening of Memories," a low-cost program that brings staff and families together to celebrate those who have passed, cementing the bond between staff and families and helping to create closure for all involved.

Another perspective in improving the care experience is shared by the team at St. Joseph Hospital–The Center for Cancer Prevention and Treatment in "A Model for Tissue Banking in the Community Setting." The authors show how this community biospecimen repository program has informed and engaged patients and providers on the importance of donating specimens to support internal and external research projects.

Finally, we can all agree that addressing "financial toxicity" is essential to improving the care experience. The economic burden of cancer continues to be a pressing issue for patients, providers, and policy makers. The financial devastation accumulates from many sources, including patient out-of-pocket costs, unreimbursed expenses to providers, and stress on payers, such as Medicare and Medicaid. These problems are particularly acute for the many ACCC member programs that treat uninsured and underinsured patient populations. To proactively address this unwanted side effect of cancer, early intervention, care coordination, and proper planning are critical. In this issue, we share practical, actionable takeaways from the ACCC Financial Advocacy Network (FAN) Learning Labs.

For more practical, replicable strategies for improving the care experience, join us at the ACCC 34th National Oncology Conference, Oct. 18-20, in Nashville, Tenn. From sessions on improving the patient experience from chemotherapy to registration to a psycho-oncology program that saw a 256% increase in referrals for crisis intervention and counseling, the conference agenda brings together the knowledge, experience, and innovations of your peers. I hope you'll join ACCC member programs from across the country to network and expand your perspective. OI

Future Ready

BY MARK S. SOBERMAN, MD, MBA, FACS

As a cancer center director and physician executive, one of my passions is patient-centered multidisciplinary care. One of the great privileges of serving as President of the Association of Community Cancer Centers is choosing a president's theme for my term in office. It is no surprise then, that the theme I have chosen is "Envisioning Next Gen Multidisciplinary Cancer Care." I think we can all agree that—whatever the shape, size, and composition of cancer care in the future—it must be patient-centered. In June at the 2017 ACCC Institute for the Future of Oncology forum, a multidisciplinary group, including ACCC-member physicians, nurses, administrators, social workers, financial advocates, pharmacists, and quality officers, as well as representatives from patient advocacy groups, engaged in a spirited discussion about what next generation cancer care might look like and who will be on the team. We were fortunate to have Kavita Patel, MD, MPH, of the Brookings Institution as facilitator.

The first topic of discussion was the care coordination imperative. To move from care organized around providers to care organized around the patient, various models, including navigation, in-person and virtual multidisciplinary clinics, tumor boards, telehealth, and better integration of primary care physicians were considered and discussed. Breaking down barriers to collaboration and specialty silos were felt to be of the utmost importance. Looking to the future, organizing the care team around the patient and his or her medical condition will not only improve patient-centeredness of care, but better facilitate the ability to improve outcomes and control the cost of care.

Discussion topic two focused on how next gen cancer care will reconcile personalized medicine with the drive to value-based healthcare. The conversation around the definition of personalized medicine was especially revealing. Prior to this discussion, I usually thought of "personalized medicine" as the need to integrate targeted therapies and immunotherapies based upon the patient's very specific tumor biology. However, many of the institute participants framed the conversation around understanding the patient's priorities and goals of treatment and designing a subsequent plan of care around those wishes and desires. Shared decision-making surfaced as a key concept in the delivery of true patient-centered care. Of course, both definitions are true and valid. And while I had always viewed these issues as separate, this year's institute discussion brought home the fact that they are not.

The final topic under consideration was the projected workforce shortages that are expected to coincide with increasing patient volumes. Some of the strategies discussed included the development of so-called "oncogeneralists," further integration of primary care physicians into the plan of care, leveraging technologies such as IBM Watson and/or telehealth, increased integration of advanced practice providers (APPs), and an increasing role for primary care and advanced practitioners in survivorship care.

All three discussion topics provided glimpses of not only what next generation cancer care may look like, but also who will be joining the team in this era of rapidly evolving cancer care. Palliative medicine, integrative oncology, pharmacy, geneticists, research nurses, financial navigators, primary care physicians, and others were all identified as needed collaborators in delivery of patient-centered care both for today and tomorrow.

Further, I'm pleased to report that this is a conversation that will be ongoing. At the end of the Institute, there was agreement that ACCC should and will provide a platform for continued discussion and refinement of these important concepts. In a value-based system of healthcare, multidisciplinary teams centered on the patient and his or her medical condition are essential to the delivery of high-quality personalized care at the most reasonable cost. OI

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- Developing a Nurse Practitioner Productivity Measurement Tool
- Life with Cancer: A Comprehensive, Holistic, Patient-Centered Approach to Cancer Management
- Aligning Cancer Center Community Needs with Network Community Needs Assessment
- A Peer Review Process Improves Quality in RT Planning

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VIDEO

ACCC Addresses Potential Impact of MedPAC Part B Proposals

In an interview with the *American Journal of Managed Care*, Leah Ralph, ACCC Director of Health Policy, discusses the impact of some of MedPAC's recent proposals on cancer patients' access to treatment, particularly those living in smaller rural communities. ajmc.com/conferences/coa-2017/leah-ralph-accc-concerned-about-potential-impact-of-medpac-proposals.

Desperately Seeking Oncology Nurses?

BLOGS

Read how 2017 ACCC Innovator Award winner Loma Linda University Cancer Center thought outside of the box to address a staffing shortage of chemotherapy skilled and oncology experienced nurses. accc-cancer.org/ACCCbuzz/desperately-seeking-oncology-nurses.

WEBINAR

Real-World Considerations When Implementing a Genomic Tumor Board Program

It requires a coordinated effort across clinical and administrative teams to successfully implement a genomic tumor board program. Gain strategies to engage clinicians, maximize meaningful participation, and lead to improved patient care. accc-cancer.org/webinars.

VIDEO

Wheels Up—Bringing Lung Cancer Education & Screening to Rural Patients

Learn how 2017 ACCC Innovator Award winner Levine Cancer Institute's mobile lung CT unit integrates technology, nurse navigation, and brick-and-mortar medical facilities and staff to serve patients in the rural Carolinas. youtube.com/watch?v=8MIdCki2cHs. Attend the 2017 ACCC National Oncology Conference, Oct. 18-20, Nashville, Tenn., to tour this one-of-a-kind mobile unit.

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fast

5 Key Findings from Report on the Costs of Cancer

1. Access to quality health insurance is essential to making cancer care affordable for patients and survivors.
2. A lower-premium insurance plan may not actually save cancer patients money; these plans often have high-cost sharing and cancer patients are high utilizers of care.
3. Even with insurance, cancer patients often face unpredictable or unmanageable costs including high co-insurance, high deductibles, having to seek out-of-network care, and needing a treatment that is not covered by their plan.
4. Newly-diagnosed cancer patients often experience their highest out-of-pocket costs in the first one to two months following a positive screening or diagnosis until they meet their applicable deductible and out-of-pocket maximums.
5. The need to pass policies that prevent cancer and its costs to patients and society by reducing tobacco use and exposure to secondhand smoke, promoting healthy eating and active living, and protecting Americans from increased skin cancer risk.

Source. ACS Cancer Action Network. The Costs of Cancer Addressing Patient Costs. acscan.org/sites/default/files/Costs%20of%20Cancer%20-%20Final%20Web.pdf.

More than 1/4 of Medicare beneficiaries—15 million people—spend at least 20% of their income on premiums and out-of-pocket expenses.

Source. The Commonwealth Fund. Medicare Beneficiaries' High Out-of-Pocket Costs: Cost Burdens by Income and Health Status. commonwealthfund.org/Publications/Issue-Briefs/2017/May/Medicare-Out-of-Pocket-Cost-Burdens.

facts

Protect the Skin You're In!

- **80%** of lifetime UV exposure occurs before a child turns **18**.
- **1 in 5** Americans will develop skin cancer in the course of a lifetime.
- Just **5** severe sunburns double your chances of developing skin cancer.
- Over the past **3** decades, more people have had skin cancer than all other cancers combined.
- More people develop skin cancer because of **tanning** than develop lung cancer because of **smoking**.
- About **90%** of non-melanoma skin cancers are associated with exposure to UV radiation from the sun.
- One person dies of melanoma every **54** minutes.

Source. prnewswire.com/news-releases/more-people-develop-skin-cancer-from-tanning-than-develop-lung-cancer-from-smoking-300461218.html.

Addressing Healthcare Disparities in Sexual & Gender Minority Populations

ASCO calls for a coordinated effort to address health disparities among SGM populations, including:

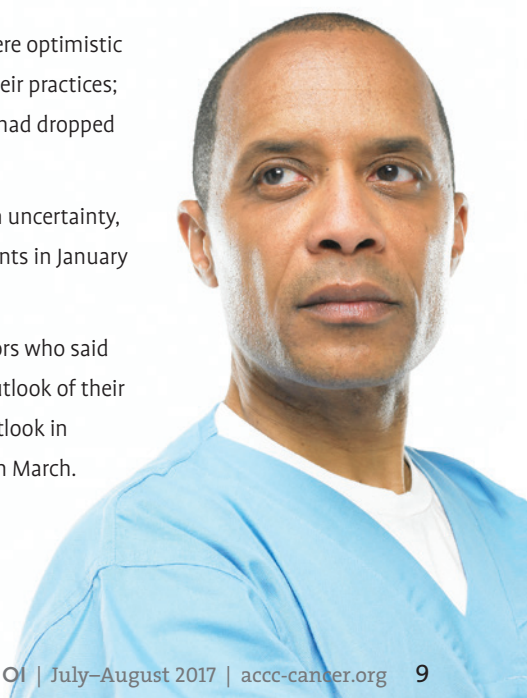
- Increased patient access to culturally competent support services.
- Expanded cancer prevention education for SGM individuals.
- Robust policies prohibiting discrimination.
- Adequate insurance coverage to meet the needs of SGM individuals affected by cancer.
- Inclusion of SGM status as a required data element in cancer registries and clinical trials.
- Increased focus on SGM populations in cancer research.

Source. Griggs J, et al. ASCO position statement: strategies for reducing cancer health disparities among sexual and gender minority populations. *J Clin Oncol*. 2017 Apr 3. doi: 10.1200/JCO.2016.72.0441 [Epub ahead of print].

MGMA Survey Finds Docs Less Optimistic about the Financial Prospects of Their Practices Under Trump Administration

- In January 2017, **45%** of doctors were optimistic about the business prospects of their practices; by the end of March, that number had dropped to **31%**.
- There was also a significant shift in uncertainty, which rose from **34%** of respondents in January to **44%** in March.
- The shift was smaller among doctors who said they were pessimistic about the outlook of their practices—**22%** had a negative outlook in January, which increased to **25%** in March.

Source: Wilkerson J. Doctors' optimism turns to uncertainty following Trump's inauguration. *Inside Health Policy*; April 5, 2017.



Supporting Patients Through Their Journey on Jakafi® (ruxolitinib)

IncyteCARES (**C**onnecting to **A**ccess, **R**eimbursement, **E**ducation and **S**upport) provides a single point of contact through a registered nurse, OCN®, to assist eligible patients and healthcare providers in obtaining access to Jakafi® (ruxolitinib) and to connect them with continuing support and resources. The program offers:

REIMBURSEMENT SUPPORT

- Insurance benefit verification
- Information about prior authorizations
- Guidance with appealing insurance denials or coverage restrictions

ACCESS ASSISTANCE

- Copay/Coinsurance assistance
- Free medication program
- Temporary access for insurance coverage delays
- Referrals to independent nonprofit organizations and foundations

EDUCATION & SUPPORT

- Access to a registered nurse, OCN®
- Educational information for your patients about their condition and Jakafi
- Patient Welcome Kit

CONNECTION TO SUPPORT SERVICES

- Referrals for transportation assistance
- Access to patient advocacy organizations for counseling and emotional support resources

Connect with IncyteCARES

For full program terms and eligibility,
visit IncyteCARES.com or call 1-855-4-Jakafi (1-855-452-5234).

IncyteCARES Connecting to Access, Reimbursement, Education and Support | Jakafi® ruxolitinib (tablets)

It's Not *All* About the ACA

BY LEAH RALPH

Summer headlines have been dominated by congressional efforts to repeal and replace portions of the Affordable Care Act (ACA) and find a politically palatable path forward to shoring up the nongroup insurance market. ACCC has strongly advocated against both the House-passed American Health Care Act (AHCA) and the current Senate proposal, the Better Care Reconciliation Act (BCRA) and advocated for health reform principles for cancer patients that include preserving access to comprehensive, affordable insurance coverage and critical protections that patients with pre-existing conditions such as cancer gained under the ACA. (At the time of writing, Congress is still wrestling with legislation that could meet these goals.)

However as stakeholders remain distracted by the politics and policy of health reform, efforts to make changes to the Medicare Part B program are flying under the radar. Reimbursement for Part B drugs remains a focus for policymakers, and patient and provider groups will need to remain vigilant in educating decision makers about the value of this program, particularly for cancer patients to continue to access life-saving treatments in their communities.

In June, the Medicare Payment Advisory Commission (MedPAC), an independent congressional agency that advises Congress on issues affecting the Medicare program, produced a series of recommendations on the Part B program that included making reductions to average sales price (ASP) reimbursement and creation of a voluntary Drug Value Program (DVP), a version of the competitive drug acquisition program CMS implemented in 2006. Specifically, in addition to imposing a number of requirements on manufacturers to hold down ASP growth, MedPAC recommends reducing wholesale acquisition cost (WAC)-based payment to WAC plus 3%, requiring HHS to use a common billing code to pay for a reference biologic and its biosimilars, and reducing the ASP add-on in tandem with the implementation of a new voluntary alternative market-based program that would allow providers to use private vendors to negotiate drug prices with manufacturers in the Medicare program. Importantly, MedPAC recommendations are just that—recommendations—but Congress often looks to these reports when it needs policy ideas or budget savings to pay for other legislative efforts.

The Administration has been less direct—and predictable—about their agenda on drug pricing reform. President Trump recently circulated a draft executive order around drug pricing, which includes policies that look very different from earlier campaign trail talking points. An early draft suggests the order would largely reduce regulatory burden for the pharmaceutical industry, as well as address topics such as pharmacy benefit managers (PBMs), value-based pricing, and narrowing the 340B program. The President's 2018 budget also directs HHS to work with Congress to develop a legislative proposal to improve the 340B program's "integrity and ensure that the benefits...are used to benefit [low-income] patients," and we expect to see legislative efforts from Congress this fall that will propose to tighten the 340B patient definition and redefine covered entity eligibility and requirements.

Last year ACCC joined hundreds of patient and provider groups to defeat the Obama Administration's misguided proposal to experiment with Part B payment rates across the country, otherwise known as the proposed Medicare Part B Drug Payment Model. We used real-world, de-identified data to show that most cancer programs, particularly smaller practices or practices in rural areas, would be devastated by the randomized cut being proposed and patient care would suffer—that such significant changes to payment structures could necessitate altering treatment plans that are currently working well for patients, creating unnecessary and potentially damaging gaps in care.

Through the noise of hyper-partisanship and on-going tensions surrounding ACA repeal, ACCC will continue that advocacy work this year, educating policymakers on the need for a collaborative, stakeholder-driven conversation about drug pricing and meaningful policy options for bringing down drug costs. In June, we joined over 250 organizations in sending a letter to Secretary Price opposing the recent MedPAC recommendations and reminding policymakers about the important role Medicare Part B plays in maintaining patient access to critical cancer therapies and services in your patients' communities. OI

Leah Ralph is ACCC Director of Health Policy.

Appropriate Imaging Through Decision Support

BY CINDY PARMAN, CPC, CPC-H, RCC

It is an act of Congress, specifically section 218 of the Protecting Access to Medicare Act (PAMA) of 2014, which requires all physicians ordering advanced imaging studies to consult government-approved, evidence-based appropriate use criteria through a clinical decision support system. The goal of these tools is to improve the accuracy of ordering advanced diagnostic imaging and ensure that appropriate studies are performed for the right reasons on the right patients.

Physicians furnishing advanced diagnostic imaging services will only be paid if the claims submitted for reimbursement confirm that this appropriate use criteria (AUC) was consulted, which clinical decision support mechanism (CDSM) was used, and whether the study ordered adhered (or not) to the final recommendation. It's important to note that, as of now, the ordering physician can override the recommendation and order the study anyway. Regardless, the AUC guidelines must be consulted, and there may come a time when ordering-physician compliance with these guidelines is mandatory.

Appropriate Use Criteria

AUC are defined as measures developed or endorsed by national professional medical specialty societies, or other provider-led entities, to assist ordering professionals in making the most appropriate treatment decision for a specific clinical condition for an individual patient. Appropriate use criteria are a collection or library of information presented to the physician in a manner that links a specific clinical condition or symptom with an assessment of the appropriateness of advanced diagnostic imaging services. These criteria would be developed or endorsed by provider-led entities, such as national professional medical specialty societies and organizations that primarily include providers who are actively engaged in the practice and delivery of healthcare.

According to the Centers for Medicare & Medicaid Services (CMS) in the November 16, 2015 Federal Register, (2016 Final Rule, Medicare Physician Fee Schedule):

> *Experience and published studies alike show that results are best when AUC are built on an evidence base that considers patient health outcomes, weighing the benefits and harms of alternative care options, and are integrated into broader care management and continuous quality improvement (QI) programs.*
>
> *There is also consensus that AUC programs built on evidence-based medicine and applied in a QI context are the best method to identify appropriate care and eliminate inappropriate care, and are preferable to across-the-board payment reductions that do not differentiate interventions that add value from those that cause harm or add no value.*

AUC are intended to be integrated into the clinical workflow and facilitate evidence-based care delivery. In addition, the ideal AUC is an evidence-based guide that starts with a patient's specific clinical condition or presentation (e.g., symptoms, provisional diagnosis, final diagnosis) and assists providers in the overall patient workup, treatment, and follow-up.

As reported by CMS in the Medicare Physician Fee Schedule Final Rule 2016:[1] "The end goal of using AUC is to improve patient health outcomes." In addition, this program is applicable to services billed under the Medicare Physician Fee Schedule (PFS), the Hospital Outpatient Prospective Payment System (OPPS), and the Ambulatory Surgical Center payment system.

Table 1, right, offers a summary of AUC program requirements.

Qualified Provider-Led Entity

A qualified provider-led entity (qPLE) is an organization of providers or practitioners who, either within the organization or outside of the organization, predominantly provide direct patient care. CMS will establish its program based on AUC that have been developed, modified, and/or endorsed by provider-led entities. Rather than reviewing each criterion for each imaging study proposed by the qPLEs, CMS will have a qualification and review process for the provider-led entities themselves. To become a qPLE, an organization must meet the following requirements:

- Have an established evidence-review process, using a formal, published, and widely recognized methodology for grading evidence.
- Grade the AUC in terms of strength of evidence.
- Be led by a multidisciplinary team with "autonomous governance" and have strict adherence to a policy on the disclosure of potential conflict of interest.

Table 1. Summary of AUC Program Requirements

Ordering professionals must consult AUC criteria for advanced outpatient imaging (CT, MR, NM, PET) orders.	Ordering professionals must access AUCs through a qualified clinical decision support mechanism.	Only AUC from qualified provider-led entities will be used.	Ordering professionals identified as outliers must obtain preauthorization as soon as Jan. 1, 2020.

