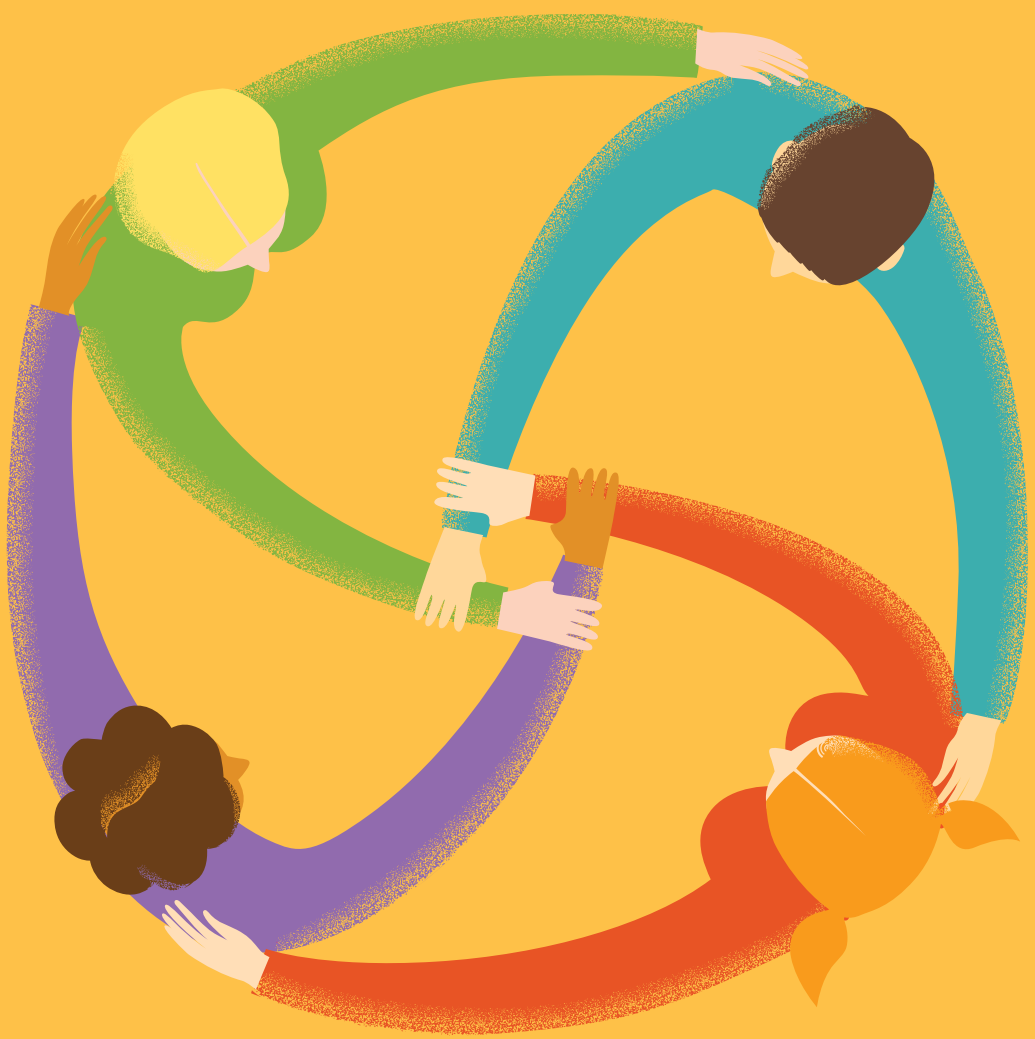
ONCOLOGY ISSUES

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

November | December 2016

Growing Supportive Care Services Through Philanthropy



ACCC
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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]*.

Distributed by:
AstraZeneca Pharmaceuticals LP, Wilmington, DE 19850

Iss. 08/16 3281701 09/16

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November | December 2016
Vol. 31 | No. 6

DEPARTMENTS

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

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

FROM THE EDITOR

Continuing the Conversation

BY CHRISTIAN DOWNS, JD, MHA

At the ACCC National Oncology Conference last month in St. Louis, the President's Theme Panel focused on patient-centered care. From contribution to engagement to responsibility, the role of the *patient* was enthusiastically debated by both panelists and audience members. At the end of the day most everyone agreed that the delivery of truly patient-centered care requires further discussion and analysis post-conference. So let's continue the conversation as we take a deeper dive into this edition of *Oncology Issues*.

In our cover article, "Growing Supportive Care Services Through Philanthropy," the Knight Cancer Institute at Oregon Health & Sciences University, Portland, Ore., shares how its patients—former and current—are driving (and in many cases funding) the integrative and supportive care services the cancer program is adding. New programs address pain management and mindfulness-based stress reduction techniques, among other identified patient needs.

In the next feature article, "Compliance with Breast Cancer Post-Therapy Surveillance," St. Joseph Hospital, Center for Cancer Prevention and Treatment, Orange, Calif., studied its breast cancer patients with state and federal safety-net funding, measuring their compliance with clinic appointments, annual mammograms, and anti-hormone therapy. The authors reiterate the importance of culturally-sensitive care and education and end their article with this statement: "[We] believe that this study serves as a real-life, practical, consistent community standard that can be achieved by similarly structured patient-centered programs."

As we all know, patient-centered care and care coordination go hand-in-hand. In "Bridging the Gap from Inpatient to Outpatient Care" author Connie Savage, LPN, shows how the creation of an inpatient coordinator role helps Cancer & Hematology Centers of Western Michigan deliver patient-centered care. Today, this inpatient coordinator schedules all outpatient appointments prior to patients being discharged from the hospital, eliminating the burden on patients and caregivers to schedule these appointments themselves. This new staff position not only improved care coordination between the inpatient (hospital) and outpatient (physician practice) setting, it also improved patient and family satisfaction scores.

In our next feature article, authors James S. Wysock, MD, and Herbert Lepor, MD, discuss improvements in screening and detection of prostate cancer and the promise these improvements have to reduce unnecessary biopsy and treatment—significantly improving the patient experience. Specifically, they share how a properly performed multi-parametric MRI of the prostate will drastically improve the disease characterization for many men and support shared decision making around treatment options.

Patient-centered care also plays a role in "Strategic Planning for Oncology." In a real-world case study, the authors share how one rural cancer program learned that patients were traveling into the city to receive what they perceived as "cutting-edge" treatment because they did not know that a group of physicians from the metropolitan practice were actually providing services in their local community. A few strategically placed billboards and a low-cost patient education campaign to raise awareness of this medical expertise provided in the community saw immediate results. As we all know, patients and families *want* to receive medical care in their own communities.

More, the patient-centered care conversation must extend beyond ACCC meetings and the Association's journal. In 2017, ACCC will launch a major education initiative around patient-centered care in the community setting. One of the key elements of the program: how providers can effectively engage patients. Because in the end, it is called patient-centered care for a reason—the patient voice is the most important voice in this conversation. OI

Engagement & Empowerment in Action

BY JENNIE R. CREWS, MD, MMM, FACP

A few weeks ago in St. Louis, leaders in the cancer care field gathered for three days of invigorating discussion and sessions at the ACCC 33rd National Oncology Conference. We had the privilege of hearing not just one, but two inspiring presentations on the topic of adolescent and young adult (AYA) cancer patients. On the provider side, clinical social worker Lauren Lux of UNC Lineberger Comprehensive Cancer Center spoke about engaging with AYA cancer patients. Lux came into her role via the *Be Loud! Sophie Foundation*. After being diagnosed with germ-cell cancer, 14-year-old Sophie Steiner expressed a strong desire to help other adolescents and young adults with cancer "stay true to their authentic selves in the face of overwhelming illness." The *Be Loud! Sophie Foundation* granted Sophie's wish by partnering with UNC Lineberger to hire Lux as their Adolescent and Young Adult Program Director. According to Sophie's parents, who also spoke at the meeting and introduced Lux, Sophie wanted any money raised from her cause to be invested in a person, not a building.

Lux spoke about the unique needs and common issues she sees in her AYA patients. Because the age range of AYA patients is typically classified as 15-39 years old, these patients often feel too mature for pediatric oncology, while also feeling out of place in the adult unit. Clinical trial enrollment for AYA patients is low, and they are less likely to access adult oncology support services. This subset of patients may also experience poor outcomes due to delays in diagnoses, non-compliance issues, and lack of insurance.

Patient-centered care is critical to AYAs. As Lux stressed to attendees, "You need to be authentic, flexible, compassionate, honest, and willing to get to know the *person*—not just the patient." With her AYA patients, Lux tries to talk about topics other than cancer and treatment, so she can better understand what may frame that patient's decision-making.

Often, Lux said, this group is making plans for the future while also making plans for their death. She empowers her AYA patients to make better treatment decisions by getting to know them and helping them articulate their aspirations and beliefs. Adapting communication styles by getting to know the personal side of a patient (not just the diagnosis) can make all the difference, Lux told meeting attendees.

On the patient side, Suleika Jaouad, Emmy Award-winning *New York Times Well* columnist, cancer survivor, and health advocate spoke to attendees about her cancer journey. At the age of 22, Jaouad was diagnosed with myelodysplastic syndrome and acute myeloid leukemia. After three years of chemotherapy, a life-saving clinical trial, and a bone marrow transplant, she is now in remission.

"We talk a lot about patient-centered care, but you can't have that unless the patient is an active part of the care conversation," Jaouad told attendees. She described feeling lost when speaking with her care team, and that their use of medical jargon felt like another language. When early in her treatment she did her own research on fertility preservation, Jaouad said she felt a breach of trust that her medical team had not mentioned this option to her. Once her care team became more attuned to Jaouad's personal needs, they could then empower her by connecting her to resources for fertility preservation. "This lack of communication showed me that open communication with my medical team is not always a given. I had to play an active role," said Jaouad.

ACCC is working with our members and oncology thought-leaders to identify patient-centered practices in oncology. The just-released white paper, *Empowering Patients, Engaging Providers: The Future of Patient-Centered Care in Oncology*, is a reflection of the conversation from the ACCC Institute for the Future of Oncology forum held in June 2016.

Truly patient-centered care requires engaged care providers like Lauren Lux, empowered patients like Suleika Jaouad, and the research talents and practice innovations of our cancer programs. So let's start those conversations with our patients. OI

Coming in Your 2017 *ONCOLOGY ISSUES*

- Developing a Nurse Practitioner Productivity Measurement Tool
- Advancing Breast Cancer Care & Survivorship Through Peer Mentor Program
- Developing a Pathway to Identify Women at Increased Risk for Breast Cancer & Providing Personalized Management & Risk Reduction
- Incorporating Telephone Triage Guidelines into Nursing Workflow
- Spiritual Care of Cancer Patients Across the Continuum: A Pilot Study
- Rural Chemotherapy Student Volunteer Support Program
- The Defeat GBM Collaborative: A Team-Based Approach to Researching Brain Cancer
- Leveraging Your Oncology Community Health Needs Assessment
- Life with Cancer: A Comprehensive, Holistic, Patient-Centered Approach to Cancer Management
- Tele-Health Technology Connects Patients with Nutrition Services

more online @ accc-cancer.org

VIDEO | Vice President Joe Biden Opens ACCC Meeting

In this inspiring video to attendees at the ACCC 33rd National Oncology Conference, Oct. 19-21, Vice President Biden talks about the Moonshot Initiative, breaking down siloes, improving access to clinical trials, the importance of receiving cancer care in the community where you live, and more. accc-cancer.org/biden.

WEBINAR | What Are Your Peers Saying about Oral Oncolytics?

ACCC's free webinars provide insight, including top barriers and challenges, adherence and toxicity issues, and more: attendee.gotowebinar.com/recording/1397447768538574852. Learn strategies to improve patient education and adherence at: attendee.gotowebinar.com/recording/5474632597402095108.

PAPER | Empowering Patients, Engaging Providers: The Future of Patient-Centered Care in Oncology

Continue the conversation started at the ACCC Institute for the Future of Oncology forum in June 2016 where participants identified seven key elements required to provide true patient-centered care. accc-cancer.org/institute/pdf/2016-WhitePaper-Empowering-Patients-Engaging-Providers.pdf.

RESOURCE | Missed the 2016 ICLIO National Conference? Download the Presentations Today

"What's Ahead in Immuno-Oncology? Indications & Combinations," "Developing Your Immuno-Oncology Dream Team: Coordination of Care and Collaboration among Specialist," "Alternative Payment Models and Methods for Immunotherapies," and more. Audio podcasts available soon. accc-iclio.org/iclio-national-conference-presentation-slides-9-30-16.

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

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

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

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

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fast

Feeling Negative Revenue Cycle Effects of High-Deductible Health Plans?

Try These 5 Tips.

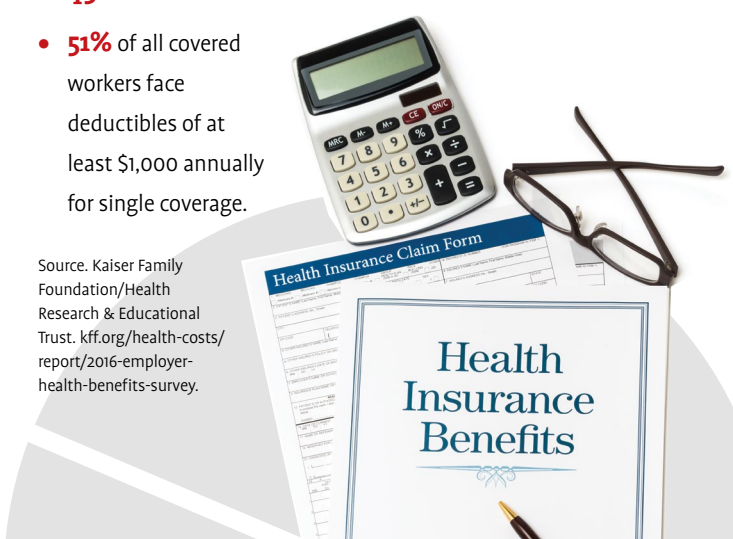
1. Communicate with your patients early about costs and options.
2. Conduct eligibility screening early.
3. Collect from patients at the point-of-care.
4. Offer patients options.
5. Have the right staff in place to help patients.

Source. MedEvolve. medevolve.com.

2016 Employer Health Benefits Survey

- Annual family premiums for employer-sponsored health insurance rose an average of **3%** to $18,142 in 2016.
- The recent trend in part reflects covered workers moving into high-deductible plans, which offer lower average premiums.
- **29%** of all workers were in high-deductible plans—up from **20%** in 2014.
- **83%** of covered workers face a deductible for single coverage that averages $1,478. That's up $159 or **12%** from 2015, and $486 or **49%** since 2011.
- **51%** of all covered workers face deductibles of at least $1,000 annually for single coverage.

Source. Kaiser Family Foundation/Health Research & Educational Trust. kff.org/health-costs/report/2016-employer-health-benefits-survey.



facts

Survey on Drug Costs: Employers Prefer Private Sector Solutions

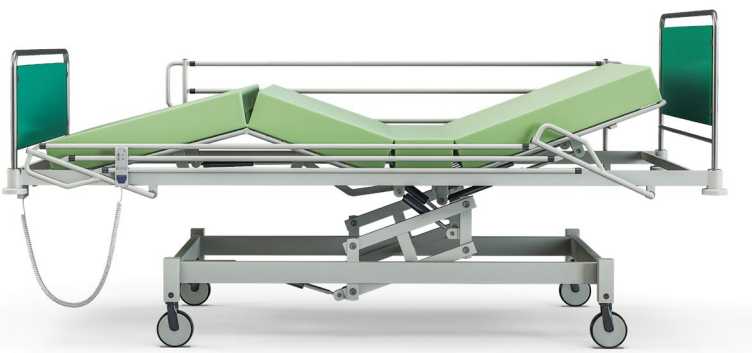
- When it comes to pharmacy benefits, employers' top concern is reducing costs; the two most important objectives: reducing overall costs (**54%**) and reducing patient premiums and other out-of-pocket costs (**45%**).
- **70%** think the private sector is better equipped than the government to manage pharmacy benefits.
- **60%** of employers say new government interventions would lead to higher prices—only **18%** say they would lower prices.
- More than half (**54%**) of employers think drug companies are primarily to blame for higher costs.