Acronym Legend

TERM	DEFINITION
AUC	Appropriate Use Criteria (AUC) are guidelines created or endorsed by qPLEs (see below) intended for use in decision support interactions. These guidelines form the backbone of knowledge that informs every decision support interaction. AUC are defined as criteria that are evidence-based (to the extent feasible) and assist professionals who order and furnish applicable imaging services to make the most appropriate treatment decisions for a specific clinical condition. Essentially, AUC link a specific clinical condition or symptom with an assessment of the appropriateness of advanced diagnostic imaging services.
CDSM	Clinical Decision Support Mechanisms (CDSMs) are the electronic portals through which clinicians would access the AUC during the patient workup. With a fully-embedded CDSM platform, practitioners interact directly with the CDSM through their primary user interface, minimizing interruption to the clinical workflow.
DSN	Every CDSM consultation must record the physician's NPI (national provider identifier) and then assign a unique Decision Support Number (DSN). The DSN serves as the "unique consultation identifier" and provides a reference to details of the CDSM consultation, including adherence and applicability of the selected service with the AUC. It contains all required data elements for a claim. CMS will define how the DSN will be used in the claims process in future rulemaking.
FP	A Furnishing Provider (FP) is the organization or health system that furnishes and bills Medicare for the ordered service provided to the beneficiary.
OP	An Ordering Provider (OP) is the individual who orders an item or service (e.g., imaging services) that will be furnished and billed by another provider or supplier (e.g., laboratory, imaging center).
PAMA	The Protecting Access to Medicare Act (PAMA) of 2014 mandates that starting Jan. 1, 2017, physicians ordering advanced diagnostic imaging exams must consult qualified, evidence-based appropriate use criteria, namely through a Clinical Decision Support Mechanism. CMS unilaterally changed the start date to Jan. 1, 2018 since a 2017 startup was not practicable.
PCA	CMS has defined eight Priority Clinical Areas (PCAs) that will be used as a tool to measure outlier ordering professionals. The PCAs represent a baseline for AUC coverage and will expand annually. In addition, there is still a requirement to document the medical necessity for each advanced imaging service ordered. The final list of PCAs includes coronary artery disease (suspected or diagnosed), suspected pulmonary embolism, headache (traumatic and non-traumatic), hip pain, low back pain, shoulder pain (to include suspected rotator cuff injury), cancer of the lung (primary or metastatic, suspected or diagnosed), and cervical or neck pain.
qPLE	A qualified Provider-Led Entity (qPLE) is responsible for the creation of sets of AUC for use in CDSM interactions. Each organization approved to create or endorse AUC follows strict guidelines and rules for criteria authoring. CMS defines a qPLE as a "national professional medical specialty society or other organization that is comprised primarily of providers or practitioners who, either within the organization or outside of the organization, predominantly provide direct patient care."

- Demonstrate transparency of the process for developing the criteria, the grading approach for the criteria, and the pipeline of criteria under consideration.

CMS adds that the agency would expect the literature review to include evidence on analytical validity, clinical validity, and clinical utility of the specified imaging study.

Provider-led entities would be required to apply and, if approved, would receive a qualification for a six-year period. Applications must include a statement regarding how the entity meets the definition of a qPLE, and once accepted, qPLEs must re-apply every five years. According to CMS, qPLEs may endorse the AUC set or individual criteria of other qualified provider-led entities, which means that qPLEs can combine their AUC to create a larger, more clinically encompassing library.

CMS acknowledges that conflicting AUC may be a concern, but generally believes that qPLEs will be using an evidence-based AUC development process that will reduce the likelihood and frequency of conflicting AUC. As a result, there may be some situations where CMS and MEDCAC (the Medicare Evidence Development & Coverage Advisory Committee) will have to review the evidence base. CMS states in the November 16, 2015, Federal Register that MEDCAC has extensive experience in reviewing, interpreting, and translating evidence.

The most recent list of qualified provider-led entities, dated June 2016, includes:[2]

- American College of Cardiology Foundation
- American College of Radiology
- Brigham and Women's Physicians Organization
- Center for Diagnostic Imaging (CDI) Quality Institute
- Intermountain Healthcare
- Massachusetts General Hospital, Department of Radiology
- National Comprehensive Cancer Network (NCCN)
- Society for Nuclear Medicine and Molecular Imaging
- University of California Medical Campuses
- University of Washington Physicians
- Weill Cornell Medicine Physicians Organization

CMS will release a list of newly approved qPLEs by June 30 of every year, so the number of qPLEs will grow over time.

Clinical Decision Support Mechanisms

A clinical decision support mechanism (CDSM) is defined as an interactive electronic tool for use by clinicians that communicates AUC information to users and assists them in making the most appropriate treatment decision for a patient's specific clinical condition. In the 2017 Medicare PFS Final Rule, CMS states that specialists may seek to align themselves with a qualified CDSM that contains AUC more exhaustive in one area of medicine to reflect the imaging services that they order most often.

Clinical decision support has two distinct parts: the appropriate use criteria (clinical guidelines) and an electronic platform that makes the guidelines accessible (an information technology tool). A CDSM may be fully integrated with, or be part of, a provider's certified EHR (electronic health record) system, partially integrated, or a stand-alone system entirely outside of the provider's existing EHR.[3] According to CMS, in the November 15, 2016 Federal Register:

> *"Ideally, CDSMs would be integrated within or seamlessly interoperable with existing health IT systems and would automatically receive patient data from the EHR or through an API* [application programming interface] *or other connection. Such integration would minimize burden on practitioners and avoid duplicate documentation."*

The requirements for a clinical decision support mechanism include the ability to make available specified AUC and the supporting documentation, while complying with privacy and security standards. This means that the CDSM must identify the AUC source consulted if multiple sources (e.g., AUC from more than one qPLE) are available for a specific clinical scenario. In addition, each CDSM will communicate the appropriateness rating to the physician ordering the diagnostic imaging study. This communication will vary, based on the program, but may include a scale of numeric ratings, indicator lights (e.g., green, yellow, red), or a yes-or-no response.

Each time the CDSM is consulted or queried, the mechanism will provide the provider ID (NPI number), adherence to AUC, and applicable AUC availability, and assign a unique consultation ID number. In addition, the CDSM must provide aggregate feedback to ordering professionals in an electronic record format on at least an annual basis, and notify ordering professionals who have been assigned outlier status. Last, the CDSM will store data electronically for a minimum of six years. According to CMS, six years is an appropriate amount of time across which ordering professionals will want to assess their ordering patterns.

Ordering providers will access the CDSM and issue an imaging order that complies with the AUC. The furnishing provider (e.g., the radiologist, imaging center, or radiology department) will submit documentation with the claim that identifies the CDSM mechanism consulted by the ordering physician, verifies adherence to the AUC, nonadherence to the AUC or whether no criteria in the CDSM were applicable to the patient's scenario, and include the NPI of the ordering professional. CMS is considering the mechanisms for appending the AUC consultation information to various types of Medicare claims (e.g., CMS1500 professional or UB04 hospital claim submissions) and expects to develop requirements for reporting such information in the calendar year 2018 PFS rulemaking process.

The noncompliance penalty for the ordering physician includes the possibility of being classified as an outlier and subsequently required to obtain preauthorization for advanced imaging studies for Medicare patients. In addition, a consequence of noncompliance for the furnishing provider includes claim denials and lack of reimbursement (this applies to both the professional and technical components of the advanced diagnostic imaging studies).

When AUC are updated or modified, CDSMs must make the updated AUC available within 12 months, have protocols in place to remove AUC determined to be potentially dangerous, and make available within 12 months AUC for new priority clinical treatment areas. The current approval timeline for clinical decision support mechanisms is:

- April 2014: PAMA signed into law, requiring provider use of AUC via CDSM for advanced imaging.
- Nov. 2, 2016: The Medicare PFS Final Rule for CY 2017 was released and established the eight clinical priority areas and clinical decision support mechanism requirements and approval process.
- March 1, 2017: Application deadline for the first round of qualified CDSMs.
- June 30, 2017: CMS is scheduled to release the first list of CDSMs.
- Jan. 1, 2018: Ordering professionals begin using CDSMs/AUC and application deadline for the second round of qualified CDSMs.
- Jan. 1, 2022: Application deadline for the first round of qualified CDSM 5-year renewals.

Outliers

Under the law, CMS must identify outlier ordering professionals, defined as professionals with low adherence to the applicable AUC, and implement prior authorization programs. While the penalties for low adherence will not be employed immediately, Section 414.94(e)(5) establishes the following priority clinical areas that will be used to determine ordering professional outliers:

- Coronary artery disease (suspected or diagnosed)
- Suspected pulmonary embolism
- Headache (traumatic and non-traumatic)
- Hip pain
- Low back pain
- Shoulder pain (to include suspected rotator cuff injury)
- Cancer of the lung (primary or metastatic, suspected, or diagnosed)
- Cervical or neck pain.

A priority clinical area (PCA) is defined as clinical topics, clinical topics and imaging modalities, or imaging modalities identified by CMS through annual rulemaking and in consultation with stakeholders that may be used in the determination of outlier ordering professionals.

This initial list of priority clinical areas was selected based on diagnostic groups with the highest associated advanced imaging volumes. In addition, a table was made available that provided stakeholders with diagnosis codes that were used to describe the proposed priority clinical areas.[4] All advanced diagnostic imaging requires the use of a clinical decision support mechanism and approved use criteria, but only consistently overriding services in priority clinical areas will result in the need to conform to a preauthorization requirement. Last, CMS plans to increase the number and scope of priority clinical areas annually.

Exceptions

Section 1834(q)(4)(C) of the Act provides for certain exceptions to the AUC consultation and reporting requirements. First, the statute provides for an exception when an applicable imaging service is ordered for an individual with an emergency medical condition. CMS believes that this exception is warranted because there can be situations in which a delay in action would jeopardize the health or safety of patients. To meet this exception, the clinician only needs to determine that the medical condition manifests itself by acute symptoms of sufficient severity such that the absence of immediate medical attention could reasonably be expected to result in placing the patient's health in serious jeopardy, serious impairment of bodily functions, or serious dysfunction of any bodily organ or part.

In addition, applicable imaging services ordered for an inpatient and for which payment is made under Medicare Part A are exempt from the requirement to consult AUC. CMS notes that if payment is made under Medicare Part A, the service is not paid under an applicable payment system.

Last, applicable imaging services ordered by an ordering professional for whom consultation with an AUC would result in significant hardship (as determined on a case-by-case basis) are exempt. For example, a hardship may include an ordering professional practicing in a rural area without sufficient Internet access, extreme and uncontrollable circumstances that prevent the healthcare professional from becoming a meaningful EHR user, practicing for less than two years, a primary specialty of anesthesiology, radiology, or pathology that qualifies for a hardship exemption, or practicing at multiple locations with the inability to control the availability of Certified EHR Technology (CEHRT).

Choosing Wisely®

While not guidelines or requirements, there are currently recommendations for advanced imaging relating to cancer care on the Choosing Wisely website (choosingwisely.org), including:

American College of Preventive Medicine

- Don't use whole body scans for early tumor detection in asymptomatic patients.

American Society of Clinical Oncology

- Don't perform PET, CT, and radionuclide bone scans in the staging of early breast cancer at low risk for metastasis.

- Don't perform surveillance testing (biomarkers) or imaging (PET, CT, and radionuclide bone scans) for asymptomatic individuals who have been treated for breast cancer with curative intent.
- Don't perform PET, CT, and radionuclide bone scans in the staging of early prostate cancer at low risk for metastasis.
- Avoid using PET or PET/CT scanning as part of routine follow-up care to monitor for a cancer recurrence in asymptomatic patients who have finished initial treatment to eliminate the cancer unless there is high-level evidence that such imaging will change the outcome.

American Society of Hematology

- Limit surveillance CT scans in asymptomatic patients following curative-intent treatment for aggressive lymphoma.
- Don't perform baseline or routine surveillance CT scans in patients with asymptomatic, early-stage chronic lymphocytic leukemia.

American Urological Association

- Don't obtain CT scan of the pelvis for asymptomatic men with low-risk clinically localized prostate cancer.

Society of Gynecologic Oncology

- Avoid routine imaging for cancer surveillance in women with gynecologic cancer, specifically ovarian, endometrial, cervical, vulvar, and vaginal cancer.

Society of Nuclear Medicine and Molecular Imaging

- Don't use PET/CT for cancer screening in healthy individuals.

Society of Surgical Oncology

- Don't perform routine PET/CT in the initial staging of localized colon or rectal cancer or as part of routine surveillance for patients who have been curatively treated for colon or rectal cancer.
- Don't routinely order imaging studies for staging purposes on patients newly diagnosed with localized primary cutaneous melanoma unless there is suspicion for metastatic disease based on history and physical exam.

The Society of Thoracic Surgeons

- Patients with suspected or biopsy-proven stage I NSCLC do not require brain imaging prior to definitive care in the absence of neurological symptoms.

Additional details on these recommendations are available on the Choosing Wisely website (choosingwisely.org).

Future Considerations

The mandate specifies that providers must consult a qualified CDSM for every Medicare diagnostic advanced imaging service (CT, MR, NM, PET) ordered. And, each claim must contain evidence of the CDSM consultation to be payable. According to a 2014 AIM Specialty Health presentation, "All things being equal, the imaging utilization of unmanaged Medicare population was 8.5% higher than managed."[5] This study highlighted that oncology specialties were responsible for 12 percent of total advanced imaging utilization.

CMS clarified in the 2017 Medicare PFS Final Rule that the delay in implementation until Jan. 1, 2018, provides ordering practitioners time to research and align themselves with a qualified CDSM. As a result, oncologists should be prepared to begin reporting data once CMS announces the claim submission details as part of the 2018 PFS Final Rule.

PAMA also introduced the controversial concept of prior authorization into Medicare. While initially limited to the small group of physicians who are image-ordering outliers, this sets a precedent for expanded application to a wider group of high-utilizers in the future.

For providers, implementing this initiative will be considerably more involved than just contacting the IT department to install a new program. Buy-in and commitment from ordering physicians, including medical, radiation, and surgical oncologists, will be critical to the successful implementation of appropriate use criteria. According to radiology specialty societies, referring physicians must be educated on the importance of using these tools and recognize that this will require both time and commitment.

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

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tools

Approved Drugs

• The U.S. Food and Drug Administration (FDA) granted accelerated approval to **Alunbrig™ tablets (brigatinib)** (Takeda Pharmaceutical Company Ltd., through its wholly owned subsidiary ARIAD Pharmaceuticals, Inc., takedaoncology.com) for the treatment of patients with metastatic anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC) who have progressed on or are intolerant to crizotinib.

• The FDA granted accelerated approval to **Bavencio® (avelumab)** (EMD Serono, Inc., emdserono.com) for patients with locally advanced or metastatic urothelial carcinoma whose disease progressed during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.

• The FDA granted accelerated approval to **Imfinzi™ (durvalumab)** (AstraZeneca, astrazeneca.com) for the treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or who have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

• Merck (merck.com) announced that the FDA has approved **Keytruda® (pembrolizumab)** in combination with pemetrexed (brand name Alimta®) and carboplatin (pem/carbo), a commonly used chemotherapy regimen, for the first-line treatment of metastatic nonsquamous NSCLC, irrespective of PD-L1 expression. The FDA also granted regular approval to Keytruda for patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

Keytruda was also granted accelerated approval by the FDA for adult and pediatric patients with unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options or with MSI-H or dMMR colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

• Novartis (novartis.com) announced that the FDA has approved the **Kisqali® Femara® Co-Pack (ribociclib tablets; letrozole tablets)** for the treatment of hormone receptor-positive, human epidermal growth factor receptor-2 negative (HR+/HER2-) advanced or metastatic breast cancer in postmenopausal women.

• The FDA approved **Rydapt® midostaurin** (Novartis Pharmaceuticals Corp., novartis.com) for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) who are FLT3 mutation-positive (FLT3+), as detected by an FDA-approved test, in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation. Rydapt is also approved to treat adults with advanced systemic mastocytosis, which includes aggressive systemic mastocytosis, systemic mastocytosis with associated hematological neoplasm, and mast cell leukemia.

• The FDA granted regular approval to **Zykadia® (ceritinib)** (Novartis Pharmaceuticals Corp., novartis.com) for patients with metastatic NSCLC whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test.

Genetic Tests and Assays in the News

• Roche (roche.com) announced FDA approval of the **Ventana ALK (D5F3) CDx Assay** as a companion diagnostic to identify ALK-positive NSCLC patients eligible for treatment with the Novartis drug Zykadia (ceritinib). The Ventana ALK (D5F3) Assay is the only immunohistochemistry test approved by the FDA as a companion diagnostic for Zykadia.

• Roche (roche.com) announced approval of the **Ventana PD-L1 (SP263) Assay** by the FDA as a complementary diagnostic to provide PD-L1 status for patients with locally advanced or metastatic urothelial carcinoma who are being considered for treatment with the FDA-approved anti-PD-L1 immunotherapy Imfinzi™ (durvalumab). OI

spotlight

Queens Medical Associates

Queens, New York

Queens Medical Associates occupies 18,000 square feet on the third floor of a mixed-use retail and professional building. The medical oncology practice is in the center of a densely populated urban area and thriving commercial district. For 16 years, Queens Medical Associates has provided medical oncology services and functions as the medical oncology division of NewYork Presbyterian Queens Hospital. The practice is the source of medical oncology services for a population of about 2.2 million people where more than 100 different languages are spoken.

Culture-Based Model

Serving such a dense and diverse patient service area requires innovative and efficient coordination of care. To better address individual patient needs, the treatment teams are largely organized around culture and ethnicity rather than by disease site.

In Queens, a primary care physician's first reflex in referral to an oncologist is based on the patient's ethnicity; patients want to be treated by someone who understands their culture. "With such diversity, we are fortunate to employ providers who speak approximately 75 different languages," explains Susan Dicosola, MS, CMPE, Executive Director of Queens Medical Associates. In complementary fashion, when our physicians refer on to downstream services, they refer to physicians they know are similarly staffed and speak the patient's language.

Translations, documents, and electronic communication are produced in five official languages: English, Spanish, Mandarin, Russian, and Korean. Plans are underway to add a sixth team, with a physician who speaks Hindi and Bengali starting in November 2017.

According to Dicosola, this team structure has been evolving since the practice's inception. The six treatment teams can connect with their patients with cultural competency, communicating in their native languages, while also recognizing how their cancer may be related to their genetic make-up.

The practice is dedicated to providing the latest treatments especially through clinical trials based on the genetic mutations in its vast gene pool. Ongoing investment in research infrastructure and staffing make Queens Medical Associates a prime contact for clinical research organizations and trial sponsors given its extreme genetic diversity. Patients are provided with translated informed consent documents and materials in the five official languages.

Staffing for the practice includes 6 physicians, 6 physician assistants, 8 medical scribes, 8 medical assistants, 11 nurses, 1 nurse navigator, 4 infusion nurse technicians, 5 pharmacists, 2 research staff, 8 laboratory technicians, 17 billing staff, and 2 social workers.

Minimum Space, Maximum Efficiency

Dicosola recognizes the challenges of serving such a large patient population in a smaller physical space, "Like equipping a boat, you must optimize every inch of space!"

While Queens Medical Associates refers patients out for radiation, surgery, and imaging, its robust in-office dispensing service has helped the practice grow. As more anticancer medications are approved in the oral form, the practice has converted a few of the infusion chairs into "non-oncology" chairs for patients receiving IV anti-transplant rejection medication or rheumatology medication, for example. And, since pharmacists are on-site, they can counsel patients chairside, discussing side effects face-to-face. Pharmacists ensure better adherence by answering patient questions and communicating with the physician directly.

The entire infusion area contains 26 treatment chairs, 4 beds, and 8 "fast-track" chairs. Dicosola describes the infusion area as very open, with some patients even visiting on their days off from treatment to check in with their friends, other patients. She credits the nursing staff with creating a sense of community among patients and throughout the practice. "There is a lot of laughter and patients actually tell us that 'this is going to sound kind of weird, but now I actually look forward to coming here'," said Dicosola.

Queens Medical Associates staff have worked over the years to develop and finesse workflow processes to yield maximum efficiency. The practice has a long experience using an EHR (electronic health record), and over the years has tweaked its system to improve workflow.

With a constant focus on efficient service delivery and robust physician

support, Dicosola's motto is "right work, right time." In a further move toward patient-centered care, each physician team includes a medical scribe to maximize physician engagement with patients during medical appointments. The structure of the treatment teams means each physician has at least one physician assistant and a scribe. These supporting staff roles are one of the best investments to support physician productivity, according to Dicosola.

To prevent lengthy patient wait times, staff work to be extremely responsive to both physicians and patients. "We make sure that we resolve provider issues quickly. If a physician walks in and says, 'I need…' we try to fix it before he or she finishes the sentence," said Dicosola.

This fine-tuned workflow allows physicians to spend more time with patients and has resulted in higher patient satisfaction scores. Dicosola describes the daily atmosphere of the practice as busy, but not rushed. Each staff member has a clear idea of his or her role on the cancer care team and they all work in concert.

Strengthening Patient Support

Like many cancer programs in the U.S., Dicosola lists unreliable transportation as an oft-cited barrier for patients to access treatment. Dicosola estimates about one-third of patients take mass transit, one-third drive, and the remaining third use some form of medical transport. For example, many patients come from the neighborhood of Flushing, which is only four miles away from Queens Medical Associates. And while New York City does have a robust transit system, some patients may have to take two buses or make several connections to get to their treatment and home, a journey that can be tiresome even without undergoing cancer treatment. The practice does have funds available for car services or gas subsidies to help ease this burden.

Queens Medical Associates uses a social work model of navigation to help patients experiencing financial hardship or barriers to treatment. Two full-time patient navigation social workers coordinate in tandem with the nurse navigator to make sure patient needs are addressed from both the clinical and social work sides.

As a participant in the Centers for Medicare & Medicaid Services Oncology Care Model (OCM), Queens Medical Associates is taking on new care initiatives. The practice is currently developing an outpatient palliative care program, which will be termed Supportive Care to overcome any stigma associated with the term palliative care, with a dedicated palliative care physician slated to begin Aug. 1, 2017.

The practice will offer full-time supportive care services on-site and will include inpatient hospital consultation. As this new program grows, Queens Medical Associates plans to launch a home-based supportive care service as well.

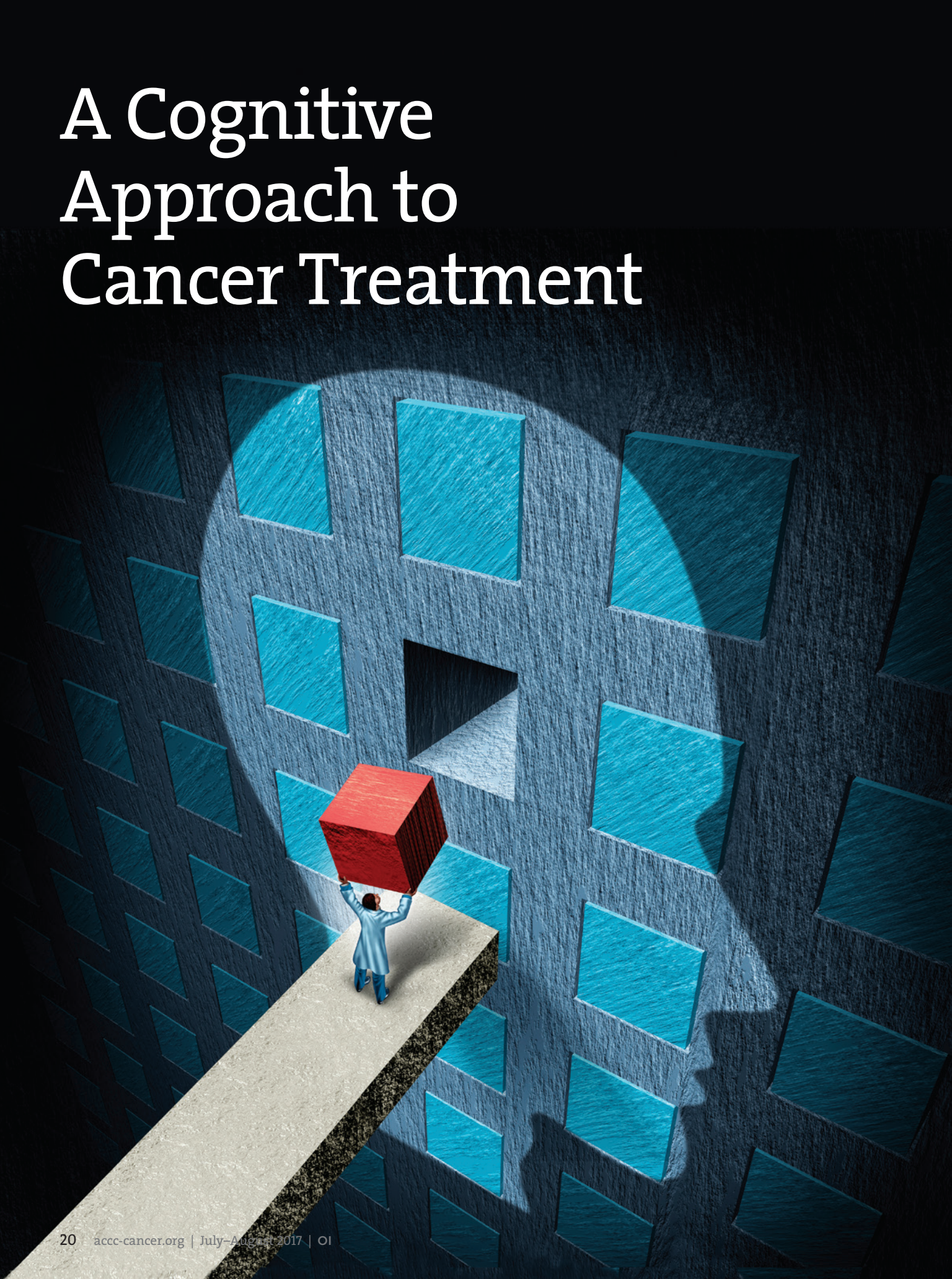
Queens Medical Associates will also embark on a new survivorship initiative with patients with metastatic disease. Dicosola notes that, in the ongoing initiative to educate patients about curative versus palliative treatment, it can be insensitive to give metastatic patients a survivorship plan, but it is also important to acknowledge their needs while in long-term treatment. Therefore, staff developed the term "Maintenance Plans" for the care plan this subset of patients will receive, signifying their need for maintenance of active treatment and moving them into the supportive care phase more naturally. OI

Select Supportive Care Services

- Social work
- Navigation
- Clinical trials
- Look Good, Feel Better

Number of new analytic cases seen in 2016: 1,500

A Cognitive Approach to Cancer Treatment



BY MARLENA RYBA, PHD

A cancer diagnosis is one of the most terrifying in medicine. The fear and anxiety most patients experience at diagnosis is expected, but for many, those debilitating emotions never fade. Instead of the hope and confidence needed for a strong immune response, despair can persist and hamper treatment. Too often, the emotional burdens accompanying cancer lead to early withdrawal from chemotherapy, for example, and poor outcomes. However, a series of clinical studies suggest psychotherapy can counter those effects, with powerful implications for patients. Applying proven mental health approaches, such as cognitive behavioral therapy, interventions are now helping patients fight back against their fears and their disease.

> Treating mental health is not just about making people feel more positive, but limiting the side effects of chemotherapy, reducing pain, lessening fatigue, and in some studies, reducing the risk of cancer recurrence.[7]

Mental Health is Not Optional for Healing

After a cancer diagnosis, patients face so many changes that it can be difficult to tease the elements apart. For many physicians, it can seem impossible to determine if emotional responses are side effects of cancer—or its treatments—or if a patient is truly experiencing depression.

Despite increasing evidence about its impact on health and recovery, psychotherapy is still not part of standard care for cancer patients, or survivors. And while integrative cancer care is expanding in the United States, depression among cancer patients is still under-diagnosed. Even when diagnosed, depression is often under-treated. Few medical personnel are well trained to recognize the symptoms, and treatments—including medication—too often fall short.[1]

Depression is not the only challenge. Pain and fatigue are also devastating for those who endure and survive cancer treatment. Pain is well recognized, but still not universally treated and fatigue is even less frequently addressed. Fatigue can hamper every aspect of cancer treatment and quality of life, yet one study found merely 5 percent of cases are treated, compared to 95 percent for pain.[2]

Research reported in 2010 reveals that these symptoms relate to hormonal changes cancer patients experience as their disease progresses. Ohio State University psychologist Lisa Thornton, PhD, and colleagues found neuroendocrine-immune models may explain why such effects are so common.[3] Controlling for disease and demographic variables, the researchers found neuroendocrine changes—shifts in levels of hormones triggered by neurological activity—predicted pain, depression, and fatigue, suggesting stress hormones as a common mechanism. Encouragingly, an earlier study from the investigators suggested a solution: psychological intervention can reduce depressive symptoms, improve immunity, and reduce inflammation, which is thought to be key to cancer onset and progression.[4]

Burdens of the Mind

When it strikes, depression may first be recognized with a slow but continuing lowering of mood or disinterest in everyday activities. When such feelings are happening more days than not, a patient may start to meet the criteria for major depressive disorder as classified in the standard of guidance for mental health, the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders (DSM-V)*.

Among cancer patients, current research suggests major depressive disorder is one of the most common psychiatric disorders, with prevalence rates ranging from 10 percent to as much as 50 percent.[5] The impact of major depressive disorder can be extensive, including such changes as increased anxiety and substance use, harmed personal relationships, poorer self-care, fewer physical activities, sexual side effects, and poor sleep, among others.[6]

Regardless of specific diagnosis, what's most important is recognizing the presence of mental illness. Physicians may not be

aware of the impact depression has on cancer treatment outcomes, beyond quality of life. Treating mental health is not just about making people feel more positive, but limiting the side effects of chemotherapy, reducing pain, lessening fatigue, and in some studies, reducing the risk of cancer recurrence.[7] More, depression is a risk factor for premature mortality, with evidence established in a 2008 clinical evaluation of breast cancer patients.[8] Treating mental health is not just about quality of life, but quality of care.

Treatment of depression can be hindered by how the disease may compound with existing, practical challenges of cancer treatment. Cancer patients are already burdened by multiple appointments. When people have a medical illness, such as cancer, therapy is not a priority even when they have severe mental health symptoms. Many patients are focused on "Let's treat the disease and then I'll worry about how I feel later," unaware that how they feel emotionally and how they cope with cancer are intimately related. Approximately 70 percent of depressed cancer patients have a range of worries beyond the disease, including:[9]

- Anxieties regarding relationships with friends (77 percent)
- Concerns about the well-being of family members (74 percent)
- Stress related to finances (63 percent).

With the high cost of treatment and the lost time at work, depression can add other economic costs to patients and to the healthcare system. For example, patients with depression have more appointments, spend more time with physicians, and have more hospital readmissions, resulting in higher healthcare costs.[10]

Over time, the risks increase beyond impact on treatment, and can lead to suicide—even long after cancer is in remission—for some cancer survivors.[11]

Cognitive Behavioral Therapy as a Cancer Treatment Solution

Cognitive behavioral therapy is the treatment of choice for depression, evidenced by hundreds of trials and multiple meta-analyses.[12] Developed by Aaron Beck, MD, in the 1960s, cognitive behavioral therapy focuses on improving thoughts and beliefs as a way to change moods and behaviors, with patients working on techniques for healthier mental habits and coping skills. Problem solving improves, and patients learn how to identify negative "automatic" thoughts and how to stop them, shattering negative self beliefs. Skills improve over time, so that eventually when stressful situations arise—or any event that might typically trigger a depressive episode—the patient can manage the crisis and move past it.

There have been few cognitive-behavioral therapy studies with cancer patients that included cases with major depressive disorder. Some have studied patients with depressive symptoms, with people reporting they feel "down," yet did not confirm the presence of clinical depression.

However, studies with cancer patients have found that mental health and wellness (overall well-being) are related; this suggests that cognitive behavioral therapy could affect both. For example, cognitive behavioral therapy reduces depressive symptoms and improves a person's health and well-being. This connection between mental health and wellness and well-being has also been observed in patients with other illnesses (especially chronic disease).

Stronger Physical Health Arises from Strong Mental Health

One landmark study conducted here at The Ohio State University Comprehensive Cancer Center through the College of Public Health established a solid baseline for understanding how mental stress impacts immunity. Led by Barbara L. Andersen, PhD, the 2004 clinical trial looked beyond patient-reported symptoms to actual biomarkers and immunity measures. The findings were clear: immunity improves as stress goes down.[13]

Andersen and colleagues found that patients receiving a psychological intervention showed significant improvements in anxiety, perceived social support, better dietary habits, and even a reduction in smoking. As important, patients receiving the intervention were also better able to maintain their chemotherapy regimens in comparison to a control group.

Social support can be critical for well-being, as cognitive behavioral therapy predicts that increased contact with reinforcers for healthy behavior (or reduced contact with reinforcers for depressed behavior) decreases depressed behavior and increases healthy behavior.[14]

In the study, the cognitive behavioral therapy intervention involved one session per week for four months and included strategies for reducing stress, improving mood, establishing good health behaviors, and adhering to cancer treatment. The healthy behaviors were particularly impressive. Compared to the control population, patients undergoing psychotherapy avoided fats, increased physical activity, and decreased the number of cigarettes smoked each day (the opposite of the smoking trend for control patients).

A 2009 Ohio State University study led by Thornton and colleagues built on those findings by observing how psychological intervention directly reduces inflammation.[4] Working with newly diagnosed cancer patients, the researchers found cognitive behavioral therapy alleviated depression, pain, and fatigue while simultaneously lowering overall white blood cell counts and improving neutrophil levels and T-cell ratios.[4]

Changing Behaviors, Changing Outcomes

Cognitive behavioral therapy studies are expanding such efforts, and evidence suggests patients can find significant benefit with only one of the therapy's components: behavioral activation for treatment of depression. The approach emphasizes improving thoughts, mood, and quality of life[15] by focusing on what leads

to depressed behavior, revisiting value systems, and resisting avoidance by focusing on emotional acceptance and behavior changes.[16] For a time, researchers had de-emphasized the behavioral aspect of cognitive behavioral therapy, but research suggests behavioral approaches may be as effective as the complete cognitive behavioral therapy treatment,[17] which is promising for people who have limited available time or need efficient interventions, such as cancer patients in a hospital setting.

For the depressed breast cancer patients with whom we worked, behavioral activation and problem-solving interventions improved psychological outcomes and quality of life.

From 2008 to 2011, I was the project coordinator involved in a behavioral activation study led by Derek Hopko, PhD, of the University of Tennessee, Knoxville,[16] and also served as a therapist. The experience was enlightening: patients in the behavioral activation arm had decreased bodily pain, not just decreased depression. In fact, nearly three quarters of patients exhibited clinically significant improvement with their depression. Further, treatment gains across outcome measures (bodily pain and depression) were maintained at 12-month follow-up, suggesting that the treatments may elicit enduring effects. For the depressed breast cancer patients with whom we worked, behavioral activation and problem-solving interventions improved psychological outcomes and quality of life.

The behavioral activation intervention for treatment of depression involved seven stages, with initial sessions assessing the function of depressed behavior, promoting efforts to weaken access to positive (e.g., sympathy) and negative reinforcement (e.g., escape from responsibilities) for depressed behavior, establishing patient rapport, and introducing treatment rationale. The sessions then provided a systematic activation approach to increase the frequency and reinforcement of healthy behavior. The emphasis then shifted to identifying behavioral goals within major life areas.

The behavioral goals defined the social environment in which treatment would progress, not just the impact of the breast cancer. For example, patients looked at their relationships with their life partners; their children, parents, and siblings; and their friends. Patients learned to honestly address both positive life experiences—such as hobbies and favorite activities—while also addressing work, finances, housing, other health problems, and legal issues.

From the Hopko study[16] and many others, to improve the patient experience and provide care that is truly patient-centered, we must return the fight to the patients, giving them the tools and the confidence to regain control of their lives, whether or not they are able to control their disease.

Bringing Cognitive Behavioral Therapy to Those Who Need It

As discussed earlier, it is important that physicians and other healthcare professionals recognize when their patients need help. When patients first arrive for cancer treatment, the admitting staff need to evaluate each patient's initial mental health needs—some will already be struggling with mental health challenges when they receive their cancer diagnosis. As important, all patients should be monitored during and after their cancer treatments, as changes in their condition or emerging fears can lead to later mental health challenges—even years after tumors have been removed and the cancer experience has ended.

At many cancer programs, resources can be limited, though many have begun distress screening of patients. That effort has been aided by guidance from the oncology community, for example, "Screening, Assessment, and Care of Anxiety and Depressive Symptoms in Adults With Cancer: An American Society of Clinical Oncology Guideline Adaptation," which appeared in the *Journal of Clinical Oncology* in 2014.[18] The guideline adaptation addresses 1 of 18 symptom topics that ASCO's Cancer Survivorship Committee has identified as important for cancer patients.[18]

The guideline provides valuable insight for screening, assessing, and caring for cancer patients and survivors struggling with psychosocial distress. Critically, the emphasis is on mental health throughout life, not just during treatment. As the authors state, physicians should evaluate all patients with cancer for symptoms of depression and anxiety periodically: at the initial visit, with changes in disease or treatment status (such as post-treatment, recurrence, progression), and if there is a transition to palliative or end-of-life care.[18]

Assessments should look for a range of anxiety and depression signs and symptoms (see the ASCO depression guideline at: asco.org/adaptations/depression), while amending standard checklists to reflect the unique patient population a clinic serves and any changes to best practices. The authors emphasize that every assessment will involve special circumstances, including (but not limited to) using culturally sensitive assessments and treatments, tailoring assessment or treatment for those with learning disabilities or cognitive impairments, and the tremendous difficulty of detecting depression in many older adults.[18]

Depression is not the only psychological response to evaluate. Many patients experience anxiety disorders, such as specific phobias and social phobia, panic and agoraphobia, generalized anxiety disorder, obsessive-compulsive disorder, and post-traumatic stress disorder.[18]

Generalized anxiety, the authors note, is the most prevalent of all anxiety disorders and commonly occurs with other mental illnesses, and patient worries generally extend to non-cancer topics and broad areas of life. Often, patients do not show symptoms of anxiety, but instead present excessive worry, too often dismissed as "concerns" or "fears." Surprisingly, such concerns can far exceed true cancer-related risk, with excessive fear of recurrence, worry about multiple symptoms, or anxiety about symptoms not associated with current disease or treatments.[18] In other words these patients' level of worry is not in proportion to their actual cancer-related risk. For example, someone with an anxiety disorder will worry excessively about the cancer spreading or about dying even if they were diagnosed with a very curable cancer and have a great prognosis. While this is typically a sign of an anxiety disorder, physicians and patients' family members will often dismiss these worries as "normal" or assume they're typical fears cancer patients experience.

As important as the guidance Andersen and her colleagues provide for identifying patients needing psychosocial support are their recommendations for ensuring that support continues. People with depression and/or anxiety often fail to follow through on referrals or comply with treatment recommendations, so the guidelines recommend the following checklist:

- Assess follow through and compliance with individual or group psychological/psychosocial referrals, as well as satisfaction with those services.
- Assess compliance with pharmacologic treatment, patient concerns about adverse effects, and satisfaction with symptom relief provided by the treatment.
- Consider tapering a patient from medications prescribed for anxiety if symptoms are under control and if the primary environmental sources of anxiety are no longer present.
- If compliance is poor, assess and construct a plan to circumvent obstacles to compliance or discuss alternative interventions that present fewer obstacles.
- After eight weeks of treatment, if symptom reduction and satisfaction with treatment are poor, despite good compliance, alter the treatment course (e.g., add a psychological or pharmacological intervention; change the specific medication; or refer the patient to individual psychotherapy if group therapy has not proven helpful).

Future Directions for Treatment

Despite the critical need for psychotherapies in cancer treatment, they are not available to all patients and are rarely covered by insurance—particularly when patients transition from active treatment

My current research at The Ohio State University Comprehensive Cancer Center–Arthur G. James Cancer Hospital and Richard J. Solove Research Institute is evaluating online cognitive behavioral therapy approaches, techniques that could both expand access and help cancer programs alleviate some of the stresses they face from an overwhelming number of patients needing emotional support. The computerized cognitive behavioral therapy treatment, Beating the Blues®, is a stand-alone platform that includes eight online sessions that mirror what a patient would review if he or she went to a psychologist:[19]

- Problem definition
- Pleasurable events
- Automatic thoughts
- Thinking errors
- Distractions
- Challenging unhelpful thinking
- Core beliefs
- Attributional style (how you explain the causes of events).

The tools include behavioral activation and problem solving—as both of those elements have a strong record in clinical trials—providing standardized exercises, multimedia, and homework online at a patient's preferred pace.