Source. Pharmaceutical Care Management Association. pcmanet.org/images/stories/uploads/2016/north%20star%20opinion%20employer%20%20memo.pdf.

Tips for Recruiting a Physician Assistant

1. Consider personality & temperament
2. Provide role clarity
3. Communicate expectations in writing
4. Hire new graduates
5. Offer a signing bonus
6. Pay attention to state laws and regulations.

Source. Cryts A. Tips for Recruiting the Perfect Physician Assistant. physicianspractice.com.



CMS Reports Hospital Rates Down Nationally

- Rates of potentially avoidable hospital readmissions fell in **49** states and the District of Columbia from 2010 through 2015; Vermont is the lone state without a decline.
- Readmission rates fell **8%** nationally over the five-year period.
- These data confirm the hard work of hospitals to reduce readmissions by improving patient safety and increasing care coordination.
- Potentially avoidable hospital readmissions that occur within **30 days** of a patient's initial discharge are estimated to account for more than **$17 billion** in Medicare expenditures annually.

Source. CMS. The CMS Blog. blog.cms.gov/2016/09/13 new-data-49-states-plus-dc-reduce-avoidable-hospital-readmissions.

With Final MACRA Rule, CMS Increases Flexibility

BY LEAH RALPH

On Friday, October 14, the Centers for Medicare & Medicaid Services (CMS) released its final rule on the MACRA Quality Payment Program (QPP), solidifying transformational changes in the way physicians will be reimbursed for Medicare Part B services. ACCC is conducting an in-depth analysis of the rule; however, an initial look reveals that CMS heard stakeholders' messages loud and clear: Make the transition to MACRA as simple and flexible as possible. Here are some top-level highlights from the final rule:

- **Low-volume threshold exemption.** The agency broadened the low-volume threshold exemption from the Merit-Based Incentive Payment System (MIPS), exempting practices with less than $30,000 in Medicare charges or fewer than 100 unique Medicare patients per year. CMS estimates this will exclude about one-third of physicians from having to report under the QPP.
- **Pick your pace.** CMS is allowing physicians to "pick their pace" in 2017, enabling physicians to avoid negative penalties in 2019 by reporting on some data (i.e., one measure in the quality, practice management, or meaningful use categories) for some period of time (less than 90 days). The takeaway: even minimal performance reporting will exempt physicians from any penalties, and opportunities for a shorter, 90-day reporting period will make providers eligible for positive adjustments. (Providers must start collecting data between January 1, 2017, and October 2, 2017, and report no later than March 31, 2018.)
- **Resource use category weighted zero in first year.** MIPS has four components, and originally the resource use (cost) category was going to account for 10 percent of your score starting in 2017. CMS has now said this category will hold zero percent weight toward your MIPS score in the first year [in 2017, the percentages will be: 60 percent quality measures, 25 percent advancing care information (EHR use), and 15 percent clinical improvement activities].
- **Expanding opportunities to participate in APMs.** CMS has also said it plans to expand opportunities to participate in models that qualify as "advanced alternative payment models" (APMs) in 2017 and 2018. The Center for Medicare and Medicaid Innovation (CMMI) also recently informed Oncology Care Model (OCM) practices that CMS is amending the program to allow OCM practices to take two-sided risk as early as January 2017 to qualify as an advanced APM (two years earlier than the model originally allowed). Although most OCM practices are not ready to take downside risk, CMS is also allowing OCM practices to substitute their reporting on quality and practice improvement activities for MIPS reporting—no additional reporting is needed.

In our comments on the proposed rule, ACCC asked for increased flexibility for practices who are still building the infrastructure to meet these requirements, and a streamlining of reporting requirements as our members increasingly engage in new delivery models and navigate the path to value-based care. ACCC's major concerns were around timeline and administrative burden. In the final rule, CMS was responsive in many ways, but ACCC will continue to work with the agency to reduce regulatory burden and make this a workable payment system for our members. We hope that CMS will provide flexibility beyond 2017 if needed.

For more information, CMS launched a website for physicians that explains the program and allows you to explore and identify different measures that are most meaningful to your practice, available at qpp.cms.gov/education?linkId=29935271. Access ACCC's archived "MACRA: What You Need to Know About the Final Rule" webinar, along with a summary of the rule, in the ACCC Resources section of MyNetwork (mynetwork.accc-cancer.org/). You can also find great checklists on how to prepare for QPP participation on both the Amercian Medical Association (ama-assn.org) and the American Society of Clinical Oncology (asco.org) websites. OI

Leah Ralph is ACCC Director of Health Policy.

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ICD-10-CM Updates!

BY CINDY PARMAN, CPC, CPC-H, RCC

Effective Oct. 1, 2016, the Centers for Medicare & Medicaid Services (CMS) and the Centers for Disease Control and Prevention (CDC) will add or update approximately 1,943 diagnosis codes in the ICD-10-CM coding classification. This large number of new codes is due to the partial freeze on updates prior to the Oct. 1, 2015, implementation of the code set. While cancer programs and oncologists will probably not use all of the new codes, here are the key revisions, updates, and new codes that will potentially impact oncology claims. There are also updates to the 2017 ICD-10-CM Official Guidelines for Coding and Reporting that impact medical record documentation, code selection, and sequencing. Adherence to the Guidelines when assigning ICD-10-CM diagnosis codes is required under HIPAA in all healthcare settings.

Guideline Updates

While there are many changes to the Official Guidelines, the following are key updates that will impact oncology providers, practices, and hospitals:

- Section 1.A.12.a: An exception to the Excludes1 definition is the circumstance when the two conditions are unrelated to each other. If it is not clear whether the two conditions involving an Excludes1 note are related, query the provider.
- Section 1.A.15: The word "with" should be interpreted to mean "associated with" or "due to" when it appears in a code title, the Alphabetic Index, or an instructional note in the Tabular List. The classification presumes a causal relationship between the two conditions linked by these terms in the Alphabetic Index or Tabular List. These conditions should be coded as related, even in the absence of provider documentation explicitly linking them, unless the documentation clearly states the conditions are unrelated. For conditions not specifically linked by these relational terms in the classification, provider documentation must link the conditions in order to code them as related.
- Section 1.A.19: The assignment of a diagnosis code is based on the provider's diagnostic statement that the condition exists. The provider's statement that the patient has a particular condition is sufficient. Code assignment is not based on clinical criteria used by the provider to establish the diagnosis.
- Section 1.B.13: When a patient has a bilateral condition and each side is treated during separate encounters, assign the "bilateral" code (as the condition still exists on both sides), including for the encounter to treat the first side. For the second encounter for treatment after one side has previously been treated and the condition no longer exists on that side, assign the appropriate unilateral code for the side where the condition still exists (e.g., cataract surgery performed on each eye in separate encounters). The bilateral code would not be assigned for the subsequent encounter, as the patient no longer has the condition in the previously treated site. If the treatment on the first side did not completely resolve the condition, then the bilateral code would still be appropriate.
- Section 1.C.1.f.1: Code only a confirmed diagnosis of Zika virus (**A92.5**, Zika virus disease) as documented by the provider. This is an exception to the hospital inpatient guideline Section II.H. In this context, "confirmation" does not require documentation of the type of test performed; the physician's diagnostic statement that the condition is confirmed is sufficient. If the provider documents "suspected," "possible," or "probable" Zika, do not assign code **A92.5**. Assign a code(s) explaining the reason for the encounter (such as fever, rash, or joint pain) or **Z20.828**, Contact with and (suspected) exposure to other viral communicable diseases.
- Section 1.C.19.3.5.b: If the intent of the poisoning is unknown or unspecified, code the intent as accidental intent. The undetermined intent is only for use if the documentation in the record specifies that the intent cannot be determined.

Neoplasm Code Updates

Notes throughout Chapter 2 of the ICD-10-CM manual to report an additional code for "history of tobacco use (**Z87.891**)" have now been changed to read "history of tobacco dependence (**Z87.891**)," which reflects the actual code description. This same verbiage change has been made across all chapters of ICD-10-CM.

A gastrointestinal stromal tumor (GIST) is an uncommon type of GI tract malignancy. GIST tumors are different from other types of malignancies because they start in

different cells, sometimes require different treatment, and may have a different prognosis. At the request of Novartis, a new subcategory **C49.A**- (*Gastrointestinal stromal tumor*) has been created, and the Neoplasm Table and Index have been updated accordingly:

- **C49**: Malignant neoplasm of other connective and soft tissue.
  - **C49.A**: Gastrointestinal stromal tumor.
    - **C49.A0**: Gastrointestinal stromal tumor, unspecified site.
    - **C49.A1**: Gastrointestinal stromal tumor of esophagus.
    - **C49.A2** Gastrointestinal stromal tumor of stomach.
    - **C49.A3**: Gastrointestinal stromal tumor of small intestine.
    - **C49.A4**: Gastrointestinal stromal tumor of large intestine.
    - **C49.A5**: Gastrointestinal stromal tumor of rectum.
    - **C49.A9**: Gastrointestinal stromal tumor of other sites.

There is also an Excludes2 Note for GIST under the regular GI malignancy codes (**C15-C26**) in the Tabular List. Remember that ICD-10-CM has two types of Excludes Notes:

- An Excludes1 code should never be used along with the code above the Excludes1 note, unless the two conditions are unrelated.
- An Excludes2 condition is not part of the condition above the Excludes2 note, but a coder may assign an additional code (if applicable) for it in addition to a code for the condition that appears above the Excludes2 note.

There is a new note under the category code for pancreatic cancer (**C25**) and the specific code for secondary digestive malignancy (**C78.89**) to also report exocrine pancreatic insufficiency (new code **K86.81**). Exocrine pancreatic insufficiency is inadequate production of pancreatic digestive enzymes, such as amylase and lipase, and it may be associated with cancer, cystic fibrosis, pancreatitis, and other disorders:

- **C25**: Malignant neoplasm of pancreas
  - Code also exocrine pancreatic insufficiency (**K86.81**).
- **C78.89**: Secondary malignant neoplasm of other digestive organs
  - Code also exocrine pancreatic insufficiency (**K86.81**).

There is a new note under prostate cancer (code **C61**) to use additional codes for hormone sensitivity status (new codes **Z19.1-Z19.2**) and/or rising PSA following treatment (new code **R97.21**):

- **C61**: Malignant neoplasm of prostate.
  - Use additional code to identify:
    - Hormone sensitivity status (**Z19.1-Z19.2**).
    - Rising PSA following treatment for malignant neoplasm of prostate (**R97.21**).

As indicated above, two new codes have been created to indicate whether a malignant neoplasm is sensitive to hormones:

- Hormone sensitivity malignancy status (**Z19**).
  - Code first malignant neoplasm—see Table of Neoplasms, by site, malignant.
    - **Z19.1**: Hormone sensitive malignancy status.
    - **Z19.2**: Hormone resistant malignancy status.
      - Castrate resistant prostate malignancy status.

These codes were created at the request of the American Urology Association (AUA) to track hormone-resistant (castrate-resistant) prostate cancer, but they may be reported with any malignant neoplasm. A note in the Tabular List indicates the neoplasm should be coded first, so these Z-codes will never be the first-listed diagnosis code. Also at the request of the AUA, the code for elevated PSA has been replaced with two new codes:

- Abnormal tumor markers (**R97**).
  - **R97**: Abnormal tumor markers.
    - **R97.2**: Elevated prostate specific antigen [PSA].
      - **R97.20**: Elevated prostate specific antigen [PSA].
      - **R97.21**: Rising PSA following treatment for malignant neoplasm of prostate.

In category **C81** (Hodgkin lymphoma), the term "classical" has been deleted from all code definitions and added as an inclusion term for the category. For example, new code descriptors for Nodular Sclerosis are:

- **C81**: Hodgkin lymphoma.
  - **C81.1**: Nodular sclerosis Hodgkin lymphoma.
    - Nodular sclerosis classical. Hodgkin lymphoma.
      - **C81.10**: Nodular sclerosis Hodgkin lymphoma,

unspecified site.
C81.11: Nodular sclerosis Hodgkin lymphoma, lymph nodes of head, face, and neck.
C81.12: Nodular sclerosis Hodgkin lymphoma, intrathoracic lymph nodes.
C81.13: Nodular sclerosis Hodgkin lymphoma, intra-abdominal lymph nodes.
C81.14: Nodular sclerosis Hodgkin lymphoma, lymph nodes of axilla and upper limb.
C81.15: Nodular sclerosis Hodgkin lymphoma, lymph nodes inguinal region, lower limb.
C81.16: Nodular sclerosis Hodgkin lymphoma, intrapelvic lymph nodes.
C81.17: Nodular sclerosis Hodgkin lymphoma, spleen.
C81.18: Nodular sclerosis Hodgkin lymphoma, lymph nodes of multiple sites.
C81.19: Nodular sclerosis Hodgkin lymphoma, extranodal and solid organ sites.

Code **D01.3** (Carcinoma in situ of anus and anal canal) has new inclusion terms for anal intraepithelial neoplasia (AIN) III and severe dysplasia of anus, as well as a new Excludes1 note for AIN I and II.

- **D01**: Carcinoma in situ of other and unspecified digestive organs.
  D01.3: Carcinoma in situ of anus and anal cancer.
  Anal intraepithelial neoplasia III [AIN III].
  Severe dysplasia of anus.
  Excludes1: anal intraepithelial neoplasia I and II [AIN I and AIN II] (K62.82).

There is a new Excludes1 note under **D07.5** (Carcinoma in situ of prostate) for prostatic intraepithelial neoplasia (PIN) II. ICD-10-CM code **N42.31** is also a new code, defined as Prostatic intraepithelial neoplasia, including PIN, PIN I, and PIN II.

- **D07**: Carcinoma in situ of other and unspecified genital organs.
  D07.5: Carcinoma in situ of prostate.
  Excludes1
  Dysplasia (mild) (moderate) of prostate (**N42.3-**).
  Prostatic intraepithelial neoplasia II [PIN II] (**N42.3-**).

There is a new code (**D47.Z2**) for Castleman disease, a type of lymphoproliferative disorder, with a Code Also note for herpesvirus 8 infection and an Excludes2 note for Kaposi's sarcoma:

- **D47**: Other neoplasms of uncertain behavior of lymphoid, hematopoietic, and related tissue.
  D47.Z: Other specified neoplasms of uncertain behavior of lymphoid, hematopoietic, and related tissue.
  D47.Z2: Castleman disease.
  Code also if applicable human herpesvirus 8 infection (**B10.89**).
  Excludes2: Kaposi's sarcoma (**C46-**).

At the request of the AUA, subcategory **D49.5** (Neoplasm of unspecified behavior of other genitourinary organs) has been expanded to include specific codes for the kidneys and other genitourinary organs:

- **D49**: Neoplasms of unspecified behavior.
  D49.5: Neoplasm of unspecified behavior of other genitourinary organs.
  D49.51: Neoplasm of unspecified behavior of kidney.
  D49.511: Neoplasm of unspecified behavior of right kidney.
  D49.512: Neoplasm of unspecified behavior of left kidney.
  D49.519: Neoplasm of unspecified behavior of unspecified kidney.
  D49.59: Neoplasm of unspecified behavior of other genitourinary organ.