Randomized, controlled trials have demonstrated the effectiveness of Beating the Blues for depression and anxiety, with data showing patients maintained progress at a six-month follow-up, and as effective as face-to-face therapy.[20]

Such interventions are becoming more important as more people transition from active treatment into survivorship. Current estimates suggest 15.5 million cancer survivors live in the United States, according to the National Cancer Institute. Following the rigors of chemotherapy, radiation therapy, or both, many will be presented with life-long physical and emotional challenges, from pain, fatigue, urinary or bowel problems, and sexual dysfunction to fear of recurrence, body image distress, job loss, or loss of personal relationships. Psychological impact can be deep and existential, leading to a loss of self or failing self-esteem, or changes in life meaning and purpose.[21]

However, no matter how daunting such challenges are, we know how to address them, and we know how to help patients fight back. While psychotherapy has long had to compete against internal medicine for public favor, society now recognizes that mental health is health, and that our minds and bodies are not independent.

Culture is changing, and processes for managing disease are changing with it. If we all work together to expand awareness of the need for psychotherapy for cancer patients—and access—outcomes will change, experiences will improve, and lives will be

saved. These are goals within reach, and now is the time to encourage the best practices that will bring them to fruition. OI

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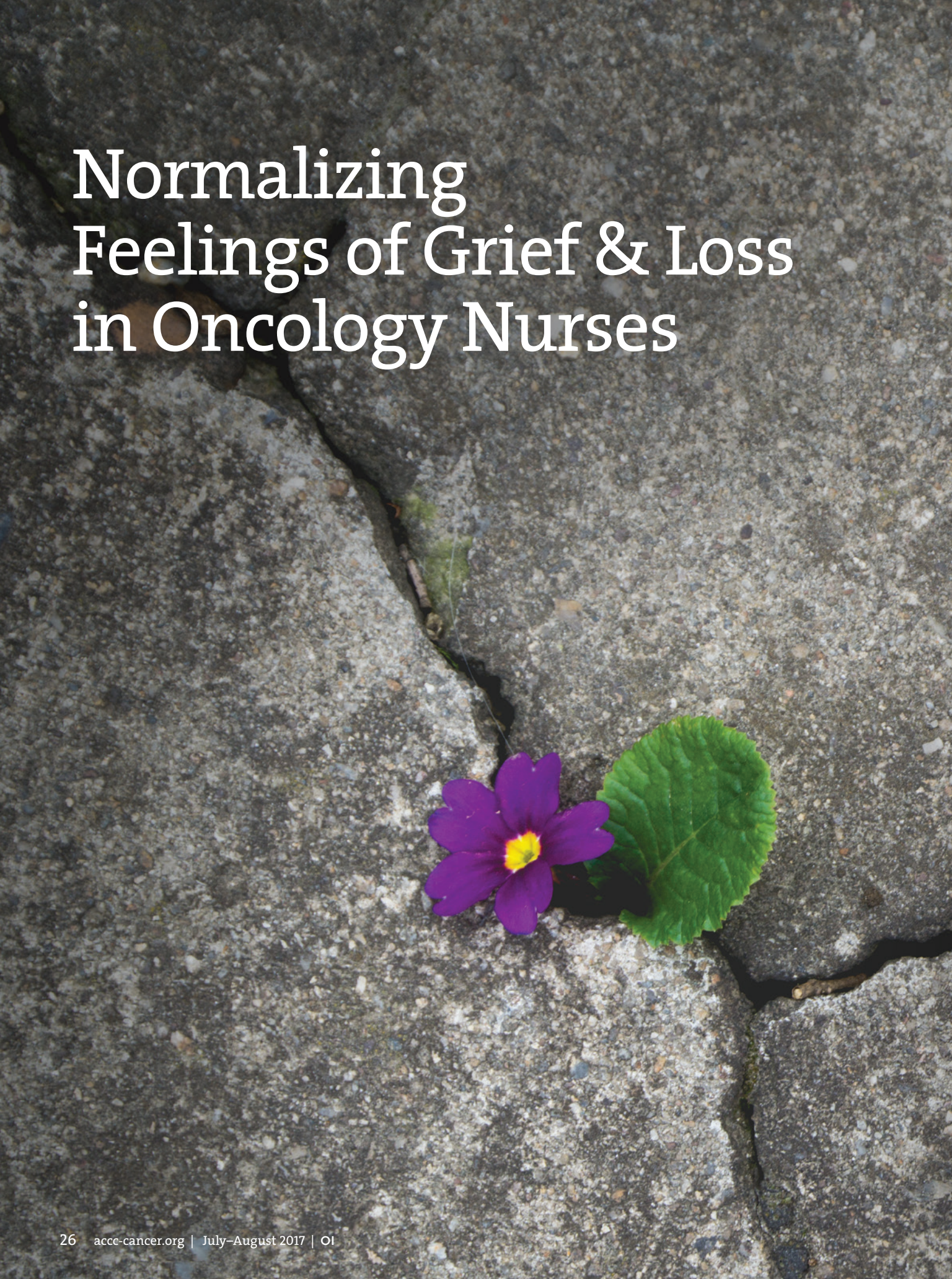
Normalizing Feelings of Grief & Loss in Oncology Nurses



BY JENNIFER COLLINS, MDIV, MS, BCC, AND
SANDRA TAN, MSW, LCSW, ACHP-SW

Piercing the wall to reveal hidden emotions

Opened in 2009, the 80,000-square-foot Sarah Cannon Cancer Institute at Johnston-Willis Hospital, Richmond, Va., offers inpatient and outpatient cancer treatment, including a radiation oncology clinic, Gamma Knife department, infusion center, cancer resource center, lymphedema clinic, a large community oncology practice, and a 24-bed inpatient unit. Like other cancer programs, the patients at Sarah Cannon Cancer Institute at Johnston-Willis Hospital often have multiple admissions lasting days to weeks. In many cases, oncology nursing staff builds relationships with these patients and their loved ones. More, caring for these patients can weigh heavily on nurses who may experience joy, sadness, anger, or frustration related to their job. Unless the nursing staff have healthy coping strategies, processing these mixed emotions can be a challenge.

In 2010, the Sarah Cannon Cancer Institute at Johnston-Willis Hospital started to explore how to best serve the emotional and spiritual needs of its oncology nursing staff. From the beginning the chaplain and social worker worked together supporting the oncology nursing staff through debriefings after an especially difficult death or an ethical or emotional situation. Due to the demands of the oncology unit, the timing of delivering this supportive care is challenging for staff, but essential to fostering caring relationships. Over time our chaplain and social worker have developed—through trial and error—complementary modalities designed to holistically support our oncology nursing staff.

Breaking Free! A Budding Flower Pushing Through the Concrete

A seed planted deep within the darkened earth is destined to be a vibrant flower yet it has so many obstacles in front of it. Deep below it is dark and there is virtually no air nor light. It is seemingly suffocating and very hard to move. This dirt seems like an impediment but it is necessary for any budding flower. It is a cell of silence and solitude and needs air, light, and water in order to arise to its full potential. Without caring support, the flower will not be able to grow and bud high enough to reach any point in the dirt that may have a crack in it. For just below the surface of this hardened soil are potential budding flowers. These budding flowers are looking for cracks above so that they can gain further light and water.

Eric Gajewski
from the work, *Fortress of the Soul*

Preventing Burnout

Research has shown that oncology nurses are at risk for developing burnout syndrome because of their significant levels of emotional involvement and a diminished sense of personal accomplishment.[1] The day-to-day practice of an oncology nurse involves addressing complex situations, which may include:[2]

- Comforting suffering patients and families
- Handling ethical issues
- Mourning
- Death.

These factors—combined with the rigorous nature of oncology nursing—can lead to high burnout in this profession.[3]

To address the risk of burnout and the emotional impact from patient deaths, the Sarah Cannon Cancer Institute at Johnston-Willis Hospital created a bereavement committee with representatives from each oncology unit: inpatient, radiation oncology, and the infusion center. The committee's first activity was the writing of personalized bereavement cards, which cancer program staff could sign and/or write a personal message, and which are delivered to families after a patient's death.

Providing Support to Oncology Nurses

Once the chaplain and social worker recognized the layers of grief experienced by oncology nursing staff, we knew more needed to be done to provide intentional, self-care opportunities for staff, allowing them to break through those layers of grief and become emotionally and spiritually stronger.

Our first organized event was a four-hour retreat off-site. The retreat focused on inspirational teaching, communication, and team building. While oncology nursing staff appreciated this self-care opportunity, we were unable to continue this event due to limited resources. Therefore, we had to think of other ways to support our oncology nursing staff that allowed the chaplain and social worker to keep a finger on the pulse of emotional needs and challenges and yet were within our budget.

One issue oncology nursing staff mentioned multiple times was that they were not always able to say goodbye to their patients or offer condolences to the family, as one might not be working at the time of the patient's death. Several bereaved family members also shared that the loss of daily interactions with cancer program staff often causes them to experience a secondary loss. With the knowledge that both oncology nursing staff and families grieved the loss of relationship with one another, our bereavement committee developed a Service of Remembrance to address this loss of connection.

A Service of Remembrance

Beginning in 2011, the Service of Remembrance allowed oncology nursing staff and families the opportunity to reconnect and to honor patients' lives. This meaningful service has evolved into a bi-annual event for the patient's loved ones. Approximately 150 families are invited and 65 to 90 people attend each service. Oncology nursing staff are encouraged to participate at a level they feel comfortable with, such as assisting with decorations, welcoming attendees, reading a piece during the service, or helping with clean up.

With the understanding that a caring and sacred space can set the stage for honest reflection, our bereavement committee developed the Reflection Service exclusively for oncology nursing staff.

On the day of the Service of Remembrance, the hospital auditorium is transformed into a place of reverence. We create a calm, healing environment with soft lighting, a soothing nature video, beautiful music performed by a harpist, and a tiered-table decorated with lit trees, paper butterflies, and fresh ivy. Framed pictures of the deceased, brought in by the families, are displayed on the tiered-table.

Oncology nursing staff welcome the guests, escort families to their seats, and pass out programs featuring readings or poems from the service. Attendees are given a paper heart infused with seeds and invited to write either a word, memory, or wish on the heart. When their loved one's name is read during the service, family members are invited to come forward, hang their hearts on the trees, and receive a bag of rosemary, the ancient symbol of remembrance. The service lasts about one hour and is followed by a reception with light refreshments, at which time oncology nursing staff and families may reconnect, reminisce, and offer words of comfort or gratitude.

The Reflection Service

Oncology nursing staff enjoyed participating in the Service of Remembrance and connecting with the families. However, our bereavement committee received feedback from staff that some felt they remained in their caregiver role and were still unable to show their true emotions while interacting with families.

The chaplain and social worker also noticed an attempt by some oncology nursing staff to try and suppress "negative feelings" for fear of being overwhelmed by them. Unfortunately, the denial of difficult emotions that arise from being around death and dying daily can result in depersonalization, and may cause individuals to deny "positive" emotions as well. Like cultivating a seed, one must attend to these negative emotions to prevent burnout. Parsing these negative emotions can be a painful part of the self-knowledge process, but it is an important part of digging to the root of the emotions to begin healing.

With the understanding that a caring and sacred space can set the stage for honest reflection, our bereavement committee devel-

In an art activity offered during the Reflection Service, nurses decorate hearts using certain colors to express specific emotions.

oped the Reflection Service exclusively for oncology nursing staff.

Based on oncology nursing staff feedback, the bereavement committee developed the following objectives for this staff-only service:

- Create a comfortable and safe environment where oncology nursing staff can express emotions and feelings.
- Be attentive to opportunities that invite checking-in with oncology nursing staff. Ask questions like, *How are you doing? What do you need? How may we serve you?*
- Offer education and stress the importance of self-care.
- Allow space to cultivate fellowship amongst oncology nursing staff through ritual, laughter, reminiscing, sharing a meal, and discussing emotions.

The Reflection Service was marketed internally to staff through emails and through cancer program leadership who shared information about the service during daily huddles.

Format of the Reflection Service

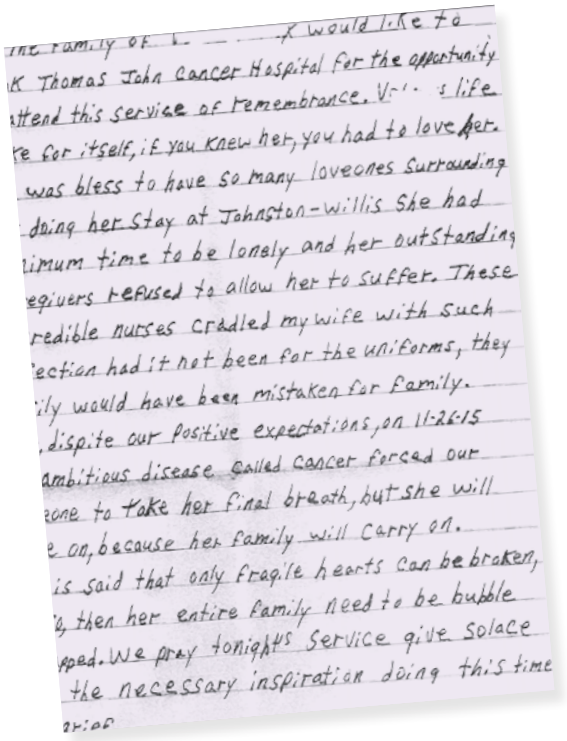
While the purpose behind this service is important, the format is critical as it can either encourage or discourage oncology nursing staff participation. We keep the service on site in the hospital, facilitating ease of attendance during shift changes. The calming environment is set with low lights, fragrant aromatherapy, and soft music, and tables are laden with inviting art supplies. To maintain the wellness theme, healthy foods are either catered or participants may provide a dish to share.

The Reflection Service has the potential to be an emotionally heavy experience, so the chaplain and social worker established ground rules at the start by creating a sacred, safe space to share. We define "safe space" as a place for honesty, no right or wrong, no judgment, and confidentiality. A slide show displays peaceful images among the names and pictures of deceased patients in the background to help balance feelings, such as grief and helplessness, with the reality that oncology nursing staff are difference makers. (In this context, a difference maker is an individual who has the ability to decrease a person's suffering and acknowledge their value.) The Reflection Service also features a lit tree filled with thank-you notes from families, bringing to mind the positive impact oncology nursing staff have on patients and families. Showing the deceased patients' names, pictures, and notes, offers oncology nursing staff a contemplative opportunity to reflect, cry, and/or laugh.

While there is no fixed schedule within the three-hour Reflection Service because staff can come and go as able, the service has both structured and unstructured activities. Structured activities include room set up and food preparation. Depending on the conversation, unstructured activities might include storytelling and/or supportive feedback.

Facilitating the Reflection Service

Appropriately-equipped and trained facilitators are key to the success of the Reflection Service. Due to the weight and potential volatility of emotions, we believe it is necessary for each facilitator to have, at a minimum, an undergraduate degree in counseling.



Photos from a recent Reflection Service.

Facilitators also must be comfortable in the presence of strong emotions, create safe space to express these emotions, and be comfortable sitting in silence with the staff's pain, when necessary.

Oncology nurses, needing to be emotionally responsible in the presence of patients and families, often struggle to give themselves permission to genuinely feel their emotions. When oncology nurses are given permission, facilitators can go beneath surface talk and gently expose those hidden feelings while guiding the conversation. Through open discussion, the facilitators:

- Affirm and normalize emotions.
- Detect struggles, deficits, and needs.
- Identify emotional similarities and differences between the department and units represented at the Reflection Service.

In the initial phase of the Reflection Service, counseling staff prepared questions that helped to guide conversation; however, with ongoing participation in the service, oncology nursing staff has become more comfortable bringing their own topics and concerns to discuss.

Challenges & Lessons Learned

Some oncology nursing staff participate in the Reflection Service on their day off; however, we are challenged to reach more staff. Oncology nursing staff attendance at the Reflection Service is likely impacted by full schedules outside of work. Further, for oncology nurses who already work long work hours, it can be burdensome coming in early or staying late. While having the Reflection Service on site is helpful, some oncology nursing staff have communicated that it can be difficult to turn the day's stress off and immediately concentrate on the service.

For some oncology nursing staff, the emotional component can be challenging, but facilitators have learned to balance heavy emotional discussions with creative, healthy outlets. While self-care is the main focus of our counseling staff and facilitators, everyone's notion of "self-care" is different. Providing creative avenues for self-care that nurture most attendees can be challenging.

Through experience, facilitators have learned that the more meaningful the activities are, the more they nurture effective thought and conversation. Oftentimes, poems or an applicable short story that relates to grief, being a caregiver, compassion fatigue or burnout, hope, or resiliency are read. Art activities are available for anyone interested, such as playdough and coloring. An art activity that continues to evoke conversation is coloring hearts where certain colors express specific emotions (see photo on page 29). While this activity is simple, its impact has been profound as oncology nursing staff gained insight and clarity, touching on the deeper layers of hidden emotions.

The Reflection Service has provided facilitators, oncology nursing staff, and hospital leadership with pertinent information about the need for continual self-care education. As the oncology nursing staff juggles numerous responsibilities at work and at home, this leaves little time for reflection and self-care. We found that oncology nurses tend to compartmentalize their emotions while working their shift, and retained a cultural mind-set of, *"I have to do this alone."* Oncology nurses often shared, *"I could/should have done more,"* revealing feelings of helplessness and frustration. Nurses wished they had more time to sit with patients and/or provide more emotional care to the bereaved family.

When asked for feedback by the chaplain and social worker, oncology nursing staff shared that when facilitators offered a listening presence and normalized emotions, staff felt validated. Staff suggestions are incorporated in future Reflection Services,

for example, it was a staff suggestion to add obituary pictures to the slide presentation. Staff also requested bereavement tools and strategies to deal with emotions, and we are planning to offer education to address those requests.

As oncology nursing staff shared with one another, new and seasoned nurses saw they were struggling with similar emotions. This realization was both painful and freeing as the facilitators encouraged and guided the nurses to begin practicing self-compassion to come out of their self-made places of isolation and heal. In this liberating process, facilitators sought to connect the oncology nursing staff with their original call to be a nurse, rekindling their commitment to patient care. While the healing process had begun, having this mindset be the unit's "new normal" required continued awareness and education.

Oncology nurses have told us that the Reflection Service has provided a safe space to reflect, share, and let go of bottled up emotions, empowering them to face the next challenge. We have also seen an increased sense of teamwork on the units, which has led to more trusting relationships and deeper care amongst the staff. With this greater sense of belonging comes a stronger sense of community, which we believe leads to a more vigorous level of care for patients and families.

We continue to offer the Reflection Service twice a year along with other educational sessions, including:

- Tools to improve self-care (mindfulness, self-compassion, journaling, etc.)
- Communication with end-of-life patients and families
- Ways to deal with grief.

Together with oncology nursing leadership, our chaplain and social worker are exploring ways to develop a ritual for staff to acknowledge a death on the unit. One proposed ritual is similar to Jonathan Bartels' "The Pause," where the staff introduce a moment of silence following a patient's death to honor the patient and their loved ones while acknowledging the efforts of the interdisciplinary team and affirm its provision of exemplary patient care.[4]

Combating burnout syndrome begins with emotional self-awareness. While self-awareness carries with it a level of vulnerability, it also provides an opportunity to grow emotionally and spiritually. Self-awareness is a journey and it needs to be nurtured to facilitate the acceptance of emotional responsibility and accountability. Our hope is that the oncology nursing staff at the Sarah Cannon Cancer Institute will continue to embody their true selves and their cumulative grief will become a catalyst for living more fully. OI

Jennifer Collins, MDiv, MS, BCC, is director of Pastoral Care at HCA, CJW Medical Center and Sandra Tan, MSW, LCSW, ACHP-SW, is a licensed clinical social worker at Sarah Cannon Cancer Institute at Johnston-Willis Hospital, Richmond, Va.