Endocrine Code Updates

Subcategory **Z79.8** reports other long-term drug therapy. The following new code reports the use of oral hypoglycemic or oral antidiabetic drugs:

- **Z79**: Long term (current) drug therapy.
  Z79.8: Other long term (current) drug therapy.
  Z79.84: Long term (current) use of oral hypoglycemic drugs.
  Long term (current) use of oral antidiabetic drugs.
  Excludes2: long term (current) use of insulin (**Z79.4**).

There is a new note under the code for volume depletion to use additional code for electrolyte or acid-base disorders.

- **E86**: Volume depletion.
  Use additional code(s) for any associated disorders of electrolyte and acid-base balance (**E87-**).

The codes in category **E87** include conditions such as hyperosmolality, hypernatremia, hypo-osmolality, hyponatremia, acidosis, alkalosis, hyperkalemia, hypokalemia, fluid overload, transfusion-related circulatory overload (TACO), hyperchloremia, hypochloremia, and other fluid overload.

Mental & Behavioral Code Updates

The DSM diagnosis "alcohol use disorder" (AUD) has been added to the inclusion terms in category **F10**. The notes indicate to code mild AUD as alcohol abuse and moderate or severe AUD as alcohol dependence. The same change has been made for drug abuse and dependence; for example, mild opioid use disorder is coded as opioid abuse and moderate is coded as opioid dependence. Sample codes with notes include:

- **F10.14**: Alcohol abuse with alcohol-induced mood disorder.
  Alcohol use disorder, mild, with alcohol-induced bipolar or related disorder.
  Alcohol use disorder, mild, with alcohol-induced depressive disorder.
- **F10.24**: Alcohol dependence with alcohol-induced mood disorder.
  Alcohol use disorder, moderate, with alcohol-induced bipolar or related disorder.
  Alcohol use disorder, moderate, with alcohol-induced depressive disorder.
  Alcohol use disorder, severe, with alcohol-induced bipolar or related disorder .
  Alcohol use disorder, severe, with alcohol-induced depressive disorder.

There are new inclusion terms under subcategory **F17.2** (Nicotine dependence) for tobacco use disorder (TUD), but all forms of TUD (mild, moderate, or severe) are coded as dependence. For example:

- **F17.200**: Nicotine dependence, unspecified, uncomplicated.
  - Tobacco use disorder, mild.
  - Tobacco use disorder, moderate.
  - Tobacco use disorder, severe.

Digestive Code Updates

New codes have been added for drug-induced constipation (**K59.03**) with a note to report the correct code to identify the drug responsible for this condition:

- **K59**: Other functional intestinal disorders.
  - **K59.0**: Constipation.
    - **K59.03**: Drug inducted constipation.
      - Use additional code for adverse effect, if applicable, to identify drug (**T36-T50** with fifth or sixth character 5).

Genitourinary Code Updates

Category **N40** (Enlarged prostate) has been renamed to "Benign prostatic hyperplasia," which is the term that is more commonly used in the United States:

- **N40**: Benign prostatic hyperplasia.
  - Includes: enlarged prostate.
  - **N40.0**: Benign prostatic hyperplasia without lower urinary tract symptoms.
  - **N40.1**: Benign prostatic hyperplasia with lower urinary tract symptoms.

At the request of the AUA, the code for dysplasia of prostate (**N42.3**) has been split into three new codes:

- **N42**: Other and unspecified disorders of prostate.
  - **N42.3**: Dysplasia of prostate.
    - **N42.30**: Unspecified dysplasia of prostate.
    - **N42.31**: Prostatic intraepithelial neoplasia (PIN).
      - Prostatic intraepithelial neoplasia I (PIN I).
      - Prostatic intraepithelial neoplasia II (PIN II).
      - Excludes1: prostatic intraepithelial neoplasia III (PIN III) (**D07.5**).
    - **N42.32**: Atypical small acinar proliferation of prostate.
    - **N42.39**: Other dysplasia of prostate.

Also at the request of the AUA, new codes have been established for specific reporting of testicular pain and scrotal pain:

- **N50.8**: Other specified disorders of male genital organs.
  - **N50.81**: Testicular pain.
    - **N50.811**: Right testicular pain.
    - **N50.812**: Left testicular pain.
    - **N50.819**: Testicular pain, unspecified.
  - **N50.82**: Scrotal pain.
  - **N50.89**: Other specified disorders of the male genital organs.
    - Atrophy of scrotum, seminal vesicle, spermatic cord, tunica vaginalis, and vas deferens.
    - Chylocele, tunica vaginalis (nonfilarial) NOS.
    - Edema of scrotum, seminal vesicle, spermatic cord, tunica vaginalis; and vas deferens.
    - Hypertrophy of scrotum, seminal vesicle, spermatic cord, tunica vaginalis and vas deferens.
    - Stricture of spermatic cord, tunica vaginalis, and vas deferens.
    - Ulcer of scrotum, seminal vesicle, spermatic cord, testis, tunica vaginalis, and vas deferens.
    - Urethroscrotal fistula.

New codes have been added in subcategory **N52.3-** for erectile dysfunction following radiation therapy and other ablative treatments of the prostate:

- **N52**: Male erectile dysfunction.
  - **N52.3**: Postprocedural erectile dysfunction.
    - **N52.35**: Erectile dysfunction following radiation therapy.
    - **N52.36**: Erectile dysfunction following interstitial seed therapy.
    - **N52.37**: Erectile dysfunction following prostate ablative therapy.
      - Erectile dysfunction following cryotherapy.
      - Erectile dysfunction following other prostate ablative therapies.
      - Erectile dysfunction following ultrasound ablative therapies.
    - **N52.39**: Other and unspecified postprocedural erectile dysfunction.

At the request of the American Association for the Surgery of Trauma, the code for inflammatory disorders of the breast (**N61**) has been replaced with specific codes for mastitis without abscess and abscess of breast and nipple:

- **N61**: Inflammatory disorders of breast.
  - **N61.0**: Mastitis without abscess.
    - Infective mastitis (acute) (nonpuerperal) (subacute).
    - Mastitis (acute) (nonpuerperal) (subacute) NOS.
    - Cellulitis (acute) (nonpuerperal) (subacute) of breast NOS.
    - Cellulitis (acute) (nonpuerperal) (subacute) of nipple NOS.
  - **N61.1**: Abscess of the breast and nipple
    - Abscess (acute) (chronic) (nonpuerperal) of areola.
    - Abscess (acute) (chronic) (nonpuerperal) of breast.
    - Carbuncle of breast.
    - Mastitis with abscess.

Signs & Symptoms Codes Update

Three new codes have been added for voiding difficulties, including the need to immediately re-void, position-dependent voiding, and other voiding difficulties:

- **R39**: Other and unspecified symptoms and signs involving the genitourinary system.
  - **R39.1**: Other difficulties with micturition.
    - **R39.19**: Other difficulties with micturition.
      - **R39.191**: Need to immediately re-void.
      - **R39.192**: Position dependent micturition.
      - **R39.198**: Other difficulties with micturition.

A new code has been created for prediabetes, in which blood sugar is higher than normal but not high enough to qualify as diabetes:

- **R73**: Elevated blood glucose level.
  - **R73.0**: Abnormal glucose.
    - **R73.03**: Prediabetes.
    - Latent diabetes.
    - **R73.09**: Other abnormal glucose.

ICD-10-CM initially classified bacteriuria as urinary tract infection (**N39.0**), but at the

request of the American Academy of Pediatrics, a new code has been created for bacteriuria:

- **R82**: Other and unspecified abnormal findings in urine.
  - **R82.7**: Abnormal findings on microbiological examination of urine.
    - Positive culture findings of urine.
    - **R82.71**: Bacteriuria.
    - **R82.79**: Other abnormal findings on microbiological examination of urine.
      - Positive culture findings of urine.

Category **R93** (Abnormal findings on diagnostic imaging of other body structures) has been expanded to include codes for abnormal findings involving renal pelvis, ureter, bladder, kidney and other urinary organs:

- **R93**: Abnormal findings on diagnostic imaging of other body structures.
  - **R93.4**: Abnormal findings on diagnostic imaging of urinary organs.
    - Excludes2: hypertrophy of kidney (**N28.81**).
    - **R93.41**: Abnormal radiologic findings on diagnostic imaging of renal pelvis, ureter, or bladder.
      - Filling defect of bladder found on diagnostic imaging.
      - Filling defect of renal pelvis found on diagnostic imaging.
      - Filling defect of ureter found on diagnostic imaging.
    - **R93.42**: Abnormal radiologic findings on diagnostic imaging of kidney.
      - **R93.421**: Abnormal radiologic findings on diagnostic imaging of right kidney.
      - **R93.422**: Abnormal radiologic findings on diagnostic imaging of left kidney.
      - **R93.429**: Abnormal radiologic findings on diagnostic imaging of unspecified kidney.
    - **R93.49**: Abnormal radiologic findings on diagnostic imaging of other urinary organs.

Complication Code Updates

Notes have been added in subcategory **T80.21-** (Infection due to central venous catheter) to indicate that these codes should also be used for infection due to pulmonary artery (Swan-Ganz) catheters:

- **T80.2**: Infections following infusion, transfusion and therapeutic injection.
  - Excludes2: Postprocedural infections (**T81.4-**).
  - **T80.21**: Infection due to central venous catheter.
    - Infection due to pulmonary artery catheter (Swan-Ganz catheter).
    - **T80.211**: Bloodstream infection due to central venous catheter.
      - Bloodstream infection due to pulmonary artery catheter.
    - **T80.212**: Local infection due to central venous catheter.
      - Local infection due to pulmonary artery catheter.
    - **T80.218**: Other infection due to central venous catheter.
      - Other infection due to pulmonary artery catheter.
  - **T80.219**: Unspecified infection due to central venous catheter.
    - Unspecified infection due to pulmonary artery catheter.

Z Code Updates

In addition to Z-codes listed in other sections of this article, a new category (**Z29**) has been established for "Encounter for other prophylactic measures," such as administration of palivizumab (Synargis) to prevent respiratory syncytial virus infection in premature infants:

- **Z29**: Encounter for other prophylactic measures.
  - Excludes 1: Desensitization to allergens (**Z51.6**).
    - Prophylactic surgery (**Z40.-**)
  - **Z29.1**: Encounter for prophylactic immunotherapy.
    - Encounter for administration of immunoglobulin.
    - **Z29.11**: Encounter for prophylactic immunotherapy for respiratory syncytial virus (RSV).
    - **Z29.12**: Encounter for prophylactic antivenin.
    - **Z29.13**: Encounter for prophylactic Rho(D) immune globulin.
    - **Z29.14**: Encounter for prophylactic rabies immune globin.
  - **Z29.3**: Encounter for prophylactic fluoride administration.
  - **Z29.8**: Encounter for other specified prophylactic measures.
  - **Z29.9**: Encounter for prophylactic measures, unspecified.

Inclusion terms have been added to codes describing a personal history of in-situ neoplasm for CIN III, VAIN III (vagina), and VIN III (vulva):

- **Z86.0**: Personal history of in-situ and benign neoplasms and neoplasms of uncertain behavior.
  - **Z86.00**: Personal history of in-situ neoplasm.
    - Conditions classifiable to D00-D09.
    - **Z86.001**: Personal history of in-situ neoplasm of cervix uteri.
      - Personal history of cervical intraepithelial neoplasia III [CIN III].
    - **Z86.008**: Personal history of in-situ neoplasm of other site.
      - Personal history of vaginal intraepithelial neoplasia III [VAIN III].
      - Personal history of vulvar intraepithelial neoplasia III [VIN III].

Last, throughout the classification, many Excludes1 notes have been changed to Excludes2 notes, and at least one Excludes2 note (category **Y62**) has been changed to Excludes1. It will therefore be important to double-check each note when using the new edition for the first time. The Official Guidelines for Coding and Reporting, Addenda, code lists and other files are available at: cdc.gov/nchs/icd/icd10cm.htm. OI

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

The Eisai $0 Co-Pay Programs

Expanding patient access to HALAVEN® and LENVIMA®

Halaven® (eribulin mesylate) Injection | 0.5 mg per mL

LENVIMA® (lenvatinib) capsules | 10 mg and 4 mg

Eisai Inc., the maker of HALAVEN and LENVIMA, offers $0 Co-Pay Programs to assist eligible, commercially insured patients with the out-of-pocket costs for their prescriptions.*

The $0 Co-pay Programs are offered through the Eisai Assistance Program, which is designed to help facilitate access and reimbursement support for health care providers and patients. Additional benefits include reimbursement information, insurance verification, alternate coverage advising, and financial assistance programs. Eisai cannot guarantee coverage or eligibility for any benefits or programs.

To learn more about the $0 Co-Pay Programs and the Eisai Assistance Program

THE EISAI ASSISTANCE PROGRAM

- Call 1-866-61-EISAI (1-866-613-4724), 8 AM to 8 PM ET, Monday through Friday
- Visit www.EisaiReimbursement.com

***Maximum benefit:** The HALAVEN and LENVIMA $0 Co-Pay Programs each provide eligible patients up to $18,000 and $40,000 per year, respectively, to assist with the out-of-pocket costs for prescriptions. Depending on the insurance plan, your patient could have additional financial responsibility for any amounts over Eisai's maximum liability. Other terms and conditions apply.

spotlight

WellSpan Good Samaritan Sechler Family Cancer Center

Lebanon, Pennsylvania

Opened in January 2016, the new WellSpan Good Samaritan Sechler Family Cancer Center brings high-tech, integrated cancer care to the small community of Lebanon, Pa. One of six cancer centers in the WellSpan organization, the Sechler Family Cancer Center is also Quality Oncology Practice Initiative (QOPI®) certified and accredited by The Joint Commission.

Prior to building the new one-story cancer center, oncology services were offered at Good Samaritan Hospital, located two miles from the new building. For hematologist Karla Ludwig, MD, access to integrated care in one location has made a difference in patients' lives. "It's very exhausting to have cancer. To be able to provide patients all of their services under one roof, especially a beautiful one like this, allows us to provide good, integrated care," said Dr. Ludwig.

Meeting Patient & Community Needs

The Sechler Family Cancer Center is truly a one-stop shop for cancer care, with medical oncology, radiation oncology, financial counseling, and supportive care all housed in the building. It's also situated close to other physician offices that patients may need to visit, including cardiologists, pulmonologists, and surgeons. All patients treated at the Sechler Family Cancer Center meet with the on-site Masters-prepared social worker. They are also seen by a registered dietitian upon starting treatment, chemotherapy, or radiation.

The on-site financial coordinator plays a huge role in assisting patients with obtaining coverage for their treatment and/or prescriptions. Last year, the financial coordinator was able to obtain $1.5 million in co-pay patient assistance for patients in Lebanon County.

Every time a physician orders oral chemotherapy, that referral immediately goes to the financial coordinator. He will then meet with the patient and determine what the cost of this drug will be, what coverage the patient has, and what assistance may be needed.

A referral to the financial coordinator can also be triggered by the nurse navigator. If a patient's initial assessment reveals distress fueled by financial worries, the navigator can immediately refer the patient to the financial coordinator.

"Patients will often ask [to be referred] but typically staff or the physicians are going to pick up on the need quicker than the patient. The coordinator is available and he'll step in often before patients are even aware there may be a problem," said Kelly Smith, MS, RN, OCN, oncology program director, Sechler Family Cancer Center.

Reflecting the Surrounding Community

In addition to taking patient convenience into account, the design of the center also reflects patient comfort and a sense of community.

"This area is a beautiful farm community. The architect did an amazing job with reflecting the bucolic setting we're in while also making it look high-tech. This cancer center really reflects the countryside," said Dr. Ludwig.