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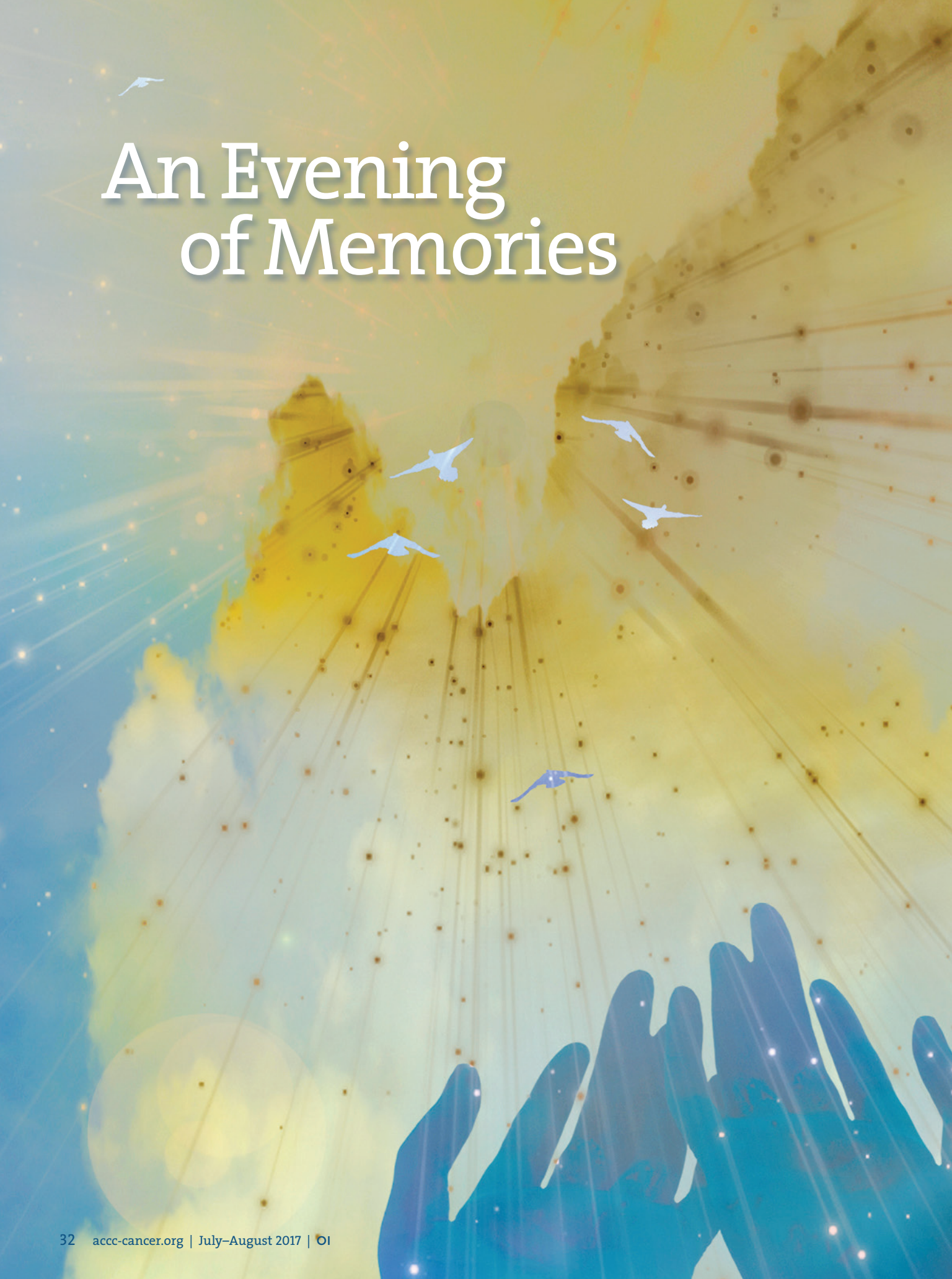
Interdisciplinary cancer care team at Sarah Cannon Cancer Institute, Richmond, Va.

An Evening of Memories



BY LINDA BILY, MA

Cancer program staff and families celebrate the lives of patients

Outpatient cancer center staff can become a second family to many patients and their caregivers. From the valet parking attendant to the receptionist at the front desk, registrars, nursing station clerks, clinical assistants, patient advocates, nurse navigators, and the oncology nurses—each team member shares a part in the patients' cancer journey. Oncology nurses, many of whom have been working in the field for more than 20 years, often form a special bond with patients and families. Treating the same patient daily, or weekly, for months or even years, nurses and patients build relationships and genuinely care about each other.

> The most amazing part of *An Evening of Memories* is how the program has grown and how family members return year after year to share with family members of the recently deceased.

In the Beginning

In 2010, a nurse at Stony Brook Cancer Center, Stony Brook, N.Y., told colleagues that she was having a difficult time dealing with the recent death of a long-term patient. The patient had passed away peacefully in home hospice, but the nurse did not have the opportunity to offer her condolences to the family members nor did she have a setting to grieve for the patient. Often the staff only finds out about a passing when the patient no longer comes for chemotherapy, and it is rare that the family returns to the cancer center.

This story was the impetus that led Stony Brook's Department of Patient Advocacy and Community Outreach to approach cancer center administrators with the idea of hosting an event to celebrate the lives of patients who had recently passed. It was believed that such an event would offer a chance for staff and family members to come together in a celebratory, but dignified, manner.

Creating Our Evening of Memories

With the full support of administration, staff created an appropriate title and tagline for this event: "*An Evening of Memories*. Remembering those we love who have passed from this life." Patient Advocacy and Community Outreach staff were careful not to use specific religious connotations, but still acknowledge the power of spirituality and prayer for those who take comfort in their beliefs. Next, the event needed a visual representation of its mission. The artist daughter of a Stony Brook staff member designed a simple cancer ribbon with wings and a halo, and this logo is used every year.

As a group, staff brainstormed the invitation wording to invite family members to this event. This simple statement said it all, "*Please join us to honor the memory of those who have touched our lives.*" The reverse side of the invitational flyer, which was sent to the families of patients who had died within the past year, explained the program in more detail.

Stony Brook Cancer Center, Stony Brook, N.Y.

We hoped not only to receive responses about attendance, but also to have family members submit photos of and write a few words about their loved one. We asked anyone who wanted to speak about their relative or friend to prepare a few words. Our first batch of invitations received more than 30 responses with 10 photos and/or reflections about the life of the loved one.

Program Nuts & Bolts

For those cancer programs looking to implement a similar program, the steps are simple.

- Identify the patients who have passed in the last year to develop your invitation list.
- Collect the necessary contact information.
- Design, print, and label your invitations in sealed envelopes to respect privacy.
- Address the invitations to "The Family of (Name of the Deceased)."
- Allow enough time for the RSVP and for family members to send a photograph and/or story. (Some older family members will send a hard copy photo in the mail.)
- If your program can afford to provide journals with photos and patient stories, the families appreciate this keepsake. (We print a limited supply in-house.) We also provide attendees with a tote bag and a blank notebook featuring our cancer program name and logo.
- Design your program and invite your speakers and musicians. Our volunteer pool is generally comprised of students from the music department at a local college and band members from local high schools. We typically have the following speakers: an administrator, an oncology nurse, a social worker, a chaplain, and any family members who wish to talk about their loved ones.
- Arrange for light refreshments. We provide a tray of cookies and bottled water from catering in our hospital dietary department.
- Set up a podium, microphone, and digital projector and screen to show a continuous loop of the photos submitted. We also include information on healing projects that we offer at the cancer center. The photo montage with background music sets the tone of the program and gives guests something to watch while they arrive. We place boxes of tissues every few seats. Battery-powered candles are on each seat for the moment of silence.

The program begins with a welcome by our nursing director, followed by a moment of silence. Then a volunteer staff member (or the chaplain) reads the names of those who have died. After, our chaplain offers a reflection and opens the floor up to reflections and/or remarks from family members. Next, an oncology nurse talks briefly on what it means to care for patients, and the evening is brought to a conclusion with a positive and empowering message from one of our social workers.

The entire event, including invitations, music, and refreshments, costs less than $500. While *An Evening of Memories* is one of our more inexpensive patient initiatives, it is also one of the most cathartic for staff, family members, and caregivers. It cements the bond between staff and families, providing an outlet to honor the loved one who has passed and creating cherished memories and a bit of closure for all involved.

Over the years, we have refined the program based on feedback from staff and family members. Sometimes we arrange for a singer to perform "Amazing Grace," a guitarist or violinist to play, or simply use an iPod with soothing background music. Social workers, nurses, navigators, and chaplains are available to talk and reminisce after the service.

The first time we hosted *An Evening of Memories*, we were unsure how many family members would want to share personal remarks. The first year of this program, only one family member volunteered. However, after she spoke, two additional families wanted to pay tribute to their loved one. We learned quickly that first year to have many boxes of tissues available, for both family members and for staff.

The most amazing part of *An Evening of Memories* is how the program has grown and how family members return year after year to share with new families of the recently deceased. The second year, a gentleman asked to speak about his beloved wife of more than 30 years. He said that he had attended the previous year at the behest of his daughter, but all he could do was numbly sit through the program. This year, he wanted to share with those who had just lost someone that it does get better. The pain never goes away, but the intensity of the grief lessens.

We also hear from our nurses how deeply they care for their patients. One nurse said it best: *"It is our honor and privilege to care for your loved ones."*

Linda Bily, MA, is cancer patient advocacy and community outreach coordinator, Stony Brook Cancer Center, Stony Brook, N.Y.

ACCC 44th Annual Meeting & Cancer Center Business Summit

March 14–16, 2018
Renaissance Washington, DC Downtown Hotel

CALL FOR PRESENTATIONS

The **Association of Community Cancer Centers (ACCC)** and **Cancer Center Business Summit** are joining forces to present one national meeting in 2018 focused on Business, Quality, Technology & Informatics, and Policy & Reimbursement.

Leading experts in oncology—including cancer care providers and business leaders—will come together to focus on innovation in oncology, including strategic service line planning, care delivery and business models, hospital and practice alignment strategies, healthcare policy, reimbursement and payment reform, data collection and reporting, alternative payment models, and more.

The call for presentations is now open. Individuals are invited to submit a presentation(s) in any of the tracks below. Key concepts may include (but are not limited to) the topics listed under each track.

TRACK 1 BUSINESS

Hospital and physician alignment strategies; marketplace consolidation; multidisciplinary and inter-professional care delivery models; implementation of precision and personalized medicine; provider burnout and quality of life strategies; marketing and social media best practices; strategies to improve provider/provider and provider/patient engagement and communication; financial and business strategic planning.

TRACK 2 QUALITY

Patient engagement models to improve symptom management and quality of life and reduce costs; quality and performance improvement initiatives; model risk assessment and financial assistance programs; strategies for improving clinical research programs and patient accrual; implementation of new treatments, including immunotherapies and genetic testing; delivery of outpatient palliative care; model supportive care programs.

TRACK 3 TECHNOLOGY & INFORMATICS

Technology tools and solutions to improve patient engagement and quality of care; redesign, realign, and streamline services; improve provider recruitment and retention efforts; transition from fee-for-service to value-based care; improve data collection and reporting; and leverage data to strengthen and grow the cancer service delivery line.

TRACK 4 POLICY & REIMBURSEMENT

MACRA and healthcare reform; drug pricing efforts; 340B Drug Pricing Program; alternative payment models; updates to oncology-specific regulations; reimbursement forecasts; site neutral payment and other policies to align reimbursement across care settings.

Submission deadline is Tuesday, September 5, 2017.
accc-cancer.org/SubmitPresentation

Submission Details: Call for presentations will be reviewed and selected by a joint ACCC and Cancer Center Business Summit Taskforce. Individuals who are selected to present will receive complimentary meeting registration, reimbursement for one night hotel, and transportation costs. Please note that ACCC will only reimburse one presenter per session. Additional presenters must pay their own expenses.

Questions? Contact Monique J. Marino, ACCC Senior Manager, Publications & Content, at mmarino@accc-cancer.org.

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A Model for Tissue Banking in the Community Setting

The Cancer Biospecimen Repository Program at St. Joseph Hospital—The Center for Cancer Prevention and Treatment

Molecular advances in cancer prevention, diagnosis, and treatment selection have led to the development of powerful analytical tools that have gained unprecedented momentum in patient care. Biospecimen repositories are key resources for the development of molecular analytics. In an era of personalized medicine, therapeutic advances based on molecular profiling of cancer as a genomic disease are superseding traditional metrics based on criteria related to disease site or general tumor and patient characteristics. Unfortunately, progress remains slow as less than 5 percent of adult oncology patients participate in clinical trials,[1] and the number of research studies available at community hospitals that diagnose and treat a large majority of patients may be limited.[2] That said, community cancer programs have a high need for rapid translation of research into evidence-based practice to benefit patients of all ages.[3,4] Importantly, banking of biological specimens can advance oncology research efforts by providing valuable resources from participants and promoting collaborative partnerships.

The Critical Need for Biorepositories

Biorepositories can provide large numbers of specimens accompanied by relevant clinical information to support molecular research for progress against cancer. Research on specimens already plays a key role in the identification of tumor markers, specific drug targets, and novel approaches for minimally invasive treatments. At the same time, more information is needed to ensure curative treatments for patients with cancer who vary not only in their diagnosis but in inherent characteristics like age, ethnicity, genetic variations, pre-existing health conditions, and other factors. While biobanking considerations are numerous and differ across disease types, biobanking remains a viable option for community hospitals. Important determinants for successful cancer biobanking include sustainable investments and proper resource allocations that support patient accrual and sample collection. A biobank must also have standardized protocols to ensure sample quality, and the ability to implement ethical, legal, financial, and policy parameters to efficiently use specimens in local and collaborative research.

> The specific aim of the repository is to collect biospecimens for use in research from patients undergoing intervention, biopsy, or surgery.

Often, biobanks result from needs in a specific medical field and can lead to relevant translational approaches. For example, the experience of established biorepositories, such as the Johns Hopkins Brady Urological Institute founded in 1994, has led to

novel development of diagnostic tests for prostate cancer.[5] Lung cancer research at the Department of Pulmonary and Critical Care, University of Toledo Medical Center in Toledo, Ohio, resulted in successful next-generation sequencing studies to identify variations in the human genome that affect cancer incidence, known as RNA polymorphisms.[6] The Canary Prostate Active Surveillance Study (PASS) involved several institutions in California, Texas, Missouri, and others with more than 900 men contributing data for genome-wide association studies to identify sequence-specific drug targets.[7] The Mayo Clinic biobank houses data from more than 50,000 patients with quality controls and samples for multiple disease processes, including several types of cancers, and researchers can access approximately 23,000 serum samples from 17,000 patients.[8]

Our comprehensive community cancer program at St. Joseph Hospital in Orange, Calif., has developed and actively maintained a cancer research program for nearly 30 years. We remain among the most active of Orange County community hospitals that participate in clinical trials, with a dedicated staff of full-time research professionals who review and implement new studies for our patients. In the past year alone, The Center for Cancer Prevention and Treatment at St. Joseph Hospital saw 1,565 new patient analytic cases, of which 391 (25 percent) consented for one of the 48 available clinical studies across several disease sites.

In this article, we describe the importance of the national biobanking effort and our ongoing success with the St. Joseph Hospital (SJO) Biospecimen Repository. The Biospecimen Repository received formal Institutional Review Board (IRB) approval in 2011, with ongoing participation in several data sharing projects.

A Brief History of the SJO Biospecimen Repository

The SJO Biospecimen Repository began as part of the combined efforts of medical personnel, staff members, and patient donors across several departments at The Center for Cancer Prevention and Treatment. In 2010, the local IRB reviewed and evaluated a written proposal submitted from our interdisciplinary team, which functions as a single institution resource for multiple types of cancer neoplasms. Protocol approval for patient consents and sample collection began on Feb. 1, 2011.

All research proposals and trials receive careful oversight to ensure patient safety and ethical study parameters from the St. Joseph local IRB, which is composed of physicians, statisticians, researchers, community advocates, and others for adequate protection of the rights of our human research participants. The Cancer Research Department is a major contributor to St. Joseph IRB activities. In the spring of 2017, the local IRB received a successful evaluation and obtained national accreditation by the Association for the Accreditation of Human Research Protection Programs.

Within The Center for Cancer Prevention and Treatment, the

After the patient has signed study informed consent, supplies are placed in the chart for draw at the time of IV placement in the pre-operative area.

Cancer Research Department brings together the varied interests of many departments that interact with our cancer patients, from those in primary care to disease site specialists in oncology, radiation, surgery, genetics, and pathology. Cancer research has been identified as a key priority for the hospital's 2015-2020 Innovating for a Healthier Community campaign (sjo.org/campaign) that pledges philanthropic support for accessibility to research studies and translational outcomes for cancer patients at St. Joseph.

Main Objectives of the SJO Biospecimen Repository

The specific aim of the repository is to collect biospecimens for use in research from patients undergoing intervention, biopsy, or surgery. Protocols are carefully followed to ensure sample quality and reliability for scientific analyses. Samples can be allocated to projects leading to the discovery of genomic and proteomic biomarkers related to tumor burden, therapeutic response, and treatment-related toxicities. In addition, the tissue can be used to test new treatment strategies in both benign and malignant conditions. Biospecimen procurement for research occurs within the clinical pathways of the institution as a routine daily procedure.

In our experience, patients give consent for their biospecimens to be used for research in the hope that the resulting knowledge might help other patients in future years. Our goal is to have every patient undergoing a cancer-related screening or treatment procedure provide informed consent to store his or her tissue for potential research purposes.

Currently, the SJO Biospecimen Repository has the flexibility to address all types of research projects by internal investigators and outside partners through an open-access policy that is available to researchers upon project review.

An Increased Need for Biospecimens

The need for specimens dedicated to cancer research is on the rise. A retrospective analysis evaluated more than 400 publications from investigators studying breast, lung, and ovarian disease processes. In the past decade, the average number of biospecimens used per study increased six-fold (<1,000 to greater than 6,000), and the average cohort size increased from approximately 50 to 200 cases.[9] In another study of more than 400 publications related to cancer research between 2010-2014 by Canadian investigators, 38 percent of studies used biospecimens obtained from either biorepositories (31 percent), hospitals (46 percent), or directly from patients (17 percent).[10]

The SJO Biospecimen Repository infrastructure and support system meets the need for readily available samples that can be routinely used for research. Especially important are analyses that identify key surface markers and immunogens needed for individualized medical treatment.

Ensuring the highest quality of samples is a high priority for the SJO Biospecimen Repository. Due to the need for high quality samples and the use of appropriate sampling procedures for every aspect of the collection and dissemination process, biorepository operations have become highly complex. As a result, the biorepository community is increasingly focused on standardization and harmonization of technical and operational practices.

> Information about biospecimens is most useful when linked to relevant clinical data. As such, relevant clinical details related to the specimen and patient are recorded in a secure database linked to the specimen code.

Approaching the Right Patients

All patients who undergo a surgical procedure as part of their cancer diagnosis or therapy are considered for participation in the SJO Biospecimen Repository. The Cancer Research Department has dedicated staff and a lab technician who manages daily referrals of patients from both hospital-employed and private practice multispecialty oncologic physicians affiliated with St. Joseph Hospital. Specimens are obtained during the planned intervention, surgical procedure, and/or at the discretion of the investigator. We have accrued a substantial collection of biospecimens obtained under highly standardized conditions that include benign, diseased, and/or normal tissue. Currently the SJO Biospecimen Repository has IRB approval for the acquisition of tissue, blood, bone marrow, and urine. This approval allows for the comprehensive collection of all samples from patients diagnosed with common cancers, rare cancers, and metastases, over lengthy periods of time (if required), enabling institutional support of several types of research projects.

The SJO Biospecimen Repository acquires biospecimen samples both prospectively and retrospectively, allowing collection of neoplastic and/or normal tissue and blood alongside corresponding pertinent clinical information. For prospective sample collection, patients are asked to sign an informed consent document at the time of the planned intervention, biopsy, or surgery. The consent form is approved by the IRB in different languages (English, Spanish, Vietnamese, Korean). Additional short-form consents help address the needs of patients who are fluent in other languages. When needed, the SJO Biospecimen Repository offers access to certified interpreters, a service that is provided for all

medical needs at our hospital and is also approved by the local IRB for use during consents to research. For acquisition of archived retrospective tissue samples, the SJO Biospecimen Repository stores samples from paraffin blocks/slides and tissue in formalin. For this patient population, the local IRB has granted a consent exemption as the tissue would otherwise be discarded, per College of American Pathologists and State of California Guidelines.

It is important to note that patients approached for participation with the SJO Biospecimen Repository are already scheduled for a procedure as part of their diagnostic and/or follow-up evaluation. Only after the collected sample has met the primary intended use for the patient, can any remaining portion of that sample be allocated for use in biospecimen research. Therefore, tissue procured for the SJO Biospecimen Repository is in excess of what is required for pathology evaluation and patient care.

A 2002 study described evidence based on feedback from donors and favorable consent rates, noting that many patients who desired and could benefit from biobank donations, were in fact not offered the opportunity.[11] However, the pre-operative approach and consent paradigm has received criticism as a barrier because of its design, which may actually limit the opportunities for patients to donate to larger biobanks.[12] While the pre-operative approach is common practice, it remains important to explore alternatives for consent and sample acquisition across a broader spectrum to maximize research participation.

In our experience overall, educated staff members and an optimal workflow can improve the ease of biospecimen donation. Patients agree to donate the excess samples for research, after diagnostic or other pathology criteria are met, and do not undergo a separate procedure or office visit only for the biospecimen program. Prior research studies vary in reporting actual screening and consent rates of patients who agree to participate in biospecimen research. For SJO Biospecimen Repository prospective samples where consent is required, the agreement to donate excess samples to research is approximately 90 percent of all those approached pre-surgery. While several measures are in place to ensure the ease of donation, barriers still exist and need to be identified and addressed to further improve knowledge and education about the importance of sample use in research.

Ensuring Sample Quality at Storage & Beyond

All biospecimens are collected and stored according to standardized techniques for subsequent use. Generally, samples include adult patients between the ages of 18 to 90 who receive surgery due to 'standard of care' procedure or perhaps a clinical trial or 'study driven' procedure. Once the initial sample is obtained, the on-site pathologist assesses adequacy of the tumor and normal tissue for diagnosis and biospecimen acquisition. With the availability of standardized lab reports, the SJO Biospecimen Repository can ensure that donors are disease-free, or have a pathologically confirmed or presumed diagnosis of neoplasia or other diseases. Specimens are provided a code and stored in appropriate media and temperature conditions as required for future access. For example, samples can be either formalin-fixed and paraffin-embedded, or undergo snap freezing with liquid nitrogen or dry ice/alcohol slurry.

Information about biospecimens is most useful when linked to relevant clinical data. As such, relevant clinical details related to the specimen and patient are recorded in a secure database linked to the specimen code. Data may include demographic characteristics and complete medical history, including cancer evaluation, diagnostic tests or imaging, treatment, trial participation (if any), and outcome. Data using specimens for scientific projects requires review and approval from members affiliated with the biospecimen program, and may be submitted for IRB approval as needed on a per-project basis. This process ensures confidentiality and adheres to best practice guidelines for protection of human subjects in research.

Lawrence Wagman, MD, executive medical director; program director, Wellness Program, at St. Joseph Hospital—The Center for Cancer Prevention and Treatment.

Figure 1. Participation in the SJO Biobank

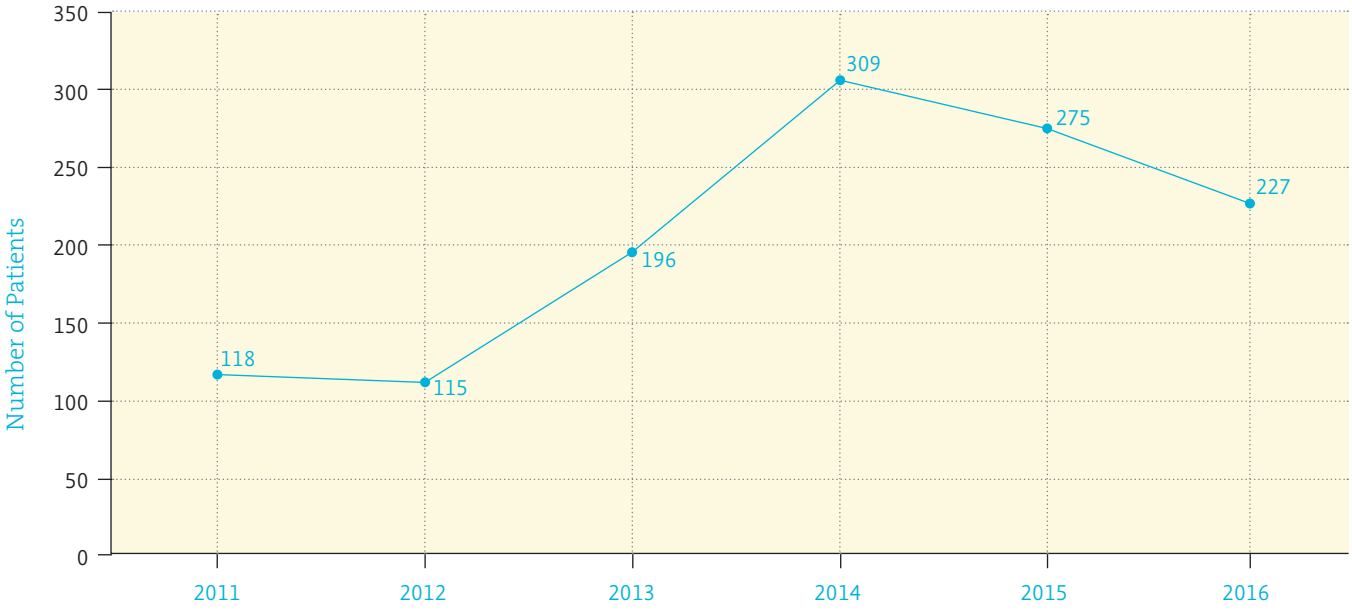

Figure 2. Age Distribution of Participants in the SJO Biobank

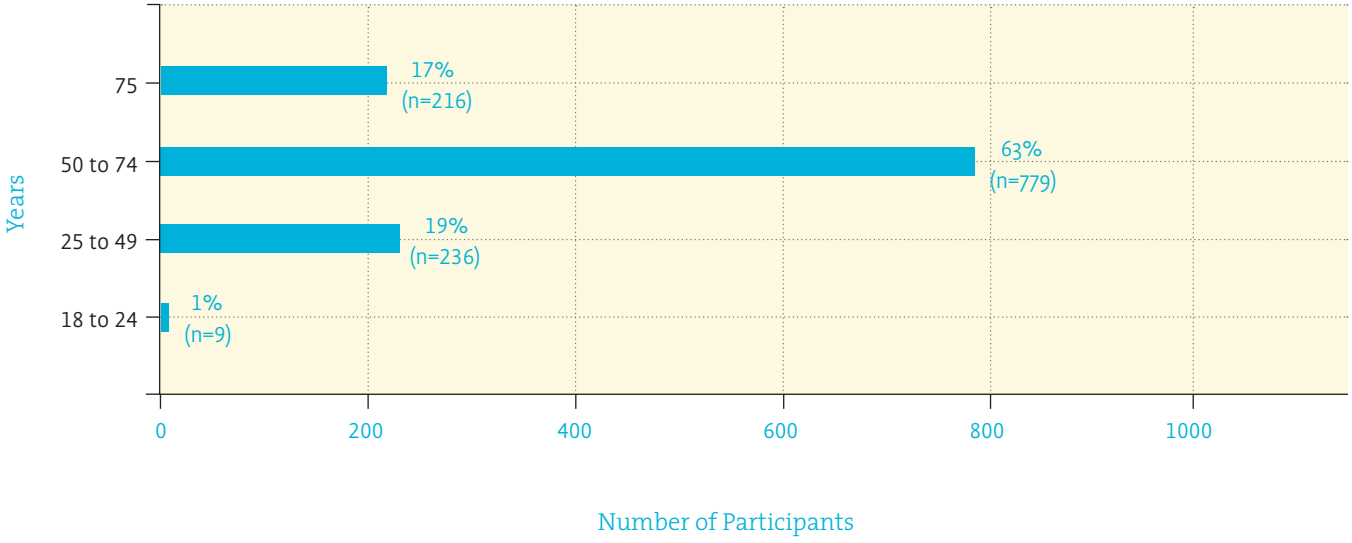

Table 1. SJO Biobank Patient Demographics		
	TOTAL (n)	PERCENTAGE
ETHNICITY		
Hispanic or Latino	118	9.5%
Not Hispanic or Latino	365	29.4%
Unknown (not reported)	757	61.1%
Total Participants	1,240	100.0%
RACE		
White	354	28.5%
Asian	46	3.7%
Black or African-American	7	0.6%
Native Hawaiian or Other Pacific Islander	6	0.5%
American Indian or Alaskan Native	3	0.2%
More Than One Race	3	0.2%
Unknown (not reported)	821	66.3%
Total Participants	1,240	100.0%

Highlights of the SJO Biospecimen Repository Samples

The Center for Cancer Prevention and Treatment sees approximately 1,500 to 2,000 cancer cases per year, with about a quarter of those individuals agreeing to participate in a research study. For example, in the year 2014 there were 1,830 cases accessioned by the cancer registry, from which 1,565 analytical cases (over 85 percent of accessioned cases) were diagnosed and/or treated at St. Joseph Hospital. In 2015 alone, approximately 25 percent of patients from analytical cases consented to one of the 48 available clinical studies across several disease sites.

The data below provide information from all samples obtained for the SJO Biospecimen Repository during a period of approximately six years from the time of IRB approval on Feb.1, 2011, through Dec. 31, 2016. Prior to this time frame, archived tissue exists, likely in the form of formalin-fixed and paraffin-embedded blocks that were routinely stored according to hospital policy for approximately ten years after completion of standard-of-care procedures. Archived tissue may be accessed for special research projects upon request and project approval. Importantly, all data presented below reflect only the sample distribution accrued specifically to the SJO Biospecimen Repository between 2011 and 2016, after the completion of any standard-of-care sample procedures related to the patient's intervention, biopsy, surgery, or pathological analyses.

The annual number of patients who consented to the SJO Biospecimen Repository each year from the start of the study in 2011 through the end of 2016 is shown in Figure 1, page 41. There is a rapid spike in patient participation in the first few years, likely due to increased recruitment efforts and knowledge about the program among physicians, staff members, and patients. There is nearly a three-fold increase in the number of consents between 2011 (n=118 patients) to 2014 (n=309 patients). Although the number of consents since 2014 has decreased, this likely represents a stabilization of the annual rate of participation over time. Overall, 1,240 unique patients consented to the SJO Biospecimen Repository during the time frame of approximately six years.

Biospecimen Patient Demographics

The SJO Biospecimen Repository acquired samples from 1,240 unique patients who were considered as potential contributors for biospecimen donation. The following are a few general characteristics of these patients. There is a disparity according to gender, with a greater number of female patients (70 percent, n=867) versus male patients (30 percent, n=373) overall. In other studies and reports, the gender gap is somewhat smaller with about 60 percent females.[6,13] Our data distribution by age is shown in Figure 2, page 41, with approximately two-thirds of patients in the range of ages 50 to 74 (63 percent), with adequate representation of patients under age 50 (20 percent), and several patients aged 75 years and up (17 percent). Interestingly, the age distribution of patients contributing to our biorepository closely matches the Mayo Clinic Biobank, which has a total of 50,000 patients. The Mayo program subjects are approximately 22 percent under age 50, about 60 percent between ages 50 to 74, and about 18 percent age 75 and up.[8]

Race and ethnicity data from the SJO Biospecimen Repository is shown in Table 1, left. While there is a fair amount of representation of minority populations, including Asian, Hispanic or Latino, and African-American individuals, it is important to note, however, that a large component of these data are currently unreported to the biospecimen program. There is an ongoing process underway to obtain ethnicity information from other existing hospital record systems.

Pictured Front Row (L to R) Martha French, RN, MSN, clinical research nurse; Viorela Pop, PhD, clinical research associate; Lavinia Dobrea, RN, MS, OCN, manager, Oncology Research & Biospecimen Program; Rachelle Alquitela, BS, clinical research associate; Virginia Trujillo Castro, RN, BSN(c), clinical research nurse. Back Row (L to R) Sonia LaBeet, executive assistant; Noah Gonzalez, biospecimen technician; Ron Bati, clinical research associate; Melinda Lima, RN, BSN, clinical research nurse.

Sample diversity remains an important factor in biospecimen research. For example, patients with a cancer diagnosis may require additional educational materials to make informed decisions about research participation and financial implications. In a recent analysis of 110 surveys from cancer research subjects, about 90 percent of participants reported being Caucasian with low representation of minority groups.[14] In the same study, more than 50 percent reported limited risk/benefit assessment of trial participation, which correlated with sociodemographic factors like increased age and lower education level.[14] When requesting biospecimen donations, a survey of more than 400 individuals identified the importance of addressing cultural factors. In a community setting during educational outreach programs to ethnic minority groups, Asian participants were more likely to agree to the donation of blood for hepatitis and liver cancer research.[13] The SJO Biospecimen Repository continues to collect a variety of information about patients that may assist in the advances of personalized treatment and therapeutic efficacy.

Biospecimen Sample Types

From the 1,240 unique patient donors, there have been patients who have the ability to donate from multiple anatomical sites and sometimes donate samples on more than one occasion. Therefore, these donors have resulted in a log of 1,364 possible unique sample collections and a total of 2,508 total samples collected as described in Table 2, below. The 2,508 total samples consist of three main category types, namely 38.7 percent blood samples (n=971), 32.5 percent tumor samples (n=814), and 28.8 percent normal samples (n=723). In many instances,

Table 2. SJO Biobank Sample Types

	TOTAL (n)	PERCENTAGE
SAMPLE TYPE		
Blood	971	38.7%
Tumor Tissue	814	32.5%
Normal Tissue	723	28.8%
Grand Total Samples	2,508	100.0%
CORRESPONDING SAMPLE COLLECTIONS (blood, tumor tissue, normal tissue)		
All three sample types available	537	39.3%
Only two sample types available	250	18.3%
Blood and tumor tissue only	70	
Blood and normal tissue only	10	
Tumor and normal tissue only	170	
Only one sample type available	397	29.1%
Blood only	354	
Tumor tissue only	37	
Normal tissue only	6	
No sample donation for research available	180	13.2%
Grand Total Collections	1,364	100.0%

Table 3. SJO Biobank Sample Availability

	TOTAL (n)	PERCENTAGE
BLOOD SAMPLES		
With additional tumor and/or normal tissue	617	63.5%
With both tumor and normal tissue	573	
With tumor tissue only	70	
WIth normal tissue only	10	
Without any additional samples available	354	36.5%
Total Blood Samples	971	100.0%
TUMOR TISSUE SAMPLES		
With additional normal tissue and/or blood	777	95.5%
With both normal tissue and blood	537	
With normal tissue only	170	
With blood only	70	
Without any additional samples available	37	4.5%
Total Tumor Tissue Samples	814	100.0%
NORMAL TISSUE SAMPLES		
With additional tumor tissue and/or blood	717	99.2%
With both tumor tissue and blood	537	
WIth tumor tissue only	170	
With blood only	10	
Without any additional samples available	6	0.8%
Total Normal Tissue Samples	723	100.0%

patients may contribute one or more sample types, depending on their cancer specification, willingness to donate, and/or tissue availability after standard-of-care procedures. As such, of the 1,364 unique sample collections available, 39.4 percent have all three sample types available for analysis, while 18.3 percent have two sample types, and 29.1 percent have only one sample type available. On occasion, logistical reasons related to patient care (e.g., insufficient sample or cancelled procedure) result in a lack of sample acquisition for the SJO Biospecimen Repository. However, such instances of missed sample collections comprise only 13.2 percent of the total sample collections consented but not acquired. Given the relatively few years of active biobanking and limitations acquiring samples using the pre-operative approach and consent paradigm, our results indicate that research participation is attainable and productive in a community setting.

Table 4. SJO Biobank Tissue Samples by Disease Site				
DISEASE SITE	BLOOD SAMPLE	TUMOR TISSUE	NORMAL TISSUE	GRAND TOTAL (n, %)
Breast	221	182	184	587 (23.4%)
Colorectal	84	85	84	253 (10.1%)
Endocrine	9	10	7	26 (1.0%)
Gastric	16	12	11	39 (1.6%)
Genitourinary	34	29	27	90 (3.6%)
Gynecologic	96	90	75	261 (10.4%)
Head and Neck	87	63	54	204 (8.1%)
Hepatobiliary	148	109	101	358 (14.3%)
Lymph Node	24	21	11	56 (2.2%)
Neuro-oncology	29	37	7	73 (2.9%)
Other	43	50	39	132 (5.3%)
Skin	4	6	6	16 (0.6%)
Thoracic	176	120	117	413 (16.5%)
Total Samples	971	814	723	2,508 (100.0%)

Samples & Their Corresponding Specimens

The data in Table 3, page 45, further evaluates the availability of individual sample types and corresponding specimens from the same collection time point. When assessing the blood samples alone, more than two-thirds (63.5 percent, 617 of 971 total) have additional normal and/or tumor tissue available alongside the blood sample. Almost all normal samples (99.2 percent, 717 of 723 total) have corresponding analytes from either a tumor site or blood sample. Most importantly, 95.5 percent (777 of 814 total) of all tumor tissue samples have either corresponding normal tissue and/or blood available for evaluation alongside the tumor specimen. Only a small 4.5 percent of tumor specimens lack corresponding samples for evaluation. This data exemplifies our ability to provide multiple sample types for each case that reaches the SJO Biospecimen Repository, therefore increasing possible research advances for individual patients.

Available Disease Sites

The data in Table 4, above, organizes all 2,508 available samples according to the type of sample and its corresponding disease site. Of all samples, the largest category is breast tissue that comprises nearly a quarter (23.4 percent) of the total samples existing in the biobank. Following breast tissue, the most abundant sample category is thoracic (16.5 percent), which is mostly composed of the lung site. Hepatobiliary (14.3 percent) samples include all liver, pancreas, and gall bladder disease sites, followed by gynecologic (10.4 percent), colorectal (10.1 percent), head and neck (8.1 percent), neuro-oncology (2.9 percent), and genitourinary (3.6 percent) cancer types. Each of the additional cancers such as endocrine, gastric, lymph node, and skin comprise less than 2 percent each of the total samples available in the biobank. The "Other" category (5.3 percent) includes any cancers in other areas such as the abdomen, pelvis, bone, or skeletal regions. The wide variety of samples available in the biobank reveals our ability to obtain a diverse set of disease sites for research purposes.

Collaborative Endeavors

Ultimately, biospecimen repositories contribute to the overall knowledge base to advance valuable insight into precision cancer care. By providing essential biologic samples, as well as comprehensive demographic and diagnostic records, the SJO Biospecimen Repository allows investigators to have access to the necessary tools for the pursuit of specific research projects. Often, successful cooperation with outside partners can benefit the larger goals in cancer research. For example, the SJO Biospecimen Repository contributed hundreds of archived tissue samples, which were collected prior to the start of the SJO Biospecimen Repository in 2011, to assist the research analyses of a third-party collaborator. In a recent study, investigators utilized the SJO Biospecimen Repository to optimize a next-generation sequencing tumor assay and showed that concurrent analysis of tumor and germline DNA improved testing accuracy and interpretation.[15]

Future Considerations

While challenges remain, they are surmountable and every sample counts and can make a difference. Next-generation science and innovative policies can be leveraged to make the best treatments available to patients. A single institution biorepository can have a consistent and effective contribution to translational science. In a pediatric tumor bank, the authors note that excellence in simple biobanking practices adequately meet the needs of major efforts with genomics that can enable the advancements expected for translational research.[4] As another group of researchers elegantly stated, "For donors, it often means having the opportunity to contribute their biospecimen and health data to drive research that can address their specific disease. For biobanks, it means access to potential donors to seek their consent to accrue biospecimens. For research users, it means finding and obtaining the right biospecimens within biobanks and navigating regulatory and oversight processes.[12]

A cancer biospecimen repository should continue to meet recommendations as outlined by the Blue Ribbon Panel in their September 2016 report to the National Cancer Advisory Board (cancerresearchideas.cancer.gov/#CancerResearchIdeasArchive). Common themes in the report included:

- Prevention and early detection
- Involvement in clinical trials
- Data sharing among centers
- Pediatric cancers
- Tumor evolution
- Standardization of biospecimens collection and processing
- Enhanced communication between the donors and biobanks
- Public engagement around biobanking.