"The building that we are in is designed to immediately set patients at ease. It is a very beautiful, peaceful place for patients to come for treatment," said Robena Medbery, MD, medical director for radiation oncology services.

With a building dedicated solely to cancer care, some services, like radiation oncology, have been able to grow. "We have the latest TruBeam™, and a program called Sun Nuclear PerFraction which gives an automated analysis of daily portal dosimetry. It detects and reports setup reproducibility and monitors linac delivery consistency on every patient, every day. We're finding this technology is only available at a handful of centers and it's usually academic centers," said Dr. Medbery.

The Sechler Family Cancer Center is also able to offer patients SBRT. The WellSpan organization includes several other radiation facilities that work in collaboration. Since the different teams perform weekly chart rounds together, patients get the opinion of multiple radiation oncologists for their treatment.

Staff and patients alike appreciate the infusion center's design. The infusion area contains nine privately separated bays overlooking a water feature resembling a pond, with each bay also containing two comfortable chairs for family and friends. "We really wanted to bring the outside in. All bays have glass windows from the ceiling down to the floor with the chairs positioned to look out onto the water feature," said Smith.

Another key design element of the building is the recognition and visibility of the community donors who helped make the new cancer center a reality. "Patients that walk through see all the donors that made

generous contributions to making this place beautiful. The lobby was donated by a family from the area, we have a spiritual center that was donated by another family from the area, and a Peace Garden donated by yet another family. Every one of the infusion bays has the donors listed so these people are familiar to the patients that come here," said Smith.

One unique feature of the new cancer center is the hitching post out front. "We do take care of the Plain community here, Mennonite and Amish, and most of them arrive in buggies so we have a hitching post for them," said Dr. Medbery.

Responding to a need within their patient population, the hospital employs a liaison for the Plain community. "There are different religious and cultural beliefs here, and we're working to establish trust with the Plain community," said Dr. Medbery.

Lebanon County also has a large Hispanic population and to reduce any language and cultural barriers, the cancer center has translators who accompany patients on their visits, rather than using a call-in phone service.

Navigation is Key

Patient navigation at the Sechler Family Cancer Center is structured to put patients at ease. Navigation begins even before the initial visit for a new patient. When a newly-diagnosed cancer patient calls to make their first appointment the oncology-certified nurse navigator fields the call and assists the patient with scheduling.

The nurse navigator accompanies new patients to their initial visit and helps them coordinate care both within the cancer center and with other physicians and other specialties as needed.

Acting as the patient's point of contact throughout the treatment journey, the navigator helps coordinate the appropriate diagnostic studies and in the event of a positive biopsy, works in tandem with the certified diagnostic navigator at Good Samaritan Hospital.

The nurse navigator also initiates survivorship care plans upon the patient beginning treatment. Between the navigator and the oncology certified nurses, the care plan is completed and the patient meets with the navigator upon the completion of treatment to review the care plan.

The Sechler Family Cancer Center partners with the local YMCA to offer a breast cancer survivorship program called Pink Complete. The program includes exercise, nutrition, and relaxation techniques with a YMCA-certified cancer recovery trainer. In addition to breast cancer patients, the certified trainer will also individually work with patients who have completed chemotherapy and want to work on getting back to their previous level of fitness.

The cancer center recognizes that completion of treatment is an important occasion to celebrate with patients. Two brass bells hang on the walls of the Sechler Family Cancer Center, one in the infusion area and one in the radiation oncology area. Often when patients are completing their therapy, they bring family members in and ring the bell and celebrate with the cancer team.

Two flatscreen televisions also hang on the walls in these areas. Dubbed "Survivor Screens," these televisions display former patients' pictures along with some words of wisdom they want to share with others.

Select Support Services

- Financial counseling
- Pet therapy
- Support groups
- Lymphedema services
- Dietitian

New analytic cases seen annually: 400

tools

Approved Drugs

• The Food and Drug Administration (FDA) has approved a supplemental biologics license application (sBLA) for the use of **Arzerra**® (**ofatumumab**) (Genmab A/S, genmab.com) in combination with fludarabine and cyclophosphamide for the treatment of patients with relapsed chronic lymphocytic leukemia (CLL).

• Amgen (amgen.com) announced that the FDA has approved the sBLA for **Blincyto**® (**blinatumomab**) to include new data supporting the treatment of pediatric patients with Philadelphia chromosome-negative (Ph-) relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

• Merck Sharp & Dohme Corp.'s (merck.com) **Keytruda**® (**pembrolizumab**) has received FDA approval in first-line non-small cell lung cancer (NSCLC). The FDA also broadened Keytruda's label, approving the drug for use in patients whose tumors express any level of PD-L1 in the second-line setting. Keytruda has also been granted accelerated approval by the FDA for the treatment of patients with recurrent or metastatic head and neck squamous cell carcinoma with disease progression on or after platinum-containing chemotherapy.

• The FDA has approved Genentech's (gene.com) **Tecentriq**® (**atezolizumab**) for people with a specific type of metastatic NSCLC.

• Astellas Pharma US, Inc. (us.astellas.com) and Pfizer Inc. (Pfizer.com) announced the FDA has approved a supplemental new drug application (sNDA) for **Xtandi**® (**enzalutamide**) **capsules** in advanced prostate cancer.

Drugs in the News

• Genentech (gene.com) has received a second breakthrough therapy designation from the FDA for **Alecensa**® (**alectinib**) for the treatment of adult patients with advanced ALK-positive NSCLC who have not received prior treatment with an ALK inhibitor.

• AbbVie (abbvie.com) submitted an sNDA to the FDA for **Imbruvica**® (**ibrutinib**) to treat patients with marginal zone lymphoma, a form of non-Hodgkin's lymphoma.

• Fate Therapeutics, Inc. (fatetherapeutics.com) announced that the FDA has granted orphan drug designation for **ProTmune**™ for "prevention of graft-versus-host disease in patients undergoing allogeneic hematopoietic cell transplantation."

Approved Devices

• Medeon Biodesign, Inc. (medeonbio.com/en) has received FDA 510(k) clearance for **AbClose**™, a single use, disposable laparoscopic port site closure device.

• GI View Ltd. (giview.com) has received FDA 510(k) clearance for the new **Aer-O-Scope**® **Colonoscope System**, a disposable, self-propelled, joystick-controlled, easy-to-use colonoscope system.

• Varian Medical Systems (varian.com) has received 510(k) clearance from the FDA to market the **Nexus DR**, a high resolution imaging system for X-ray imaging using a digital X-ray detector.

Approved Genetic Tests & Assays

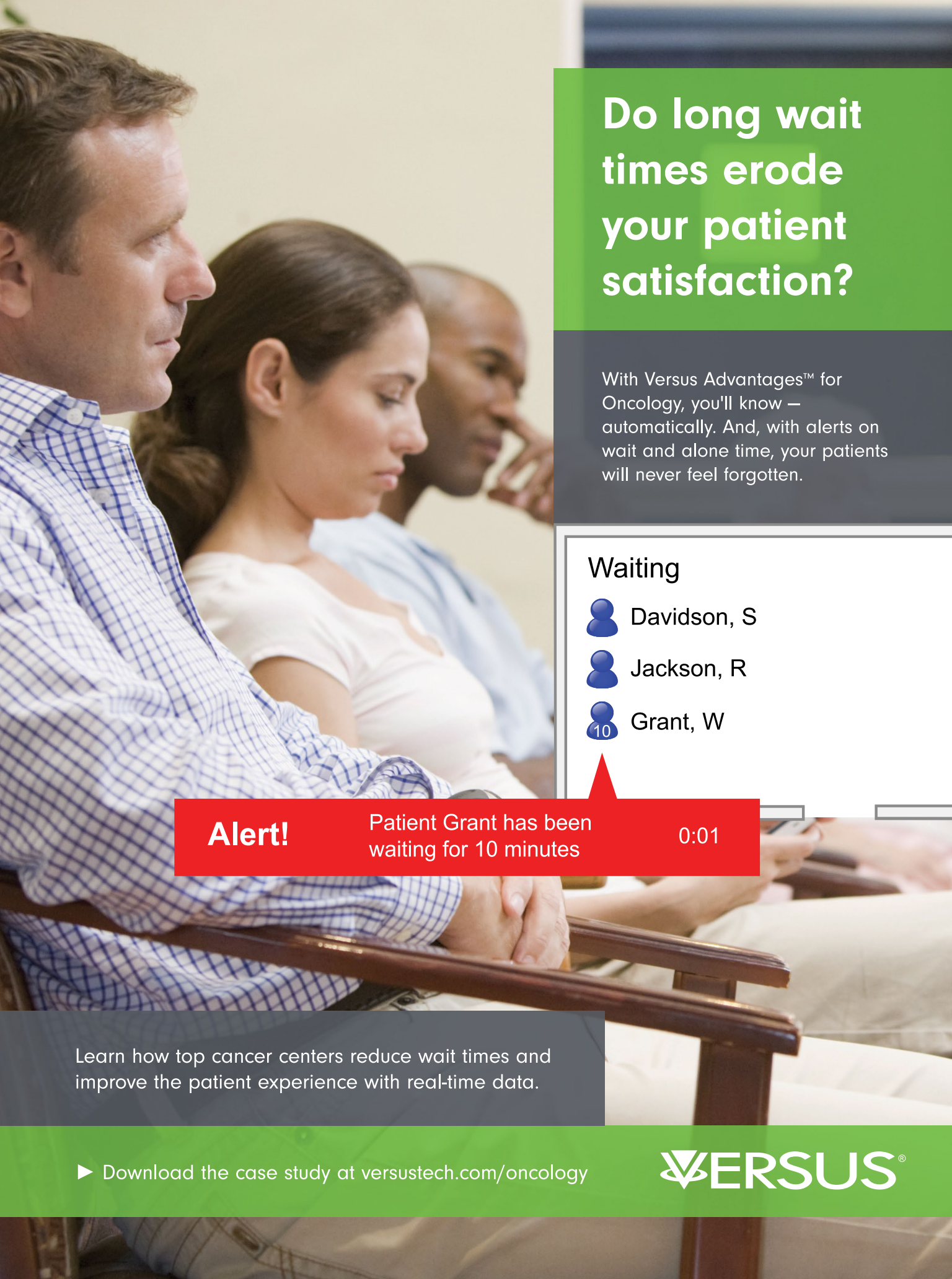
• AstraZeneca (astrazeneca-us.com) announced that the FDA has approved a blood-based companion diagnostic for **Tagrisso**® (**osimertinib**). OI

FDA Approves Two-Dose Vaccination Regime

The FDA has approved a 2-dose vaccination regimen for **Gardasil**® **9** (**Human Papillomavirus 9-valent Vaccine, Recombinant**), for use in girls and boys 9 through 14 years of age.

FDA Modifies the Indication for Tarceva

FDA modified the indication for **Tarceva**® (**erlotinib**) (Astellas Pharma US, Inc., us.astellas.com) for the treatment of NSCLC to limit use to patients whose tumors have specific epidermal growth factor receptor (EGFR) mutations.


Do long wait times erode your patient satisfaction?
With Versus Advantages™ for Oncology, you'll know – automatically. And, with alerts on wait and alone time, your patients will never feel forgotten.
Waiting
Davidson, S
Jackson, R
10
Grant, W
Alert!
Patient Grant has been waiting for 10 minutes
0:01
Learn how top cancer centers reduce wait times and improve the patient experience with real-time data.
► Download the case study at versustech.com/oncology
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Indication

IRESSA is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test.

There's marking time...

and there's making memories

Efficacy was demonstrated in the IFUM* study

- IRESSA achieved a 50% objective response rate (ORR) (95% confidence interval [CI]: 41, 59) by blinded independent central review (BICR) and a 70% ORR (95% CI: 61, 78) by investigator assessment

Efficacy was confirmed by the IPASS† study

- 3.5-month improvement in progression-free survival (median) vs chemotherapy—10.9 months with IRESSA vs 7.4 months with carboplatin/paclitaxel (HR=0.54; 95% CI: 0.38, 0.79) by BICR

Safety was established in the ISEL‡ study

- The most frequent adverse reactions (incidence of >20% and greater than placebo) reported in IRESSA-treated patients were skin reactions (47%) and diarrhea (29%)
- ≤5.1% of IRESSA-treated patients experienced severe adverse reactions
- Approximately 5% of IRESSA-treated patients and 2.3% of placebo-treated patients discontinued treatment due to an adverse event; the most frequent adverse reactions that led to discontinuation in patients treated with IRESSA were nausea (0.5%), vomiting (0.5%) and diarrhea (0.4%)

Limitation of Use: Safety and efficacy of IRESSA have not been established in patients with metastatic NSCLC whose tumors have EGFR mutations other than exon 19 deletions or exon 21 (L858R) substitution mutations.

Important Safety Information

- There are no contraindications for IRESSA
- Interstitial Lung Disease (ILD) or ILD-like reactions (eg, lung infiltration, pneumonitis, acute respiratory distress syndrome, or pulmonary fibrosis) occurred in 1.3% of 2462 IRESSA patients; of these, 0.7% were Grade ≥3 and 3 cases were fatal. Withhold IRESSA and promptly investigate for ILD in any patient who presents with worsening of respiratory symptoms such as dyspnea, cough and fever. Permanently discontinue IRESSA if ILD is confirmed
- In patients who received IRESSA, 11.4% of patients had increased alanine aminotransferase (ALT), 7.9% of patients had increased aspartate aminotransferase (AST), and 2.7% of patients had increased bilirubin. Grade ≥3 liver test abnormalities occurred in 5.1% ALT, 3.0% AST, and 0.7% bilirubin of patients. The incidence of fatal hepatotoxicity was 0.04%. Obtain periodic liver function testing. Withhold IRESSA in patients with worsening liver function and discontinue in patients with severe hepatic impairment
- Gastrointestinal perforation occurred in three (0.1%) of 2462 IRESSA patients. Permanently discontinue IRESSA in patients who develop gastrointestinal perforation
- Grade ≥3 diarrhea occurred in 3% of 2462 IRESSA patients. Withhold IRESSA for severe or persistent (up to 14 days) diarrhea
- Ocular disorders [keratitis (0.1%), corneal erosion and aberrant eyelash growth (0.2%), conjunctivitis, blepharitis and dry eye (6.7%)] occurred in 2462 IRESSA patients. The incidence of Grade 3 ocular disorders was 0.1%. Interrupt or discontinue IRESSA for severe or worsening ocular disorders
- Bullous conditions including toxic epidermal necrolysis, Stevens Johnson syndrome and erythema multiforme have been reported from treatment with IRESSA. Erythema multiforme and dermatitis bullous have been reported in two patients (0.08%) across NSCLC trials. IRESSA treatment should be interrupted or discontinued if patients develop severe bullous, blistering or exfoliating conditions
- Based on its mechanism of action and data from animal reproduction studies IRESSA can cause fetal harm when administered to a pregnant woman. In animal reproductive studies, oral administration of gefitinib from organogenesis through weaning resulted in fetotoxicity and neonatal death at doses below the recommended human dose. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with IRESSA and for at least two weeks following completion of therapy
- Advise women to discontinue breast-feeding during treatment with IRESSA
- The most commonly reported adverse drug reactions reported in more than 20% of patients and greater than placebo, were skin reactions (47%) and diarrhea (29%)

Please see brief summary of complete Prescribing Information on adjacent pages.

*IRESSA efficacy was evaluated in a multicenter, single-arm, open-label study as a first-line treatment of 106 Caucasian patients with EGFR mutation–positive metastatic NSCLC. IFUM=IRESSA Follow-Up Measure.