The SJO Biospecimen Repository continues to align with these recommendations and refine processes to ensure goals are met. There is a need for quick improvement on the research front of personalized medicine. This is especially true for understanding the benefits of minimally-invasive biopsies (e.g., liquid or aspiration biopsies), the meaning of genetic differences between sample types and genetic changes over time, and the improved correlations between imaging and pathology findings of the same tissue. One example of using multiple modalities was in breast cancer patients. In a prospective analysis comparing data from core-needle biopsy identification of ductal carcinoma in situ alongside specific pre-operative features, researchers proposed an algorithm to assist in a better evaluation of risk factors during staging, diagnosis, surgery, and additional treatment planning.[16] The evolution of metastatic disease also remains a high priority, and there is a need to further explore the biological and environmental reasons for the occurrence of metastases in some tissues, while other sites are spared. For example, by collecting metastatic and non-metastatic tumor samples, liquid and normal samples, biospecimen repositories can provide resources that will generate data and knowledge for discovery. It also remains important to continue advances in the discovery of precise driver mutations, treatment targets, prognostic factors, and protective factors to improve curative therapies in oncology.

As years pass and samples accrue, it's important to prepare for changes in operational logistics and implement procedures related to biobank legacy planning.[17] The operational phases following continued sample collection, immediate and long-term use, collaborative distribution, and project completion will necessitate best practices for transfer and/or destruction of materials as samples become unusable.

There are also considerations regarding databases for local tracking and for collaborations. As translational genomic research becomes an international collaborative effort, biobanking networks have become more common.[5,12,18] One network sharing model uses a computer-based Text Information Extraction System (TIES) across several cancer centers. It allows management of biospecimen data and resources at the institutional level, and facilitates collaborations within regulatory guidelines among member institutions.[18] Computerized systems can also help track information effectively and easily, as exemplified by the iPhone interface for project management.[5]

St. Joseph Hospital is actively participating in collaborations that engage the community. With continued vigilance over all aspects of the SJO Biospecimen Repository, the biorepository remains a key step to the advancement of scientific progress and beneficial outcomes for patients and families. OI

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ACCC INTRODUCES

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2016 FAN Learning Labs

Practical strategies to address financial toxicity

FINANCIAL ADVOCACY NETWORK (FAN)

Resources & Tools for the Multidisciplinary Team

As the cancer community gains a deeper understanding of how financial burdens impact patient care, more emphasis is being placed on effective interventions that can minimize financial toxicity. Studies have shown that financial toxicity is associated with greater pain, more symptom burden, and poorer quality of life in cancer patients undergoing active treatment.[1] While the immediate costs of treatment often cause distress during the active treatment period, a review of 25 research studies found that up to 78 percent of cancer survivors continue to experience financial hardship due to their cancer diagnosis and treatment.[2]

The ACCC Financial Advocacy Network

Cancer programs are all on different parts of an ongoing journey to provide better financial counseling, navigation, and advocacy services to patients. Since 2011, ACCC has led national efforts to provide practical education, training, tools, and resources through its Financial Advocacy Network (FAN) initiative. In 2016 and 2017, ACCC continued the FAN initiative with a series of case-based regional workshops, on-site learning labs at member cancer programs, and the launch of the Financial Advocacy Boot Camp (accc-cancer.org/FANbootcamp). To date, more than 1,200 individuals have enrolled in this online course.

FAN Case-Based Regional Workshops

In 2016, ACCC held three case-based regional workshops for financial advocates, counselors, social workers, administrators, and clinicians. The 2016 FAN workshops were held May 23 in Cleveland, Ohio; Aug. 17 in Dallas, Tex.; and Sept. 29 in Philadelphia, Pa. Attendees at each meeting were actively engaged in learning as they spent time discussing de-identified patient cases in small groups and listened to presentations. The patient cases illustrated real-world examples of financial interventions that could transform a patient's experience by effectively reducing the financial burden associated with various treatments. The cases included a mix of common cancers (lung and colon cancer) and less common cancers (lymphoma). The all-day sessions wrapped up with actionable takeaways on how to apply process changes and implement effective practices for financial advocacy within a community cancer program. Highlights from the meetings include:

- ***Recognizing and proactively assisting patients who are underinsured.*** Although most patients now have some form of health insurance, those with high out-of-pocket responsibilities and/or those with limited income may be functionally underinsured. Proactive interventions can help some of these patients, if implemented in a timely fashion.
- ***Understanding the complexities of Medicare and the need to educate clinicians and patients about all the different options.*** This includes Medicare Advantage, Medicare Supplement (Medigap), Medicare Select, the four types of Medicare Savings Programs, Medicare Low Income Subsidy (Extra Help), and much more.
- ***Improving communication across all members of the cancer care team regarding the patient's financial questions and concerns.*** Since this information is often not documented in the patient's electronic health record (EHR), it may be difficult for clinicians to know how these concerns are impacting the care journey. Improving those lines of communication could lead to more proactive ways to reduce financial toxicity.
- ***Establishing processes and metrics to track the financial savings achieved by the financial advocacy team.*** Almost every cancer program may direct patients to pharmaceutical drug assistance programs, but some cancer programs have difficulty tracking this information and coordinating reimbursement with their billing office.

FAN Learning Labs

In 2016, ACCC also went on-site and conducted Learning Labs at four member programs in August and September. Learning Lab attendees spent several hours discussing how they currently provide financial advocacy services and identified specific and practical opportunities for improvement. The 2016 FAN Learning Lab sites were:

- Ohio Valley Medical Center in Wheeling, W. Va.
- NewYork-Presbyterian Weill Cornell Medical Center, New York, N.Y.
- St. Luke's University Health Network Cancer Program, Easton, Pa.
- Nebraska Medical Center, Omaha, Nebr.

Following the Learning Labs, each cancer program developed and implemented several process improvement plans using the Plan-Do-Study-Act (PDSA) cycle for improvement and then reported their progress to ACCC after three months. Below are strategies from these improvement plans, including practical strategies for cancer programs looking to address financial toxicity. Access the PDSA Worksheet and user instructions at: ihi.org/resources/Pages/Tools/PlanDoStudyActWorksheet.aspx.

Strategy 1. Establish Processes to Proactively Address Financial Distress

As a cancer patient receives treatment, the financial burden may evolve over the course of time. Therefore, cancer programs should have a systematic process in place to screen for financial distress to proactively address concerns in a timely fashion.

Routine psychosocial distress screening processes may not consistently identify cancer patients who are at-risk of experiencing significant financial distress. Cancer patients generally pay higher out-of-pocket costs compared to patients suffering from other chronic conditions.[3] Some have suggested that financial burden and financial toxicity should be assessed based on whether cancer patients accrued debt, sold assets to cover treatment costs, skipped vacations due to financial pressures, refinanced their home, borrowed money, or experienced a 20 percent or greater decline in their annual revenue as a result of treatment-related expenses.[4] Researchers have also proposed specific questionnaires designed to reliably measure financial toxicity in cancer patients.[5] While it may not be practical or feasible to use these research instruments in routine practice, cancer programs may consider modifying their current distress screening tools to better identify patients who are at-risk for experiencing significant financial distress.

Many cancer programs use screening tools, such as the NCCN Distress Thermometer, but they may not be capturing every patient who may benefit from early financial counseling interventions. Several of the cancer programs that participated in the FAN Learning Labs agreed that they could improve how they identify cancer patients who may benefit from receiving financial advocacy and counseling services earlier in their course of treatment.

To continue improvements spurred by the FAN Learning Lab, St. Luke's University Health Network Cancer Program identified the need for a lead financial counselor role. The financial counseling team developed a process to provide financial counseling services as early as possible. When new patients call to schedule their initial appointment, new patient schedulers now follow this process:

- ***Step 1.*** Gather and review health insurance information at the time of appointment scheduling.
- ***Step 2.*** Check and review a list of criteria to see if the patient meets the requirements for a referral to financial counseling.
- ***Step 3.*** Refer patients who meet criteria for financial counseling.

This practical, easily replicable process has led to more patients being seen by financial counseling before their first visit.

At St. Luke's University Health Network Cancer Program, new patients who have been referred for financial counseling have received guidance or interventions that have helped reduce or minimize their risk for experiencing financial toxicity. Some of these interventions may include a change to better health insurance coverage or awareness of different types of patient assistance programs. Since health insurance policies and coverage details change at the beginning of each calendar year, the financial advocacy team spends time educating the schedulers about these major updates. The new process has led to more communication and feedback between the schedulers and the financial advocates. Given that the schedulers are now spending more time on the phone when new patients call for appointments, the cancer program has recognized the need to hire additional schedulers.

Nebraska Medical Center made changes in its EHR to include more specific questions about financial distress. The routine distress screening tool that had been built into the EHR simply did not have enough financial-specific questions. After Nebraska Medical Center made changes to incorporate additional financial distress questions, it worked with the IT team to generate reports based on these newly added questions. Each month, the financial advocacy team reviews these reports and assesses how well they are proactively providing interventions for patients who are experiencing financial distress.

Practical Suggestions for Improvement

- Consider modifying screening forms and questionnaires to include more questions about financial distress.
- Assess whether some cancer patients may benefit by receiving financial counseling earlier in their care journey.
- Discuss whether all of the appropriate patients are receiving financial counseling. If some are getting missed, explore ways to capture those patients earlier in their treatment course.

Strategy 2. Develop Processes for Improving Health Literacy

Limited health literacy has been linked to worse clinical outcomes in cancer patients because they have a limited capacity to obtain, process, and understand information about the services they are receiving.[6] Healthcare bills and Explanation of Benefits (EOB) letters may cause significant anxiety, especially when patients do not understand what they are reading.[7] Researchers have stressed the importance of educating and engaging patients around the topic of financial distress.[8]

At NewYork-Presbyterian, the financial advocacy team committed to proactively communicate with patients to alleviate their anxieties about medical bills. The team recognized that some patients would form piles of unopened medical bills at home because they knew that they would not be able to pay those bills. Patients would not answer their phones when the hospital would call, fearing that those calls would be from the billing department. The financial advocates developed a process to speak with patients

at every appointment to alleviate those concerns and to assure them that they would find ways to find assistance programs. The financial advocates also encouraged patients to bring those bills and EOBs with them to their clinic visits so they could help them understand what was written in those letters. The team recognized that patients appreciated learning how to interpret their bills, and they felt a sense of relief when they knew that an EOB was not a medical bill.

Practical Suggestions for Improvement

- Use visual aids and easy-to-understand materials when explaining health insurance terms to patients.
- Offer to educate patients about specific issues like the difference between an EOB and a medical bill, the difference between co-pay and coinsurance, etc.
- Provide patients with ongoing reassurance that financial advocates and counselors are there to help and support patients through their treatment journey.

Strategy 3. Guide Patients through the Medicare Maze

Every cancer program that participated in the FAN Learning Labs agreed that the Medicare landscape can be very confusing for patients. There are so many options, and providers and patients often get terms confused or may not know about programs and resources that are designed to help Medicare beneficiaries. Medicare is so complex that patients often get lost in the Medicare "maze" of options that include Medicare Supplement Plans; Medicare Advantage Plans; Medicare Parts A, B, C, and D; and much more.

At the Ohio Valley Medical Center, the financial advocacy team used a two-pronged approach to provide education about Medicare coverage and options:

1. Educate clinicians and support staff so they can speak more clearly and effectively with patients about Medicare.
2. Educate patients prior to Medicare open enrollment so patients can make better coverage decisions.

To educate patients, Ohio Valley Medical Center's financial advocacy team developed a public educational seminar and promoted this to eligible patients prior to the Medicare open enrollment period. The education has helped new Medicare patients become more knowledgeable about their options. However, many existing Medicare patients still continue to struggle because they lack prescription drug coverage (Part D) or do not have supplemental coverage. Ohio Valley Medical Center saw the value of educating clinicians and support staff about some of these topics, so their compliance department now requires staff to participate in training focused around specific parts of Medicare.

Nebraska Medical Center also saw the benefit of proactively educating staff and patients about Medicare issues, so it trained financial counselors to provide individualized education about Medicare options to patients throughout the year. Financial advocates became more knowledgeable about the different types of Medicare options including the four types of Medicare Savings Programs:

1. Qualified Medicare Beneficiary Program
2. Specified Low-Income Medicare Beneficiary Program
3. Qualifying Individual Program
4. Qualified Disabled and Working Individuals Program.

The team also learned about Medicare Extra Help for Part D, also called the Low Income Subsidy.

Practical Suggestions for Improvement

- Consider providing a patient education seminar about Medicare before the open enrollment period.
- Provide staff with ongoing training about important Medicare topics and issues, including the four types of Medicare Savings Programs and Extra Help for Part D.
- Be sure that patients and staff clearly understand the differences between Medicare Supplement Plans versus Medicare Advantage Plans, as these are often confused or misunderstood.

Strategy 4. Improve Coordination During Care Transitions

At NewYork-Presbyterian, the financial advocacy team recognized an opportunity to improve the patient experience as cancer patients are discharged from the hospital and begin their outpatient chemotherapy. Before NewYork-Presbyterian made changes, patients who were discharged had to call several different phones numbers to schedule clinic appointments and chemotherapy treatments because the scheduling systems were not linked. Moreover, some patients might have experienced delays in outpatient treatments because the necessary prior authorizations were not completed in a timely fashion. To minimize these delays and frustrations, NewYork-Presbyterian instituted a new process when hospital inpatients were preparing to be discharged:

- The hospital social worker or financial advocate would coordinate and schedule the outpatient clinic and treatment appointments before the patient leaves the hospital.
- The outpatient treatment center would receive all the health

insurance information and begin the process of filling out the required paperwork and prior authorizations to ensure that treatments could begin in a timely fashion.

This process has led to significant improvements in care coordination, reduced delays in treatments, and improved patient experience scores. The multidisciplinary cancer team continues to discuss how it may improve care coordination as patients transition from the inpatient to the outpatient setting. In 2017, NewYork-Presbyterian will be switching to a centralized scheduling system to streamline outpatient clinic and treatment schedules.

Practical Suggestions for Improvement

- Identify opportunities to improve care coordination as patients transition from inpatient care to outpatient treatment plans.
- Hold meetings with the inpatient and outpatient social workers and financial advocates to uncover gaps or delays that may occur during care transitions.
- Collect feedback from patients about their experience transitioning from inpatient to outpatient care to find opportunities for improvement.

Strategy 5. Develop Metrics and a Process to Measure Cost-Savings and the Effectiveness of Financial Advocacy Interventions

While many cancer programs use spreadsheets to manually track some of the financial savings achieved by their financial advocates, this process may not provide enough metrics on the overall effectiveness of the team. During the 2016 FAN Learning Labs, financial advocates and administrators discussed ways to improve tracking and reporting so they can gain a deeper understanding of their effectiveness.

Following its Learning Lab, Nebraska Medical Center built a decision matrix for its financial advocates and trained staff on how they can properly enroll patients into the right patient assistance programs. The ACCC *Patient Assistance and Reimbursement Guide* served as a template as the team created an algorithmic process that every financial counselor could follow to find the right types of patient assistance program. After training its financial advocates, Nebraska Medical Center customized a tracking tool in its EHR by creating a new task that was linked to a report that measures how much time financial advocates spent on patient assistance. The report would also indicate how many patients were being enrolled into patient assistance programs.

Ohio Valley Medical Center developed a financial advocacy tracking sheet to measure how much money this team saves the hospital. Using information from an electronic cancer navigation file that lists every newly-diagnosed patient, the financial advocacy team added columns to that file so they could track the effectiveness of their financial advocacy interventions. The new columns included:

- Original primary insurance
- Secondary insurance
- Deductible and out-of-pocket limits
- New primary insurance
- New secondary insurance
- New deductible and out-of-pocket limits
- Co-pay card assistance monetary amount
- Co-pay card assistance company
- Drug replacement monetary amount and company
- Oral drug co-pay assistance monetary amount and company
- Free oral drug monetary amount and company
- Grant assistance monetary amount and grant program.

Formulas were built into the spreadsheet to calculate and total the monetary assistance that patients received. After creating this tool, the team calculated that they had received nearly half a million dollars ($487,500) in assistance in 2016. The team also discovered that 95 percent of the patients evaluated for financial assistance received some form of assistance.

At NewYork-Presbyterian, the financial advocacy team refined its manual tracking process and collected more detailed information about co-pay and patient assistance programs. Over a period of several months in 2016, the team tracked a savings of $300,000. Moreover, they improved lines of communication with their pharmacy and billing departments to ensure that the hospital was being reimbursed from drug replacement and co-pay assistance programs. Financial advocates made sure to collect the Explanation of Benefits (EOB) paperwork from patients so that they could submit all the required paperwork to receive reimbursement.

Practical Suggestions for Improvement

- Partner with your IT department to develop better reports that reflect the financial advocacy team's time spent on specific tasks and its overall productivity.
- As your program tracks savings from co-pay and patient assistance programs, be sure to track how your hospital is being reimbursed from these programs.

Looking Ahead

Given that financial distress directly impacts overall suffering and quality of life for patients with advanced cancer and their families, cancer programs must continuously find ways to improve how they are addressing financial distress.[9] As cancer programs adopt a mindset of continuous improvement across all the members of the care team, financial advocates and counselors have a special

opportunity to play a role in significantly improving the patient experience. Small changes and structured pilot projects may lead to measurable improvements, especially when those ideas are generated from those providers interacting directly with patients. As mentioned previously, in April 2017, ACCC launched the online Financial Advocacy Boot Camp, a free resource for cancer programs across the country. The Boot Camp is designed to educate and equip financial advocates across five major domains through a series of 14 online learning modules. ACCC remains committed to providing ongoing resources for cancer programs that are looking for ways to improve their financial advocacy services. OI

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Real-World Experiences in Immunotherapy Delivery

In 2016 and 2017, the American Society of Clinical Oncology (ASCO) named cancer immunotherapy the "advance of the year" in its Annual Cancer Progress Report.[1,2] As of May 2017, the U.S. Food and Drug Administration (FDA) has approved immune checkpoint inhibitors for the treatment of many different types of malignances including skin cancers, lung cancer, head and neck cancer, bladder cancer, kidney cancer, and lymphoma. The next evolution of immunotherapy, which ASCO has referred to as Immunotherapy 2.0, focuses on personalizing the use of these agents so that the right patients receive therapies that are most likely to work best in them. Immunotherapy 2.0 also addresses issues around treatment resistance mechanisms and better ways to reduce the toxicities associated with immunotherapy.

While excitement around cancer immunotherapy continues to grow, cancer programs need guidance around practical implications surrounding the real-world delivery of immunotherapy. The ACCC education project, "Real-World Experiences in Immunotherapy Delivery," addresses some of the practical issues that cancer programs must navigate to provide immunotherapy safely and effectively in their own communities.

EMD Serono

This project is made possible by an educational donation from EMD Serono.

For this project, ACCC conducted interviews with cancer clinicians at two ACCC member programs who provided input about their real-world experiences using immunotherapy to treat cancer patients:

- Sandra & Malcolm Berman Cancer Institute at Greater Baltimore Medical Center, Towson, Md.
- The Center for Cancer Prevention and Treatment at St. Joseph Hospital of Orange County, Orange, Calif.

Strategy 1. Identifying Local Experts & Resources

As cancer programs consider how they will be providing immunotherapy for various types of cancers, assessing the levels of experience across members of the cancer care team is an important first step. While some clinicians may have many years of experience using immunotherapies for clinical research, others may have very limited experience and may have difficulty identifying and managing immune-related adverse events (irAEs). Cancer clinicians at The Center for Cancer Prevention and Treatment and the Sandra & Malcolm Berman Cancer Institute noted that the oncologists and nurses who had experience using immunotherapies in clinical trials became recognized as "local experts" and as resources for other oncology providers who were starting to use immunotherapies in their practice. Since some of these local experts may have treated patients using higher doses of immunotherapy agents for clinical trial protocols, they may also have more experience managing more severe forms of irAEs.

Local experts may also provide formal education to other oncologists and nurses in the region. A recent survey of oncologists found that nearly 75 percent report being only somewhat confident or not confident in their abilities to work interprofessionally and manage patients receiving immunotherapy.[3] Since some oncologists are not able to attend annual national educational conferences, there are missed opportunities to inform and educate these providers about the optimal use of immunotherapies in real-world settings. Using grand rounds, tumor boards, and case conferences, the local immunotherapy experts at both The Center for Cancer Prevention and Treatment and the Sandra & Malcolm Berman Cancer Institute have been educating their colleagues about the use of these newer agents by sharing case presentations and reviewing the science of immunotherapy.

Practical Suggestions for Improvement

- Identify local oncologists and nurses with extensive experience using immunotherapy so that they can be a resource for other clinicians in your region. Some may be willing to provide formal education to other providers in established settings, such as tumor boards or grand rounds.
- Increase awareness about ongoing clinical research opportunities around the use of immunotherapy. Some large studies such as ALCHEMIST (The Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trials) now include an immunotherapy treatment arm.

Strategy 2. Coordinating the Management of Immune-Related Adverse Events

Given that immune-related adverse events may be difficult to identify and manage, cancer programs need to educate and engage emergency medicine, urgent care, primary care, and radiology clinicians about the unique differences between irAEs and toxicities that may occur from standard chemotherapy or the use of molecularly targeted agents. Some of the main irAEs associated with checkpoint inhibitors include:[4]

- Diarrhea
- Colitis
- Hepatitis
- Skin problems
- Hypophysitis (inflammation of the pituitary gland)
- Pneumonitis
- Thyroid dysfunction.

Early recognition and proper treatment remain essential in patients receiving treatment with immunotherapy agents.[5]

Emergency medicine clinicians may not recognize that certain symptoms are irAEs, so patients may not receive the required

therapies in a timely fashion. For example, cancer patients treated with certain immunotherapies may develop gastrointestinal symptoms that require urgent treatment with high doses of corticosteroids. If the emergency room clinicians do not identify the problem and coordinate care with medical oncology, then the patient may leave the ER hydrated, but inadequately managed. The use of high doses of corticosteroids remains a critical component of the treatment algorithm when cancer patients treated with immunotherapy present with emergent symptoms.[6]

In another example, a patient may undergo a radiologic study and the radiologist may not recognize that the unusual findings are due to an irAE or may be due to a phenomenon known as pseudoprogression. Radiologists may need to learn how to distinguish hypophysitis from other brain abnormalities on MRI scans.

The team at St. Joseph Hospital of Orange County The Center for Cancer Prevention and Treatment is planning a formal education project for their emergency medicine clinicians. Their nurses are also involved with the International Association for the Study of Lung Cancer (IASLC) nursing committee and have been corresponding with nurses around the world about the optimal management of irAEs in the real-world setting. The team is currently planning to deliver a series of educational in-service programs for teams of emergency medicine providers and nurses who work at their hospital. Some of the irAE topics to be covered are pneumonitis, colitis, rashes, and other common reactions. The educational curriculum will be based on resources like the Oncology Nursing Society "Putting Evidence into Practice: Immunotherapy-Induced Diarrhea."[7]

In addition to educating emergency department clinicians, St. Joseph Hospital of Orange County The Center for Cancer Prevention and Treatment is evaluating other ways to educate and inform patients and family members about the differences in immunotherapy toxicities. One consideration is to provide patients with some form of identification, such as a laminated medical identification card that informs emergency medicine clinicians that the patient is on an immunotherapy agent for cancer. This type of card can help empower patients and family members to advocate for emergency care that is always coordinated with oncology providers. In addition to providing the card, clinicians are spending extra time to educate patients about immunotherapy using resources, including:

- ASCO Answers: Understanding Immunotherapy[8]
- The American Cancer Society's, *What is Cancer Immunotherapy?*[9]
- The American Lung Association's, *What You Need to Know About Lung Cancer Immunotherapy*,[10]
- The Lung Cancer Alliance's, *Immunotherapy for Lung Cancer: A Guide for the Patient*[11]
- The Cancer Research Institute's videos, *Immunotherapy & Chemotherapy: What's the Difference?* that explain to patients the concept of how immunotherapy will work to combat their cancer.[12]

Practical Suggestions for Improvement

- Develop a coordinated outreach, communication, and education plan to inform emergency medicine, urgent care, and radiology clinicians in your region about the identification and coordinated management of irAEs.
- Engage team members in ongoing discussion and dialogue by presenting unusual findings during case conferences and inviting other specialists, such as dermatologists, radiologists, gastroenterologists, and pathologists, to learn about the unique aspects of irAEs.
- Since the concept of immunotherapy can be confusing for patients, leverage existing patient education resources that are clear, concise, and produced at the appropriate health literacy level.
- Engage and empower patients to have a more active role in their care if they develop signs of irAEs. If they need to go to an emergency room, have a caregiver or family member notify the medical oncology office.

Strategy 3. Ensuring Adequate Patient Access & Communication

In the state of Maryland, the All-Payer Model has led hospitals to be more vigilant when tracking and managing drug inventory based on patient treatment schedules.[13] The Sandra & Malcolm Berman Cancer Institute at Greater Baltimore Medical Center has a dedicated oncology pharmacist who performs these tasks and helps to monitor drug acquisition costs, prior authorizations, medication billing, and reimbursements to the hospital. Oncology pharmacists can also play a key role in detecting signs and symptoms of irAEs and resources like the NCCN Immunotherapy Teaching/Monitoring Tool (nccn.org/immunotherapy-tool/pdf/NCCN_Immunotherapy_Teaching_Monitoring_Tool) can be incorporated into treatment plans to ensure that the right questions are being asked to assess for potential toxicities.

Both the Sandra & Malcolm Berman Cancer Institute and The Center for Cancer Prevention and Treatment have strong teams of financial advocates who use copay and patient assistance programs to reduce the risk of financial toxicity in patients treated with immunotherapies. The Affordable Care Act has led to more patients entering the cancer care system with health insurance. When immunotherapy agents are used on-label, patients do not seem to have difficulty getting coverage from their health insurance plans. However, researchers have noted that when these agents

are not used for their specific indications, the costs of these therapies to patients and health systems can be significant.[14]

The Center for Cancer Prevention and Treatment sees many cancer patients who are highly educated and knowledgeable about the latest medical advances and research developments. As a result, the cancer program often gets direct inquiries from patients and family members about the possibility of receiving immunotherapy for their cancer. Clinicians need to know how to manage demands and expectations from patients by properly discussing the appropriate use of immunotherapy, as well as offering opportunities for clinical trial enrollment if patients are eligible. At The Center for Cancer Prevention and Treatment, an integrated approach to improve access to immunotherapy has impacted the clinical workflow in several ways:

- Physicians spend more time in team-based discussions to plan and coordinate care with other medical specialists and nurses. These discussions may also include brief educational opportunities and patient case studies.
- Oncology nurses, infusion nurses, and nurse navigators coordinate their approach to educating patients and documenting and communicating patient-reported symptoms. This care coordination allows the team to collect information from patients when they come for follow-up appointments, when they come for their treatments, or when they call with questions.

Practical Suggestions for Improvement

- Work with oncology pharmacists to manage and track drug orders and inventory based on treatment schedules. Identify potential bottlenecks in the process that may lead to drug delivery delays so that treatment schedules are not affected.
- Leverage copay and patient assistance programs for all patients, including those who appear to have adequate health insurance coverage.

Going Forward

Advances in immunotherapy will lead to more cancer programs offering these treatments to patients. While these therapies are exciting developments for oncologists, patients receiving them may require carefully coordinated monitoring and treatment by non-cancer clinicians in the surrounding community. Patients treated in real-world settings are often more complex than those represented in clinical trials and multiple specialists working in different health systems may get involved with the identification and management of pseudoprogression and irAEs. OI

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A Reminder from ACCC's Bylaws Committee

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

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Del Rep: Jason Ervin, MBA
Website: ocsri.org

Northside Hospital Cancer Registry is Generating Treatment Summaries

BY EBONY JOHNSON, CTR

According to the American Cancer Society report, *Cancer Treatment & Survivorship Facts & Figures: 2016-2017*, more than 15 million people in the U.S. are living as cancer survivors and by 2026 this number is expected to grow to more than 20 million. To better meet the needs of these patients, the American College of Surgeons Commission on Cancer (CoC) developed a new edition of its Cancer Program Standards that went into effect in 2016. Specifically, Standard 3.3 instructs accredited facilities to develop a process to distribute treatment summaries and follow-up care plans to those survivors who have completed cancer treatment.

As a pilot site in the NCI Community Cancer Center Program (NCCCP), Northside Hospital Cancer Institute in Atlanta, Ga., was in an excellent position develop a program to meet that standard. (Among many NCCCP goals, pilot sites were called on to develop and deliver cancer treatment summaries and follow-up care plans to cancer survivors completing therapy.) Northside Hospital recognized early on that registry data were invaluable in creating patient treatment summaries. Hospital CTRs were already responsible for collecting data on every cancer patient's diagnosis and treatment for the purpose of reporting to the state and National Cancer Database (NCDB), so asking nurse navigators to collect the same information when developing survivorship care plans and treatment summaries would be duplicating efforts and stretching resources thin.

Instead, using NCCCP program funding, Northside Hospital recruited a certified tumor registrar (CTR) to abstract the top five primary sites in real-time, focusing first on breast cancer. Over time, this position evolved into a full-time treatment summary registrar. Today this CTR works alongside their registry software vendor, survivorship coordinator, other registry abstractors, nurse practitioners, and additional members of the care team to continually advance the survivorship program and deliver treatment summaries and survivorship care plans (SCPs) to meet current CoC standards.

In 2013, the treatment summary registrar reached out to Northside's registry software vendor to create custom templates that would generate patient-friendly treatment summary documents utilizing data already coded in the abstracts. These custom templates were created based on the data elements set forth by the American Society of Clinical Oncology (ASCO) and allowed Northside Hospital to maintain facility branding. The templates have been through several iterations and Northside continues to improve them as they implement additional primary sites based on feedback from steering committee physicians.

While Northside's treatment summary process engages several staff members, it is streamlined. At the time of case identification in the cancer registry, staff estimate the month that patient is likely to finish treatment based on the patient's current stage and NCCN treatment guidelines. The treatment summary CTR runs a report using custom data fields in the software that can easily identify which patients are ready to be abstracted and shares that with a team of abstractors. These patients become their top priority for abstraction. Once abstraction is complete and all information is collected (including information from other treatment facilities), the CTR performs quality checks on the treatment summary fields. The quality checks take an average of about 35 to 40 minutes per patient, but quality is a top priority at Northside Hospital. After all treatment summary fields are verified, a treatment summary is created for each patient. Because the templates are built into the database software, it only takes another 5 minutes to generate and save the final treatment summary. From start to finish, once a case is abstracted, QA and treatment summary delivery takes a total of 40-45 minutes per patient.

When treatment summaries are complete, each patient's summary is uploaded to his or her abstract for document retention. It is also placed into a shared folder on the hospital network drive so that nurses and mid-levels can access it. Once clinical staff sees the new treatment summaries in the shared folder, they reach out to the patients and schedule the survivorship visit.

Prior to the patient's visit, clinicians prepare the survivorship care plan folder. It includes a survivorship care plan that is specific to the patient's disease site, fitness and nutrition information, the Cancer Support Community calendar, support group information, survivorship class schedules, and more. These survivorship care plan folders and documents are prewritten and preprinted by a company that prints all of Northside's marketing materials and forms. Each physician practice

Northside Hospital's Cancer Registry team celebrates National Cancer Registrars Week with a proclamation signed by Georgia Governor Nathan Deal.

that is delivering SCPs has the forms on hand so when the patient comes for their visit, the nurse puts one of each sheet into the folder and hands it to the patient. Because these forms are preprinted, it takes the nurse less than 5 minutes per patient to stuff the folder before the visit. Sometimes the oncology analytics department gets volunteers who are happy to stuff these folders as well, and they get delivered to the doctor offices all ready. The treatment summary that was uploaded to the shared drive is then reviewed with the patient, printed, and added to the survivorship care folder. Once the visit has taken place, the treatment summary CTR updates the registry records with the visit date so information can feed into a dashboard created in Excel to ensure ongoing CoC compliance.

Beginning in 2016, CoC-accredited programs were required to deliver survivorship care plans to 25 percent of eligible cases. Northside Hospital surpassed that goal and is working on delivering survivorship care plans to 50 percent of patients by the end of 2017. In 2018 and beyond, CoC-accredited programs will need to offer survivorship care visits to 75 percent of eligible patients. Currently Northside Hospital focuses on breast, melanoma, endometrium, sarcoma, and cervical cancer, with plans to incorporate ovarian, non-small cell lung cancers, and colorectal by the end of the 2017.

Northside Hospital has earned the CoC Outstanding Achievement Award for five consecutive survey cycles (2004, 2007, 2010, 2013, 2016). The hospital strives for this award every survey cycle because this is a quantifiable way to show the quality care of care it provides to patients. OI

Ebony Johnson, CTR, is the oncology analytics treatment summary specialist at Northside Hospital Cancer Institute, Atlanta, Ga.

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WARNINGS AND PRECAUTIONS

Seizure

Seizure occurred in 0.5% of patients receiving XTANDI in clinical studies. In placebo-controlled studies, 8 of 1671 (0.5%) patients treated with XTANDI and 1 of 1243 (0.1%) patients treated with placebo experienced a seizure. In patients who previously received docetaxel, 7 of 800 (0.9%) patients treated with XTANDI experienced a seizure and no patients treated with placebo experienced a seizure. Seizure occurred from 31 to 603 days after initiation of XTANDI. In a placebo-controlled study in chemotherapy-naïve patients, 1 of 871 (0.1%) treated with XTANDI and 1 of 844 (0.1%) patients treated with placebo experienced a seizure. In bicalutamide-controlled studies conducted in chemotherapy-naïve patients, 3 of 380 (0.8%) patients treated with XTANDI and 1 of 387 (0.3%) patients treated with bicalutamide experienced a seizure. Patients experiencing seizure were permanently discontinued from therapy and all seizure events resolved. There is no clinical trial experience re-administering XTANDI to patients who experienced seizure.

Limited safety data are available in patients with predisposing factors for seizure because these patients were generally excluded from the trials. 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, and brain arteriovenous malformation. Study 1 excluded the use of concomitant medications that may lower the seizure threshold, whereas Study 2 permitted the use of these medications.

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

Posterior Reversible Encephalopathy Syndrome (PRES)

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

ADVERSE REACTIONS

Clinical Trial Experience

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

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

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

Study 1: XTANDI versus Placebo in Metastatic CRPC Following Chemotherapy

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

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

Table 1. Adverse Reactions in Study 1

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

a CTCAE v4.
b Includes asthenia and fatigue.
c Includes dizziness and vertigo.
d Includes amnesia, memory impairment, cognitive disorder, and disturbance in attention.
e Includes nasopharyngitis, upper respiratory tract infection, sinusitis, rhinitis, pharyngitis, and laryngitis.
f Includes pneumonia, lower respiratory tract infection, bronchitis, and lung infection.

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

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

Table 2. Adverse Reactions in Study 2

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

a CTCAE v4.
b Includes asthenia and fatigue.
c Includes dizziness and vertigo.
d Includes amnesia, memory impairment, cognitive disorder, and disturbance in attention.
e Includes dyspnea, exertional dyspnea, and dyspnea at rest.
f Includes nasopharyngitis, upper respiratory tract infection, sinusitis, rhinitis, pharyngitis, and laryngitis.
g Includes pneumonia, lower respiratory tract infection, bronchitis, and lung infection.

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

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

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

Table 3. Adverse Reactions in Study 3

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

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

Laboratory Abnormalities

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

Infections

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

Falls and Fall-related Injuries

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

Hypertension

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

Post-Marketing Experience

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

Neurological Disorders: posterior reversible encephalopathy syndrome (PRES)

DRUG INTERACTIONS

Drugs that Inhibit CYP2C8

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

Drugs that Induce CYP3A4

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

Effect of XTANDI on Drug Metabolizing Enzymes

Enzalutamide is a strong CYP3A4 inducer and a moderate CYP2C9 and CYP2C19 inducer in humans. At steady state, XTANDI reduced the plasma exposure to midazolam (CYP3A4 substrate), warfarin (CYP2C9 substrate), and omeprazole (CYP2C19 substrate). Concomitant use of XTANDI with narrow therapeutic index drugs that are metabolized by CYP3A4 (e.g., alfentanil, cyclosporine, dihydroergotamine, ergotamine, fentanyl, 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.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

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

Animal Data

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

Lactation

Risk Summary

XTANDI is not indicated for use in females. There is no information available on the presence of XTANDI in human milk, the effects of the drug on the breastfed infant, or the effects of the drug on milk production.

Females and Males of Reproductive Potential

Contraception

Males

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

Infertility

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

Pediatric Use

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

Geriatric Use

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

Patients with Renal Impairment

A dedicated renal impairment trial for XTANDI has not been conducted. Based on the population pharmacokinetic analysis using data from clinical trials in patients with metastatic CRPC and healthy volunteers, no significant difference in enzalutamide clearance was observed in patients with pre-existing mild to moderate renal impairment (30 mL/min ≤ 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.

Patients with Hepatic Impairment

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

OVERDOSAGE

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

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility

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

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

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

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

Marketed by:
Astellas Pharma US, Inc., Northbrook, IL 60062
Medivation, Inc., San Francisco, CA 94105

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Rx Only

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Indication and Important Safety Information

Indication

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

Important Safety Information

Contraindications

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

Warnings and Precautions

Seizure occurred in 0.5% of patients receiving XTANDI in clinical studies. In placebo-controlled studies, 8 of 1671 (0.5%) patients treated with XTANDI and 1 of 1243 (0.1%) patients treated with placebo experienced a seizure. In patients who previously received docetaxel, 7 of 800 (0.9%) patients treated with XTANDI experienced a seizure and no patients treated with placebo experienced a seizure. In a placebo-controlled study in chemotherapy-naïve patients, 1 of 871 (0.1%) patients treated with XTANDI and 1 of 844 (0.1%) patients treated with placebo experienced a seizure. In bicalutamide-controlled studies conducted in chemotherapy-naïve patients, 3 of 380 (0.8%) patients treated with XTANDI and 1 of 387 (0.3%) patients treated with bicalutamide experienced a seizure. Permanently discontinue XTANDI in patients who develop a seizure during treatment.

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

Adverse Reactions

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

In the study of patients taking XTANDI who previously received docetaxel, Grade 3 and higher adverse reactions were reported among 47% of XTANDI patients and 53% of placebo patients. Discontinuations due to adverse events were reported for 16% of XTANDI patients and 18% of placebo patients. In the placebo-controlled study of chemotherapy-naïve patients, Grade 3-4 adverse reactions were reported in 44% of XTANDI patients and 37% of placebo patients. Discontinuations due to adverse events were reported for 6% of both study groups. In the bicalutamide-controlled study of chemotherapy-naïve patients, Grade 3-4 adverse reactions were reported in 38.8% of XTANDI patients and 37.6% of bicalutamide patients. Discontinuations due to adverse events were reported for 7.6% of XTANDI patients and 6.3% of bicalutamide patients.

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

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

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

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

Drug Interactions

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

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

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

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

References: 1. XTANDI [package insert]. Northbrook, IL: Astellas, Inc. **2.** Shore ND, Chowdhury S, Villers A, et al. Efficacy and safety of enzalutamide versus bicalutamide for patients with metastatic prostate cancer (TERRAIN): a randomised, double-blind, phase 2 study. Lancet Oncol 2016;17(2):153-63. **3.** Beer TM, Armstrong AJ, Rathkopf DE, et al., for the PREVAIL Investigators. Enzalutamide in metastatic prostate cancer before chemotherapy. N Engl J Med 2014;371(5):424-33.

astellas MEDIVATION

Xtandi® (enzalutamide) 40 mg capsules

Data vs bicalutamide

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

TO EXTEND SURVIVAL[1]

23% reduction in risk of death with XTANDI + GnRH therapy vs placebo + GnRH therapy in PREVAIL‖¶[1]

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

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

CONVENIENT DOSING[1]

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

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

Learn more about XTANDI at **StartXtandi.com**

Indication

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

Select Safety Information

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

Seizure occurred in 0.5% of patients receiving XTANDI in clinical studies. Permanently discontinue XTANDI in patients who develop a seizure during treatment.

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

CI, confidence interval; HR, hazard ratio; mCRPC, metastatic castration-resistant prostate cancer; NR, not reached; OS, overall survival; rPFS, radiographic progression-free survival.

*Radiographic progression-free survival was defined as the time from randomization until first objective evidence of radiographic disease progression based on the assessments by Independent Central Review (ICR) or death, whichever occurred first.[1]

†Or after bilateral orchiectomy.[1]

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

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

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

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

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

Xtandi®
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40 mg capsules