†IPASS included an exploratory analysis of a subset of a randomized, multicenter, open-label trial conducted in patients with metastatic adenocarcinoma histology NSCLC receiving first-line treatment. Patients received IRESSA 250 mg orally once daily (n=88) or up to 6 cycles of carboplatin/paclitaxel (n=98). IPASS=IRESSA Pan-Asia Study.

‡Common adverse reactions were evaluated in ISEL, a randomized, multicenter, double-blind, placebo-controlled study of 1692 metastatic NSCLC patients. Patients received IRESSA 250 mg daily (n=1126) or placebo (n=562). ISEL=IRESSA Survival Evaluation in Lung Cancer. A pooled safety database from 3 randomized trials was used to evaluate for serious and uncommon adverse drug reactions.

IRESSA®
gefitinib

AstraZeneca

IRESSA® (gefitinib) tablets for oral use

Brief Summary of Prescribing Information.
For complete prescribing information consult official package insert

INDICATIONS AND USAGE

IRESSA is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test *[see Clinical Studies (14) in the full Prescribing Information]*.

Limitation of Use: Safety and efficacy of IRESSA have not been established in patients with metastatic NSCLC whose tumors have EGFR mutations other than exon 19 deletions or exon 21 (L858R) substitution mutations *[see Clinical Studies (14) in the full Prescribing Information]*.

DOSAGE AND ADMINISTRATION

Patient Selection

Select patients for the first-line treatment of metastatic NSCLC with IRESSA based on the presence of EGFR exon 19 deletion or exon 21 (L858R) substitution mutations in their tumor *[see Indications and Usage (1)* and *Clinical Studies (14) in the full Prescribing Information]*. Information on FDA-approved tests for the detection of EGFR mutations in NSCLC is available at: http://www.fda.gov/CompanionDiagnostics.

Recommended Dose

The recommended dose of IRESSA is 250 mg orally once daily with or without food until disease progression or unacceptable toxicity.

Do not take a missed dose within 12 hours of the next dose.

Administration to Patients Who Have Difficulty Swallowing Solids

Immerse IRESSA tablets in 4 to 8 ounces of water by dropping the tablet in water, and stir for approximately 15 minutes. Immediately drink the liquid or administer through a naso-gastric tube. Rinse the container with 4 to 8 ounces of water and immediately drink or administer through the naso-gastric tube.

Dose Modification

Dose Modifications for Adverse Drug Reactions

Withhold IRESSA (for up to 14 days) for any of the following:

- Acute onset or worsening of pulmonary symptoms (dyspnea, cough, fever) *[see Warnings and Precautions (5.1) in the full Prescribing Information]*
- NCI CTCAE Grade 2 or higher in ALT and/or AST elevations [*see Warnings and Precautions (5.2) in the full Prescribing Information*]
- NCI CTCAE Grade 3 or higher diarrhea *[see Warnings and Precautions (5.4) in the full Prescribing Information]*
- Signs and symptoms of severe or worsening ocular disorders including keratitis *[see Warnings and Precautions (5.5) in the full Prescribing Information]*
- NCI CTCAE Grade 3 or higher skin reactions *[see Warnings and Precautions (5.6) in the full Prescribing Information]*

Resume treatment with IRESSA when the adverse reaction fully resolves or improves to NCI CTCAE Grade 1.

Permanently discontinue IRESSA for:

- Confirmed interstitial lung disease (ILD) *[see Warnings and Precautions (5.1) in the full Prescribing Information]*
- Severe hepatic impairment *[see Warnings and Precautions (5.2) in the full Prescribing Information]*
- Gastrointestinal perforation *[see Warnings and Precautions (5.3) in the full Prescribing Information]*
- Persistent ulcerative keratitis *[see Warnings and Precautions (5.5) in the full Prescribing Information]*

Dose Modifications for Drug Interactions

Strong CYP3A4 Inducers

Increase IRESSA to 500 mg daily in the absence of severe adverse drug reaction, and resume IRESSA at 250 mg seven days after discontinuation of the strong CYP3A4 inducer *[see Drug Interactions (7)* and *Clinical Pharmacology (12.3) in the full Prescribing Information]*.

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

Interstitial Lung Disease (ILD)

ILD or ILD-like adverse drug reactions (e.g., lung infiltration, pneumonitis, acute respiratory distress syndrome, or pulmonary fibrosis) occurred in 1.3% of the 2462 patients who received IRESSA across clinical trials; of these, 0.7% were Grade 3 or higher and 3 cases were fatal.

Withhold IRESSA and promptly investigate for ILD in any patient who presents with worsening of respiratory symptoms such as dyspnea, cough and fever. Permanently discontinue IRESSA if ILD is confirmed [*see Dosage and Administration (2.4) and Adverse Reactions (6.1) in the full Prescribing Information*].

Hepatotoxicity

In patients who received IRESSA across clinical trials, 11.4% of patients had increased alanine aminotransferase (ALT), 7.9% of patients had increased aspartate aminotransferase (AST), and 2.7% of patients had increased bilirubin. Grade 3 or higher liver test abnormalities occurred in 5.1% (ALT), 3.0% (AST), and 0.7% (bilirubin) of patients. The incidence of fatal hepatotoxicity was 0.04%.

Obtain periodic liver function testing. Withhold IRESSA in patients with worsening liver function and discontinue in patients with severe hepatic impairment *[see Dosage and Administration (2.4)*, *Adverse Reactions (6.1)*, and *Use in Specific Populations (8.7) in the full Prescribing Information]*.

Gastrointestinal Perforation

Gastrointestinal perforation occurred in three (0.1%) of the 2462 IRESSA-treated patients across clinical trials [*see Adverse Reactions (6.1) in the full Prescribing Information*]. Permanently discontinue IRESSA in patients who develop gastrointestinal perforation [*see Dosage and Administration (2.4) in the full Prescribing Information*].

Severe or Persistent Diarrhea

Grade 3 or 4 diarrhea occurred in 3% of 2462 IRESSA-treated patients across clinical trials. Withhold IRESSA for severe or persistent (up to 14 days) diarrhea *[see Dosage and Administration (2.4)* and *Adverse Reactions (6.1) in the full Prescribing Information]*.

Ocular Disorders including Keratitis

Ocular disorders [keratitis (0.1%), corneal erosion and aberrant eyelash growth (0.2%), conjunctivitis, blephritis and dry eye (6.7%)] occurred in the 2462 IRESSA-treated patients across clinical trials. The incidence of Grade 3 ocular disorders was 0.1% [*see Adverse Reactions (6.1) in the full Prescribing Information*]. Interrupt or discontinue IRESSA for severe, or worsening ocular disorders [*see Dosage and Administration (2.4) in the full Prescribing Information*].

Bullous and Exfoliative Skin Disorders

Bullous conditions including toxic epidermal necrolysis, Stevens Johnson syndrome and erythema multiforme have been reported from treatment with IRESSA. Erythema multiforme and dermatitis bullous have been reported in two patients (0.08%) across NSCLC trials (Study 2, Study 3 and Study 4). IRESSA treatment should be interrupted or discontinued if the patient develops severe bullous, blistering or exfoliating conditions.

Embryo-fetal Toxicity

Based on its mechanism of action and data from animal reproduction studies IRESSA can cause fetal harm when administered to a pregnant woman. In animal reproductive studies, oral administration of gefitinib from organogenesis through weaning resulted in fetotoxicity and neonatal death at doses below the recommended human dose. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with IRESSA and for at least two weeks following completion of therapy [*see Use in Specific Populations (8.1, 8.3) in the full Prescribing Information*].

ADVERSE REACTIONS

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

- Interstitial Lung Disease *[see Warnings and Precautions (5.1) in the full Prescribing Information]*
- Hepatotoxicity *[see Warnings and Precautions (5.2) in the full Prescribing Information]*
- Gastrointestinal Perforation *[see Warnings and Precautions (5.3) in the full Prescribing Information]*
- Severe or Persistent Diarrhea *[see Warnings and Precautions (5.4) in the full Prescribing Information]*
- Ocular Disorders including Keratitis *[see Warnings and Precautions (5.5) in the full Prescribing Information]*
- Bullous and Exfoliative Skin Disorders *[see Warning and Precautions (5.6) in the 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 safety of IRESSA is based on the data from 2462 patients with NSCLC who received IRESSA 250 mg daily monotherapy in three randomized clinical studies (Study 2, Study 3 and Study 4). Patients with a history of interstitial lung disease, drug-induced interstitial disease, radiation pneumonitis that required steroid treatment or any evidence of clinically active interstitial lung disease were excluded from these studies.

Controlled Studies:

Study 2 was a randomized, multicenter, open-label trial in which 1217 patients were randomized to receive first-line treatment for metastatic NSCLC; 607 patients received IRESSA 250 mg daily and 589 patients received carboplatin/paclitaxel. The median duration of treatment with IRESSA was 5.9 months. The study population characteristics were: median age 57 years, age less than 65 years (73%), female (79%), Asian (100%), NSCLC adenocarcinoma histology (100%), never smoker (94%), light ex-smoker (6%), ECOG PS 0 or 1 (90%).

Study 3 was a randomized, multicenter, double-blind, placebo-controlled trial in which 1692 patients were randomized to receive second- or third-line treatment for metastatic NSCLC; of which 1126 patients received IRESSA 250 mg daily and 562 patients received placebo. The median duration of treatment with IRESSA was 2.9 months. The study population characteristics were: median age 62 years, age less than 65 years (60%), female (33%), Caucasian (75%), Asian (21%), NSCLC adenocarcinoma histology (48%), never smoker (22%), ECOG PS 0 or 1 (65%), PS 2 (29%), PS 3 (5%) and two or more prior therapies (51%).

Study 4 was a randomized, multicenter, open-label trial in which 1466 patients were randomized to receive second-line treatment for metastatic NSCLC; 729 patients received IRESSA 250 mg daily and 715 patients received docetaxel. The median duration of treatment with IRESSA was 2.4 months. The study population characteristics were: median age 61 years, age less than 65 years (61%), female (36%), Caucasian (79%), Asian (21%), NSCLC adenocarcinoma histology (54%), never smoker (20%), ECOG PS 0 or 1 (88%) and two or more prior therapies (16%).

The pooled safety database from the three randomized trials was used to evaluate for serious and uncommon adverse drug reactions. Common adverse reactions were evaluated in Study 3. The most frequent adverse reactions in Study 3 (incidence of >20% and greater than placebo) reported in IRESSA-treated patients were skin reactions (47%) and diarrhea (29%). The most frequent fatal adverse reactions in IRESSA-treated patients were respiratory failure (0.9%), pneumonia (0.8%), and pulmonary embolism (0.5%).

Approximately 5% of IRESSA-treated patients and 2.3% of placebo-treated patients discontinued treatment due to an adverse event. The most frequent adverse reactions that led to discontinuation in patients treated with IRESSA were nausea (0.5%), vomiting (0.5%) and diarrhea (0.4%).

Table 1 – Selected Adverse Drug Reactions Occurring with an Incidence Rate ≥5% and an Increase of >2% of IRESSA-treated Patients in Study 3

	Percentage (%) of patients			
	IRESSA (N=1126)		Placebo (N=562)	
Adverse Reaction	**All Grades**	**Grade 3 and 4**	**All Grades**	**Grade 3 and 4**
Skin and subcutaneous tissue disorders				
Skin reactions[1]	47%	2%	17%	0.4%
Nail disorders[2]	5%	0.1%	0.7%	0%
Gastrointestinal disorders				
Diarrhea[3]	29%	3%	10%	1%
Vomiting	14%	1.2%	10%	0.4%
Stomatitis[4]	7%	0.3%	4%	0.2%
Metabolism and nutrition disorders				
Decreased appetite	17%	2.3%	14%	2.0%

Table 1 – Selected Adverse Drug Reactions Occurring with an Incidence Rate ≥5% and an Increase of >2% of IRESSA-treated Patients in Study 3 (cont'd.)

	Percentage (%) of patients			
	IRESSA (N=1126)		Placebo (N=562)	
Adverse Reaction	**All Grades**	**Grade 3 and 4**	**All Grades**	**Grade 3 and 4**
Eye disorders				
Conjunctivitis/blepharitis/dry eye[5]	6%	0%	3.2%	0%

[1] Includes Acne, Acne pustular, Dermatitis, Dermatitis acneiform, Dermatitis exfoliative, Drug eruption, Dry skin, Erythema, Exfoliative rash, Folliculitis, Pruritus, Pruritus generalized, Rash, Rash erythematous, Rash generalized, Rash macular, Rash maculo-papular, Rash papular, Rash pruritic, Rash pustular, Rash vesicular, Skin exfoliation, Skin toxicity, Xeroderma
[2] Includes Ingrowing nail, Nail bed infection, Nail disorder, Nail infection, Onychoclasis, Onycholysis, Paronychia
[3] Includes Diarrhea, Feces soft, Frequent bowel movements
[4] Includes Aphthous stomatitis, Cheilitis, Glossodynia, Mouth ulceration, Mucosal inflammation, Oral mucosal blistering, Stomatitis, Tongue disorder, Tongue ulceration
[5] Includes Blepharitis, Conjunctival hyperemia, Conjunctivitis, Dry eye, Eye irritation, Eye pruritus, Eye swelling, Eyelid irritation, Eyelid edema, Eyelids pruritus

Table 2 – Treatment Emergent Laboratory Abnormalities Occurring More Frequently in IRESSA-Treated Patients in Study 3

	IRESSA		Placebo	
Adverse Reaction	**All Grades %**	**Grade 3 and 4 %**	**All Grades %**	**Grade 3 and 4 %**
Alanine aminotransferase increased[1]	38%[2]	2.4%	23%[2]	1.4%[4]
Aspartate aminotransferase increased[1]	40%[3]	2.0%	25%[3]	1.3%[5]
Proteinuria	35%	4.7%	31%	3.3%

[1] Patients were allowed to enter the clinical study with lab values of ALT or AST CTCAE grade 1 or 2
[2] 14% gefitinib patients and 10% placebo patients were CTC grade 1 or 2 ALT at baseline
[3] 15% gefitinib patients and 12% placebo patients were CTC grade 1 or 2 AST at baseline
[4] 0.2% of placebo patients were CTC grade 3 at baseline
[5] 0.4% of placebo patients were CTC grade 3 at baseline

The following adverse reactions have been reported with IRESSA across NSCLC trials (Study 2, Study 3 and Study 4) and are not listed elsewhere in Section 6: nausea (18%), asthenia (17%), pyrexia (9%), alopecia (4.7%), hemorrhage (including epistaxis and hematuria) (4.3%), dry mouth (2%), dehydration (1.8%), allergic reactions including angioedema and urticaria (1.1%), elevations in blood creatinine (1.5%), and pancreatitis (0.1%).

Postmarketing Experience

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

Renal and urinary disorders: cystitis, hemorrhagic cystitis

Skin and subcutaneous tissue disorders: cutaneous vasculitis

DRUG INTERACTIONS

Drugs Affecting Gefitinib Exposure

CYP3A4 Inducer

Drugs that are strong inducers of CYP3A4 increase the metabolism of gefitinib and decrease gefitinib plasma concentrations. Increase IRESSA to 500 mg daily in patients receiving a strong CYP3A4 inducer (e.g., rifampicin, phenytoin, or tricyclic antidepressant) and resume IRESSA at 250 mg 7 days after discontinuation of the strong inducer [*see Dosage and Administration (2.4)* and *Clinical Pharmacology (12.3) in the full Prescribing Information*].

CYP3A4 Inhibitor

Drugs that are strong inhibitors of CYP3A4 (e.g., ketoconazole and itraconazole) decrease gefitinib metabolism and increase gefitinib plasma concentrations. Monitor adverse reactions when administering strong CYP3A4 inhibitors with IRESSA.

Drugs Affecting Gastric pH

Drugs that elevate gastric pH (e.g., proton pump inhibitors, histamine H_2-receptor antagonists, and antacids) may reduce plasma concentrations of gefitinib. Avoid concomitant use of IRESSA with proton pump inhibitors, if possible. If treatment with a proton-pump inhibitor is required, take IRESSA 12 hours after the last dose or 12 hours before the next dose of the proton-pump inhibitor. Take IRESSA 6 hours after or 6 hours before an H_2-receptor antagonist or an antacid [*see Clinical Pharmacology (12.3) in the full Prescribing Information*].

Hemorrhage in Patients taking Warfarin

International Normalized Ratio (INR) elevations and/or hemorrhage have been reported in some patients taking warfarin while on IRESSA therapy. Patients taking warfarin should be monitored regularly for changes in prothrombin time or INR.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

Based on its mechanism of action and animal data, IRESSA can cause fetal harm when administered to a pregnant woman. In animal reproductive studies, oral administration of gefitinib from organogenesis through weaning resulted in fetotoxicity and neonatal death at doses below the recommended human dose (*see Animal Data*). Advise pregnant women of the potential hazard to a fetus or potential risk for loss of the pregnancy.

The background risk of major birth defects and miscarriage for the indicated population is unknown; however, the background risk in the U.S. general population of major birth defects is 2-4% and miscarriage is 15-20% of clinically recognized pregnancies.

Data

Animal Data

A single dose study in rats showed that gefitinib crosses the placenta after an oral dose of 5 mg/kg (30 mg/m^2, about 0.2 times the recommended human dose on a mg/m^2 basis). When pregnant rats were treated with 5 mg/kg from the beginning of organogenesis to the end of weaning there was a reduction in the number of offspring born alive. This effect was more severe at 20 mg/kg (approximate the human clinical dose on a mg/m^2 basis) and was accompanied by high neonatal mortality soon after parturition. In rabbits, a dose of 20 mg/kg/day (240 mg/m^2, about twice the recommended dose in humans on a mg/m^2 basis) caused reduced fetal weight.

Lactation

Risk Summary

It is not known whether IRESSA is excreted in human milk. Animal studies indicate the gefitinib and its metabolites are present in rat milk at a concentration higher than those in maternal plasma. Because of the potential for serious adverse reactions in nursing infants from IRESSA, advise women to discontinue breast-feeding during treatment with IRESSA.

Data

Animal Data

Levels of gefitinib and its metabolites were 11-to-19-fold higher in milk than in blood, after oral exposure of lactating rats to a dose of 5 mg/kg.

Females and Males of Reproductive Potential

Contraception

Based on its mechanism of action and animal data, IRESSA can cause fetal harm when administered to a pregnant woman [*see Use in Specific Populations (8.1) in the full Prescribing Information*]. Advise females of reproductive potential to use effective contraception during treatment with IRESSA and for at least two weeks following completion of therapy.

Infertility

IRESSA may result in reduced fertility in females of reproductive potential [*see Nonclinical Toxicology (13.1) in the full Prescribing Information*].

Pediatric Use

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

Geriatric Use

Of the 823 patients enrolled in two randomized, active-controlled clinical trials 374 patients (45%) were 65 years and older, and 93 patients (11%) were 75 years and older. No overall differences in safety were observed between patients 65 years and older and those younger than 65 years. There is insufficient information to assess for differences in efficacy between older and younger patients.

Renal Impairment

Less than four percent (<4%) of gefitinib and its metabolites are excreted via the kidney. No clinical studies were conducted with IRESSA in patients with severe renal impairment.

Hepatic Impairment

The systemic exposure of gefitinib was compared in patients with mild, moderate, or severe hepatic impairment due to cirrhosis (according to Child-Pugh classification) and healthy subjects with normal hepatic function (N=10/group). The mean systemic exposure ($AUC_{0-\infty}$) was increased by 40% in patients with mild impairment, 263% in patients with moderate impairment, and 166% in patients with severe hepatic impairment. Monitor adverse reactions when IRESSA is administered to patients with moderate and severe hepatic impairment.

In a study comparing 13 patients with liver metastases and moderate hepatic impairment (addition of CTC grade of baseline AST/SGOT, ALP, and bilirubin equals 3 to 5) to 14 patients with liver metastases and normal hepatic function, the systemic exposure of gefitinib was similar [*see Warnings and Precautions (5.2) in the full Prescribing Information*].

OVERDOSAGE

Twenty three patients were treated weekly with doses from 1500 mg to 3500 mg, and IRESSA exposure did not increase with increasing dose. Adverse events were mostly mild to moderate in severity, and were consistent with the known safety profile of IRESSA. In the event of suspected overdose, interrupt IRESSA, institute supportive care, and observe until clinical stabilization. There are no specific measures/treatments that should be taken following IRESSA overdosing.

PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labelling (Patient Information).

Interstitial Lung Disease: Advise patients to immediately contact their healthcare provider for new onset or worsening of pulmonary symptoms such as dyspnea, cough and fever [*see Warnings and Precautions (5.1) in the full Prescribing Information*].

Hepatotoxicity: Inform patients that they will need to undergo lab tests to monitor for liver function. Advise patients to contact their healthcare provider to report any new symptoms indicating hepatic toxicity [*see Warnings and Precautions (5.2) in the full Prescribing Information*].

Gastrointestinal Perforation: Advise patients that IRESSA can increase the risk of gastrointestinal perforation and to seek immediate medical attention for severe abdominal pain [*see Warnings and Precautions (5.3) in the full Prescribing Information*].

Severe or Persistent Diarrhea: Advise patients to contact their healthcare provider for severe or persistent diarrhea [*see Warnings and Precautions (5.4) in the full Prescribing Information*].

Ocular Disorders including Keratitis: Advise patients promptly to contact their healthcare provider if they develop eye symptoms, lacrimation, light sensitivity, blurred vision, eye pain, red eye or changes in vision *[see Warnings and Precautions (5.5) in the full Prescribing Information].*

Bullous and Exfoliative Skin Disorders: Advise patients that IRESSA can increase the risk of bullous and exfoliative skin disorders and to seek immediately medical attention for severe skin reactions [*see Warnings and Precautions (5.6) in the full Prescribing Information*].

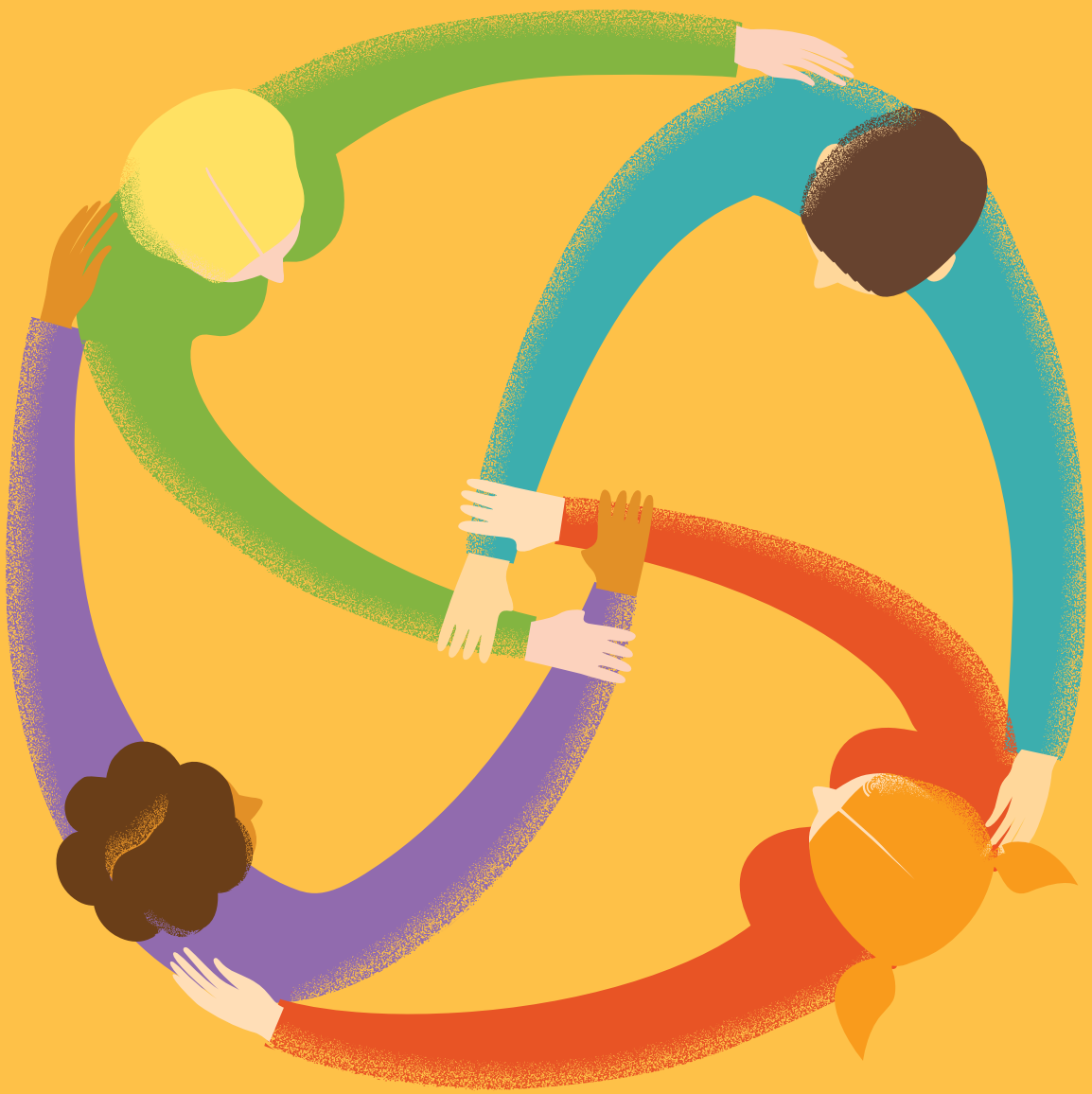
Embryo-fetal Toxicity: Advise pregnant women of the potential risk to a fetus or potential risk for loss of the pregnancy [*see Warnings and Precautions (5.7) and Use in Specific Populations (8.1) in the full Prescribing Information*]. Advise females of reproductive potential to use effective contraception during treatment with IRESSA and for at least two weeks following completion of therapy [*see Use in Specific Populations (8.3) in the full Prescribing Information*].

Lactation: Advise women to discontinue breast-feeding during treatment with IRESSA [*see Use in Specific Populations (8.2) in the full Prescribing Information].*

IRESSA is a trademark of the AstraZeneca group of companies.

Manufactured for:
AstraZeneca Pharmaceuticals LP Wilmington, DE 19850
By: AstraZeneca UK Limited Macclesfield, Cheshire, England Product of Belgium

3148105 7/15 Issued: 07/15



Growing Supportive Care Services Through Philanthropy

BY SUSAN HEDLUND, MSW, LCSW

A community comes together to meet the needs of its cancer patients

An estimated 14.5 million cancer survivors live in the U.S. today, and that number is expected to increase to 19 million by 2024.[1] Previously considered a death sentence, cancer is now viewed as a treatable, sometimes curable, cluster of diseases. Cancer is also regarded as a chronic illness, with greater emphasis on managing late effects and enhancing quality of life (QOL). Side effects from cancer—and cancer treatment—include physical, psychological, social, spiritual, and financial concerns, which have potential long-term impact on cancer patients and their families. As a consequence, cancer survivorship is now a public health issue.

Increasingly, cancer survivors are seeking guidance and support as they transition out of active treatment into ongoing surveillance and a return to "normal" life. These individuals seek services and tools to help them to adjust while maintaining wellness in the post-treatment phase of life.

In 2002 *CA: A Cancer Journal for Clinicians* reported that "increased use of outpatient services for cancer treatment, shortened hospital stays, longer survival, and the rise in the number of patients receiving home health services have created a greater need for assistance with regard to transportation, home medical care, activities of daily living, and out of pocket expenses."[2] The authors went on to further describe that community-based and philanthropic organizations often provided cancer patients with essential services that were unavailable from traditional medical services.

> The hospital foundation strategically cultivates relationships with generous donors to understand and be true to the donor's interests and desires. To support these efforts, the hospital foundation develops "menus of giving" that suggest services donors can support.

A Changing Landscape

Research suggests that as many as 90 percent of cancer patients use some form of integrative medicine compared to 40 percent of the general population.[3] Historically, cancer patients were often challenged to find these integrative services on their own; oncology providers were often unaware of the additional services pursued by their patients. It soon became clear to providers that they must find ways to bridge the gap between traditional medicine and the integrative medicine that patients desired.

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2015-2016 Patient and Family Support Services Program Highlights

Launched in 2011, the OHSU Knight Cancer Institute's Patient and Family Support Services Program has grown and thrived because of generous gifts from many contributors. Under the leadership of Susan Hedlund, M.S.W., L.C.S.W., and with cumulative philanthropic support we have been able to sustain, expand and create a range of patient- and family-centered support and care programs. This past year, we:

- Launched drop-in stress management breath-by-breath class in addition to offering ongoing mindfulness based stress reduction classes. Mindfulness is a practice of moment-to-moment observation, and can be highly effective in helping bring calm and clarity to the pressures of daily life. This is a powerful adjunct to therapy or medical treatment, and has proven beneficial for health conditions such as cardiovascular disease and chronic pain disorders.
- Offered three popular yoga classes, including gentle yoga for women healing from cancer. Classes are taught by a nationally certified cancer yoga teacher.
- Expanded acupuncture services to Knight Community Hematology Oncology clinic in Beaverton.
- Created, under the leadership of social work team members Nancy Boyle and Keren McCord, a quarterly well-attended cancer survivorship series for patients with hematologic malignancies. Topics have included: dealing with cancer and treatment related fatigue, chemo brain, exercise.
- Collaborated with a program dietician to pilot healthy cooking classes for breast and gynecological cancer survivors.
- Moderated successful therapeutic writing groups for adult patients and added a new program specifically for adolescent and young adult oncology patients and survivors.
- Partnered with Children's Healing Art Project to provide inpatient art therapy to help patient and family members reduce stress, pain, isolation and anxiety.
- Continued to fund a massage therapy program for inpatient with plans to expand to offer massage in outpatient clinics.
- Provided nearly $70,000 in emergency patient assistance to help with transportation, medication and lodging costs.
- Established the Jill Austin Cancer Pain Management Fund to support educational, research and care initiatives to help patients with cancer pain return to their highest level of functioning and to help them restore their quality of life.

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Recent trends in cancer care delivery also suggest there is increasing awareness of—and need for—services beyond those historically provided by cancer programs. This article describes the experience of one NCI-designated Cancer Center that has received extensive philanthropic funds to develop supportive care services for cancer patients.

Our Story

Five years ago, the Knight Cancer Institute at Oregon Health & Sciences University (OHSU), Portland, Ore., created a department within the cancer center called Patient & Family Support Services. Recognizing the need to create services that supported patients and families through the continuum of treatment and into survivorship, the new program had the backing of hospital leadership, as well as the philanthropic support of the hospital's foundation.

Indeed, the hospital foundation provided essential early support into program development. For example, in 2010, when conversations began about the need for supportive care services beyond medical treatment, the foundation helped recruit leadership for this program, and promised to provide funding for half of this FTE position for the first three years. The hospital made a commitment to pick up the funding for that role after the first three years. Soon, patients, families, and cancer program staff began to ask how they could make donations specifically for patient support.

At that time, in addition to 5 social workers, we offered one yoga class, thanks to an estate gift that specifically acknowledged the benefit of yoga in cancer recovery. This program was continued largely through the support of an oncology nurse who also believed in the programs' benefits.

Fast forward to today, our cancer program has experienced unprecedented growth in recent years. Over the past five years we've developed a robust program of supportive care services, including 12 oncology social worker positions (10.7 FTEs) funded by the hospital—essentially doubling our social work staff.

Expanding Our Services Through Philanthropy

The hospital foundation strategically cultivates relationships with generous donors to understand and be true to the donor's interests and desires. To support these efforts, the hospital foundation develops "menus of giving" that suggest services donors can support. Below are some of the supportive care services we've been able to fund through philanthropy.

Emergency assistance fund. Our oncology social workers assess all cancer patients for financial need and then recommend assistance based on this assessment. Each year patient need increases. (Of note, Oregon is primarily a rural state, and we are the only academic medical center in the state and the only cancer center with NCI-Cancer Program designation.)

High school senior Krysta Kilmer (left) raised funds for the Patient & Family Support Services program in honor of her mother and cancer survivor Mary Kilmer (right). The family benefited from the program when Mary traveled to the Knight Cancer Institute at Oregon Health & Sciences University from her home in Idaho for treatment and wanted to pay it forward. Accepting the generous donation is Nancy Boyle, LCSW.

One grateful patient asked her oncologist how she could help other patients. He directed her to the hospital foundation, and in 2011, the patient hosted the first of what has become an annual fundraiser. Hosted at the patient's catering business during the holidays, *Wine, Dine, and Be Merry* is now in its fourth year and is well-attended by hospital and cancer program staff, patients, families, and friends. Much of the funds raised at this annual event support a Patient & Family Emergency Assistance Fund. This fund has proved to be critical for serving some of our most vulnerable patients. This past year alone we provided approximately $60,000 of emergency assistance to patients. Most assistance went towards providing housing and/or transportation to patients who would not have been able to access care.

Recently two other family foundations have offered generous philanthropic support to the emergency assistance fund. The Dominic Fouts Memorial Cancer Fund uses their gift to honor the brother of the foundation's administrator, who died of cancer at age 38. The Bess Spiva Timmons Foundation also supports this important fund.

Integrative therapies. Another OHSU patient, who had been a childhood cancer survivor, and was now being treated for CML as an adult, had a family foundation. He met with representatives from the hospital foundation and asked how they might partner together. He and his wife were specifically interested in the use of integrative therapies to accompany traditional medical treat-

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A Special Report
August 2016

Fund Purpose and History

Established in October 2015, the Jill Austin Cancer Pain Management Fund provides vital support for educational, research and care initiatives to help patients so that they are able to return to their highest level of functioning and to help them restore their quality of life. Gifts to this fund make a huge difference in the lives of these patients and their loved ones.

Your Support

Thank you for supporting the Jill Austin Cancer Pain Management at the OHSU Knight Cancer Institute. Nearly one-third of the patients treated for cancer experience pain, which may significantly alter their quality of life. Acute or chronic pain affects basic daily activities becoming a contributing factor to fatigue, depression and stress. The OHSU Knight Cancer Institute and the OHSU Comprehensive Pain Center are committed to making sure that all cancer patients who experience pain have access to resources and care to reduce their pain and return to their day-to-day activities. When pain is controlled people may eat and sleep better and participate in the daily activities that are meaningful to them. For loved ones who support cancer patients during treatment this relief may provide an immeasurable sense of comfort. Your support is making it possible for OHSU to develop and implement strategies to specifically address care, education and research initiatives around cancer pain management.

> "Jill always gave to others and never asked anything in return. In this loving spirit we hope to help ease the pain of others. **Thank you for your support."**
>
> — *The Sorenson Family*

It is important to OHSU and the Sorenson family that you know how your support is making a difference. Please read more about the impact your gifts are making.

Jill Austin

In memory of Jill, Richard Sorenson, her widower, created the Jill Austin Cancer Pain Management Fund to help others who suffer from debilitating pain. Jill was the life of the party, up for new adventures, and constantly playing and laughing with her grandchildren. She loved gardening, hosting big parties, being a wonderful mother, and a devoted friend to countless people. Before Jill lost her battle with cancer, the pain took away her amazing quality of life—it took her life before cancer did. This gift is to help patients and their loved ones become better equipped to conquer pain associated with their cancer.

— *The Sorenson Family*

(continued from page 29)
ment. Through the family foundation's gift, we were able to add two additional yoga classes and a program on *Mindfulness-Based Stress Reduction*.

Massage and healing touch. As Patient & Family Support Services continued to evolve, we found that financial gifts inspired other, larger gifts. Simply put: our cancer patients very much wanted to help other cancer patients. Two former patients—both with hematological malignancies treated with bone marrow transplantation—worked as national marketing representatives for Nike, the athletic company. They approached us and indicated that they were having an annual fundraiser, and wanted our cancer program to be the recipient of this benefit.

As Patient & Family Support Services grew, we wanted to be sure that the services we offered were in line with the needs of patients and loved ones. To do so, we conducted five focus groups with cancer survivors in 2014.

When talking with these former patients about what was important to them, one indicated that the only time she was touched "non-medically" during transplant was by the oncology massage volunteer.

The benefit raised $85,000 for our cancer program, and we committed all funds to grow our cancer massage services. We now have five oncology-trained massage therapists who work part-time on our inpatient oncology units and in the outpatient oncology clinics. We also have a massage internship program for licensed massage therapists seeking to learn the specialized skills needed for working with an oncology population.

We have begun to evaluate the impact of massage for our oncology inpatients by administering a pre- and post-massage survey to measure the impact of massage on the patient experiences of anxiety, fatigue, and pain.

Last year, we provided 1,434 massages on our inpatient oncology units. The results have been impressive. Before implementing this service, 22 percent of patients reported high levels of anxiety; only 8 percent reported anxiety after. We saw similar improvements in pain scores: 22 percent of patients reported pain before massage services were added, and only 10 percent reported pain after implementing the massage program. We also realized an improvement in patient-reported fatigue, with 21 percent of patients reporting fatigue prior to these services, and 17 percent reporting fatigue after. Clearly the addition of massage services helped to reduce the distress of our cancer patients.

Pain management. Another donor gifted money and helped raise funds to support our Jill Austin Cancer Pain Management Fund, in the hope that cancer patients will not have to suffer as a result of cancer-related pain. To meet this need, the oncology program is partnering with the hospital's department of anesthesiology to develop a program to improve treatment of cancer-related pain and ensure patient access to these critical services. See box at left for more on this fund.

Adding the Right Staff

Through philanthropy, the Patient & Family Support Services was able to hire its first acupuncturist. The hospital agreed to pay for the acupuncturist on a part-time basis until she was able to be largely self-supporting through billing. Cancer program staff navigated the acupuncturist through the credentialing process and set up billing mechanisms for her services. We hired a practitioner who had been an oncology nurse in our healthcare system prior to becoming a licensed acupuncturist and naturopath. This decision was critical because she understood cancer, cancer treatment, and the related side effects. While she is currently practicing as an acupuncturist, Patient & Family Support Services is exploring how we might add her naturopathic skills to our practice setting.

It has been important to recruit integrative medicine providers who are willing to collaborate with more traditional Western medicine practitioners. Thus, in the massage program, we set the bar high by requiring that the massage therapists had specific and in-depth training in cancer-specific massage techniques.

Our mindfulness-based stress reduction and yoga teacher has extensive experience working with cancer patients, offering trainings at Duke University, as well as having one of the first evidence-based NCI research studies on the efficacy of mindfulness-based intervention for cancer patients.

These staffing choices have been intentional, and have resulted in great acceptance and support of services that could potentially been perceived as "unconventional" by providers and staff.

Identifying New Needs

As Patient & Family Support Services grew, we wanted to be sure that the services we offered were in line with the needs of patients and loved ones. To do so, we conducted five focus groups with cancer survivors in 2014. We also conducted a one-month survey of cancer survivors inquiring as to what services they most wanted to see added. The results from 374 patients surveyed identified these top three needs:

- Fitness classes: 18 percent
- Nutrition classes: 18 percent
- Traditional support groups: 12 percent.

Knight Cancer Institute's Patient & Family Support Services benefits greatly from the ongoing philanthropic support of its community. In 2010 and 2011 Patty Reed, owner and president of Patty Reed Designs, gave generously in support of breast cancer research and patient care. (Reed is pictured holding the check.)

Additional feedback from the focus groups reflected the desire for classes on chemotherapy-related cognitive changes, fatigue, stress management, and integrative medicine. All have been added as a result.

We have since added expressive arts to our service line offerings. Currently, we offer three writing groups: one for women with cancer, one for men with cancer, and one for adolescents and young adults with cancer. All groups are led by trained writing facilitators. Our experience is that these groups are often attended by people who might not attend more traditional support groups.

Patient & Family Support Services also supports:

- A large and active prostate cancer support group—11 years strong—and a support group for young adults with cancer
- A healing arts program on the inpatient transplant unit

- Survivorship classes
- A "Cooking for Wellness" monthly pilot in conjunction with the Center for Women's Health and the hospital's Nutrition Department
- Classes on dealing with fatigue, chemo brain, and intimacy issues after cancer.

All services are offered free-of-charge with the exception of acupuncture, which is a fee-for-service offering, and the mindfulness-based stress reduction, which is offered at half the normal cost for the series.

Sharing Lessons Learned

Hospital foundation leaders share that there is sometimes a misconception that "things just happen," meaning supportive care services simply get created. The reality: it takes people who understand the needs and wishes of people with cancer, combined with the required resources, to create these services. It is simply not realistic to expect that all of these resources can come from within the hospital system itself, which is often managing multiple competing priorities.

Leveraging philanthropy to seed fund some of these supportive care programs helps lay the foundation for programs that ultimately become self-sustaining, as was the case for our acupuncturist. In other instances, the supportive care programs inspire ongoing and larger gifts. Family foundations, memorial gifts, and/or the desire to leave a legacy are all aspects of philanthropic support.

Another lesson we can pass on is the critical nature of relationship building. It has been essential for Patient & Family Support Services to maintain and proactively seek relationships with our donors on a personal level. We cannot emphasize enough that being "good stewards" to the donors' intent is of utmost importance. Letting donors know how funds are received and used and how their gifts truly make a meaningful difference in the lives of patients is essential.

We make a concerted effort to let donors who cannot give large amounts know that every gift makes a difference. For example, a gift of $25 immediately becomes a gas card to help a patient get to treatment.

An inspiring component of this evolution is how much our staff, who spend each day working with oncology patients and their loved ones, want to support Patient & Family Support Services. Staff attend our annual fundraiser—both as volunteers and donors—and are enthusiastic about their support. It is inspiring and humbling to see their efforts.

Staying current with what patients need and want is also important as cancer patients and survivors have a range of needs. Periodic focus groups and surveys help us keep our fingers on the pulse of those needs.

Relationships between Patient & Family Support Services and key foundation directors are also essential. We offer education to members of the hospital foundation about our current offering of supportive care services; the foundation has found this ongoing education helpful to make solicitations. Patient & Family Support Services has also created print materials and reports to share with potential donors (see pages 28 and 30). Finally, sharing patient stories of how lives have been touched by these supportive care services is powerful. We keep our momentum going by being available to meet with donors, giving community presentations, and, most importantly, always expressing gratitude.

Most people with cancer and their loved ones tell us that it takes more than medicine to help them heal. The role of supportive care services cannot be underplayed, yet expecting our hospitals and health systems to pay for this support is unrealistic. We are so fortunate that donors in our community have stepped up to help, supporting our efforts to create a robust offering of supportive care services to our patients and their loved ones.

The most critical takeaway for cancer programs looking to leverage community philanthropy is this: prepare for it to be an ongoing endeavor. Fundraising is not a single event in time. Building on relationships with donors, measuring the impact on cancer patients, soliciting patient feedback, and letting donors know that their gifts indeed change lives is essential. OI

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COMPLIANCE
with Breast Cancer Post-Therapy Surveillance

BY MELISSA CARANDANG, MD; WESLEY BABARAN, MD; LAWRENCE WAGMAN, MD; LIANNE NACPIL, MPH, CTR; TIMOTEA LARA, RN, MSN, NP-C; NORMA CASTRO; AND SHANNIN GREENE

IN BRIEF

The multidisciplinary breast cancer clinic at St. Joseph Hospital, Center for Cancer Prevention and Treatment (CCPT), Orange, Calif., was designed with a specific infrastructure to serve women with state and federal safety net funding. In 2011 CCPT initiated a study to measure patient compliance with post-therapy surveillance in this population, conducting a descriptive retrospective chart review on previously diagnosed breast cancer patients seen at the multidisciplinary breast cancer clinic during the two years from 2011 to 2013. Post-therapy surveillance compliance was assessed in three categories: clinic appointments (n=82), annual mammography for patients with one or both breasts intact (n=75), and yearly evaluation for those prescribed anti-hormone therapy (n=61). CCPT compared compliance rates based on patient characteristics: age, stage, distance from the clinic, insurance carrier, race, and ethnicity.

Study results found the average per patient combined compliance for all post-therapy surveillance to be 92.5 percent at 12 months, 54.4 percent at 18 months, and 82.4 percent at 60 months. When comparing characteristic groups by test categories, CCPT found no clinically significant patterns or trends; however, overall annual mammogram compliance was consistently higher than both clinic appointment and anti-hormone therapy compliance.

The St. Joseph Hospital, Center for Cancer Prevention and Treatment established its multidisciplinary breast cancer clinic in 2008 as a component of the National Cancer Institute Community Cancer Centers Program (NCCCP) grant. The goal: to serve women with a confirmed breast cancer diagnosis and "safety net" financial status—the patient population for the study discussed in this article.

Clinic components include scheduling, nursing, culturally geared navigation, operating services, breast imaging, electronic health records, translation services, and research (Table 1, page 37). As the breast cancer clinic is staffed by both hospital-employed and private practice multispecialty oncologic physicians, CCPT has developed guidelines for physician participation in the cancer program. Some physicians treat patients in the hospital's outpatient department and bill under 1206(d) in the Outpatient Prospective Payment System (OPPS), while others see patients in their private physician practice offices and bill for services under the Physician Fee Schedule (PFS).

The CCPT multidisciplinary breast cancer clinic follows National Comprehensive Cancer Network (NCCN) guidelines for breast cancer post-therapy surveillance, including clinic appointments, mammograms, and confirmation of anti-hormone therapy use. During this study period, the standard practice was to advise patients in accordance with NCCN post-therapy surveillance. Note: this analysis precedes the multidisciplinary breast cancer clinic's consistent distribution of a formal breast-cancer-specific treatment summary survivorship plan, which is currently required by the Commission on Cancer (CoC).

Study Methods

In 2014 CCPT conducted a retrospective, descriptive chart review on 82 previously diagnosed breast cancer patients seen at the multidisciplinary breast cancer clinic between 2011 and 2013. Post-therapy surveillance consisted of:

- Clinic appointments every 4 to 6 months for the first 5 years after treatment.
- Annual mammograms for the first 5 years after treatment.
- Annual compliance with recommended anti-hormone therapy use for the first 5 years after treatment.

As is expected in the breast cancer patient population, CCPT believed that primary care providers, in a variety of settings, would potentially assume patients' long-term cancer surveillance.

Individual patient and test results were tallied and analyzed for compliance. All 82 patients were evaluable for clinic appointment compliance. For annual mammograms, the patients who were included in the study had one or both breasts intact (n=75), while patients with a history of bilateral total mastectomies were excluded. CCPT also assessed the compliance of all patients who had been prescribed anti-hormone therapy (e.g., aromatase inhibitors or tamoxifen); data was collected to document evidence of assessment and adherence at the follow-up appointments (n=61). Patients who were not prescribed anti-hormone therapy were excluded.

CCPT then compared compliance for the three main parameters based on subject characteristics:

- Age
- Stage at diagnosis
- Distance from home to clinic
- Type of insurance
- Race
- Ethnicity.

Table 2, page 38, shows the subject characteristics of the study.

Study Results

Overall, during the 5-year study period, the compliance rate for attending scheduled clinic appointments for all 82 patients ranged from 54.3 percent to 96.3 percent. Patient compliance with mammograms completed for 75 patients ranged from 78.6 percent to 97.3 percent. Finally, compliance with reported anti-hormone therapy use for 61 patients ranged from 62.5 percent to 93.3 percent. CCPT saw a large dropoff in the average per patient combined compliance for the three parameters 18 months post-treatment, but compliance increased and remained consistently higher after 2-years post-treatment (see Figure 1, page 40).

During analysis of the compliance with clinic appointments based on patient age, the average was approximately 70 percent throughout the groups. The average compliance of reported anti-hormone therapy use based on age groups was slightly higher at 81 percent, while mammogram compliance was the highest overall, with averages ranging from about 80 percent to 90 percent.

All patients in the study were newly diagnosed and staged at their initial multidisciplinary breast cancer clinic evaluation. When measuring the compliance with clinic appointment based on stage at diagnosis, the range was large—59.3 percent at Stage 0 to 80.6 percent at Stage III. The compliance with reported anti-hormone use based on stage at diagnosis was slightly higher with a range of 75.1 percent (Stage 0) to 87.5 percent (Stage IV). Mammograms completed showed the highest compliance, ranging from 85.1 percent (Stage II) to 91.7 percent (Stage IV).

As the distance from the clinic increased, the average compliance of all three post-therapy surveillance measurements did show a slight downward trend. For clinic appointments, the compliance was highest for patients who traveled 0.0 to 9.9 miles for treatment (76.6 percent), whereas the patients who traveled more than 20 miles had a slightly lower average (67.6 percent). The compliance with reported anti-hormone therapy use was around 77 percent. Again, mammograms completed were the highest all around, ranging from 81 percent (patients traveling 10 to 19.9 miles) to 93.5 percent (patients traveling 0 to 9.9 miles).

Table 1. Multidisciplinary Breast Cancer Clinic Infrastructure Elements
SPACE
• 3,300 square feet
• 4 examination rooms
• Scheduling desk
• A private consultation room
• A nurse practitioner room
• A navigator room
PERSONNEL
• Medical director
• 2 administrative assistants
• Medical assistant
• Nurse practitioner
• Financial navigator
• 2 nurse navigators
• 12 breast specialty physicians
• Social worker
• Translator (plus telephonic support)
EQUIPMENT
• Ultrasound machine

Based on insurance carriers, MediCal HMO patients had the highest percentage of compliance (95 percent; n=2). After that, the ranking was as follows:

- 73.7 percent compliance for patients under the Breast Cancer Early Detection Program (n=9)
- 68.6 percent for patients with Cal Optima (n=63)
- 68.2 percent for Medicare patients (n=2)
- 63.1 percent for MediCal patients (n=6).

While CCPT identified no statistical trends when stratifying the data by insurance carrier, compliance was overall higher (average of 90 percent) when compared to clinic appointment (average of 74 percent) and reported anti-hormone therapy use compliance (average of 87 percent). Of note: evaluation of the patients under the Breast Cancer Early Prevention Program revealed an 83.3 percent composite compliance.

The average compliance for clinic appointments based on ethnicity was approximately 70 percent throughout all groups, while average compliance for mammogram completed was around 88 percent. However, looking at reported anti-hormone therapy use compliance, the averages ranged from 52.5 percent (Other) to 80.4 percent (Asian). The average compliance for ethnicity mirrored race.

Patient Compliance in the Community Setting

The journey through cancer care is long and arduous, resulting in a stronger relationship between patient and provider. Patients tend to place a higher level of trust in their cancer care professionals. In addition, cancer treatments are becoming readily available in the community setting, providing patients with more options close to home. While some patients still favor receiving care in an academic or tertiary care setting, a growing number of patients look to receive care in their community or close to home. (In general, 80 percent of initial cancer care is believed to be delivered in the community environment.)

Physicians make treatment recommendations and educate patients on both the benefits of following through and the risk factors of not adhering to these recommendations; however, socioeconomic and cultural factors interact and influence health-

(continued on page 39)

Table 2. Subject Characteristics

DEMOGRAPHICS	
Total number of patients assessed for compliance with clinic appointments	n=82
Total number of patients assessed for compliance with mammography	n=82
Total number of patients assessed for compliance with anti-hormone therapy	n=61
AGE GROUPS (AVERAGE=53.5 YEARS; RANGE 32.7 YEARS TO 69.8 YEARS)	
<40 years	3
40 to 49 years	25
50.0 to 59.9 years	37
60.0 to 69.9 years	17
STAGE AT DIAGNOSIS	
Stage 0	13
Stage I	24
Stage II	25
Stage III	18
Stage IV	2
DISTANCE TO CLINIC	
0.0 to 9.9 miles	32
10.0 to 19.9 miles	30
>20 miles	20
TYPE OF INSURANCE	
BCEDP (Breast Cancer Early Detection Program)	9
MediCal HMO	2
Medicaid	6
Cal Optima	63
Medicare	2
RACE	
White	49
Asian	30
Other	3
ETHNICITY	
Non-Spanish	55
Spanish NOS	19
Spanish Surname Only	8

(continued from page 37)
care compliance patterns and real-life factors affect adherence. Whether external—distance from the clinic, financial issues, the patient having to see multiple providers—or internal—competing priorities or educational status—the reasons for non-compliance are usually multi-faceted and difficult to assess using standard measurements. While there is not enough evidence to definitively identify these individual or group of factors at this time, this study documents the favorable outcomes that can be achieved in a multidisciplinary breast clinic designed with a population and culturally-sensitive infrastructure.

> ...the multidisciplinary breast cancer clinic is developing a well-structured process for transferring survivorship care to oncological or primary care facilities closer to the patients' residences.

Consistent with other reports analyzing post-cancer treatment adherence, this study documents a general dropoff in compliance at the 18-month mark. There are a number of potential reasons for this pattern, including financial burdens and a lower perceived notion of recurrence once the cancer is treated.[1] Patients may feel that once they are cancer free or have clear findings during the first year of post-cancer treatment screenings, they are no longer on "high-alert" for recurrence. Studies suggest that by verbally emphasizing the importance of annual screening at each patient encounter, and sending reminder notes and/or telephone calls, patient compliance can be improved. Specific educational interventions may be needed in survivorship care that can influence both survival and quality of life outcomes.[1,2] The practice at CCPT is to counsel each patient at the end of each clinic visit, tailoring education based on individual socioeconomic and cultural considerations. This counseling includes educating patients about the timing importance of follow-up tests and adherence to medication.

The consistently high overall compliance levels that were achieved in this study were likely a result of CCPT's well-designed and executed patient-centric infrastructure (e.g., financial navigator, language specific scheduling) and its ability to eliminate expected non-compliance patterns.

Compliance & Scheduling

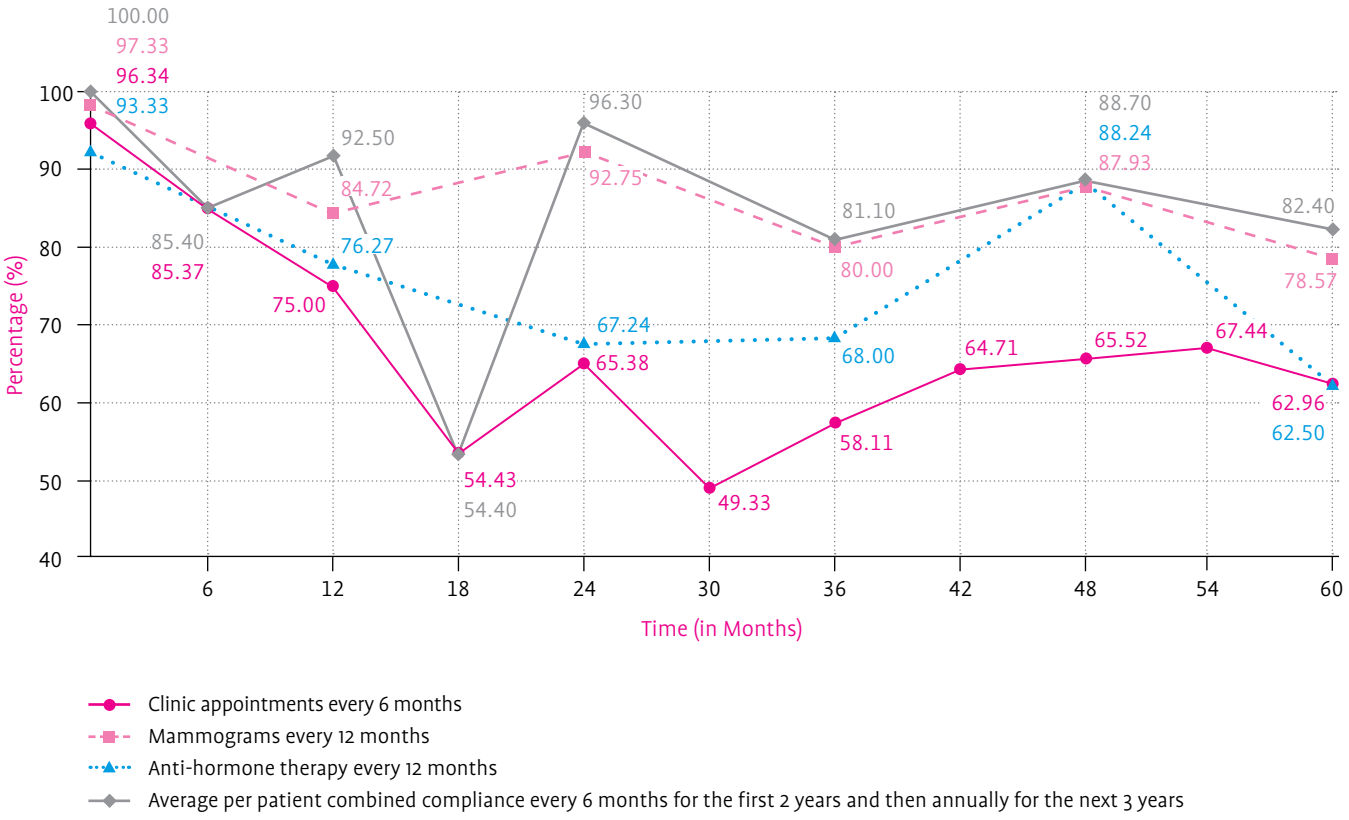
When comparing the three post-therapy surveillance parameters, overall mammogram compliance was consistently higher than clinic appointment and anti-hormone therapy compliance. Study data showed that many patients had appointments for mammograms and clinic appointments on separate days. This was done to ensure that providers had mammography reports and films at the time of the clinic appointment. Based on study data, this scheduling process affected the return of patients for their clinic appointments. To improve compliance with clinic appointments, the multidisciplinary breast cancer clinic now schedules mammograms and clinic appointments for the same day, pairing the highly compliant mammogram encounter with the slightly lower performing clinic appointment and anti-hormone therapy events (Figure 1, page 40).

Also, since the multidisciplinary breast cancer clinic is privately funded and resources are limited, CCPT is decreasing post-therapy surveillance care from 5 years to 3 years—with a return to the primary care provider for follow up, which may help CCPT manage patient volume. In accordance with recommendations from Advani et al., the multidisciplinary breast cancer clinic is developing a well-structured process for transferring survivorship care to oncological or primary care facilities closer to the patients' residences.

Compliance & Age of Patient

One study revealed a relationship between clinic attendance and age, where each year of increased age was associated with a 7 percent greater likelihood of re-attendance, as well as compliance to breast cancer screening practices like mammography.[3] Another study measured the adherence of hormone therapy after breast surgery and found that the lower rate among younger patients

Figure 1. Compliance of Post-Treatment Surveillance by Month



was thought to be related to the adverse effects on sexuality, fertility, and menopausal symptoms.[4] According to Calvocoressi et al., another factor that may explain low adherence among younger patients (<50 years) is that screening procedures, such as mammography, may not yet have become a habit for many younger women.[5]

In this study, CCPT observed no age-dependent pattern. If the sample size had been larger, a clearer trend or pattern may have emerged. While the low number of patients may explain the failure to identify a variation, this lack of variation may also be supported by the hands-on approach of the multidisciplinary breast cancer clinic staff to keep patients well-informed about importance of post-therapy surveillance.

Compliance & Stage of Disease

According to Brito et al., a correlation exists between adherence to anti-hormone therapy in breast cancer patients after surgery and stage of disease.[4] Specifically, there was a lower compliance among patients at non-curable stages (Stages III and IV).[4]

In this study, CCPT saw consistency throughout all groups when evaluating stage of disease and compliance. To eliminate any pattern of non-compliance, care must focus on patient-specific needs, which includes culture, language, and individual concerns. CCPT support staff maintained compliance for this patient population by adapting education and management techniques to fit the specific needs of individual patients.

Compliance & Travel Time

In the CCPT study, a mildly inverse relationship occurred—as the distance between the patient's residence and the multidisciplinary breast cancer clinic increased, patient compliance decreased. A more significant pattern between travel distance and patient compliance may have been apparent with a larger study group. For example, one study measured adherence to breast cancer survivorship surveillance care and found an association with compliance and the distance from the patient's residence to the cancer center for follow-up.[2] Researchers saw that the distance that patients had to travel to receive care was significantly associated with a lack of follow-up after treatment completion and with non-adherence to survivorship care guidelines.[2] Similarly, a comprehensive review of multiple studies revealed a strong relationship between travel burden and poorer prognosis due to non-compliance.[6] Also, it has been suggested that patients who live further away may have continued their care with a provider closer to their place of residence.

Communication between healthcare providers and a formal "hand-off" may be beneficial. Of interest, the referral patterns for the group of patients described in the CCPT study are generally geographically restricted by county and administrative criteria. Thus, the referring physician's practice has often pre-selected geographically desirable breast cancer facilities. Even the greatest distances observed in this community-based care delivery network may not be significant enough to impact compliance. Yet, this data emphasizes the importance of supporting community-based cancer delivery systems.

Compliance & Insurance

In general, access to medical insurance can play a role with a patient's adherence to healthcare. Cancer patients without insurance or who are under-insured may be hesitant to seek care, follow therapy, and/or comply with post-therapy examinations. Personal and family financial burdens are also cited in the literature. For example, one study analyzed different socioeconomic predictors of regular mammography use among African-American women and found that loss or lack of healthcare insurance adversely affected adherence to mammography guidelines.[7]

In the CCPT study, all patients had some form of insurance coverage, explaining the lack of variation and consistency across all groups. Along with Medicare, MediCal, and state of California sponsored breast cancer support programs, CCPT has the philanthropic means to financially support care-based costs, including travel, co-pays, short-term rent, and personal expenses. Since access to insurance was constant across all groups, a different predictor (e.g., social, cultural, psychological) must have played a role in non-compliance.

Compliance, Race & Ethnicity

Based on both race and ethnicity, compliance levels were not different in the CCPT study. This uniformity could be explained by the culturally sensitive, language-specific education offered by staff at the multidisciplinary breast cancer clinic.

In one analysis measuring the treatment adherence and outcome in women with inflammatory breast cancer, results showed that race or ethnicity did not appear to impact treatment adherence with African Americans or Caucasians.[8] However, another study demonstrated a significant interaction between Hispanic ethnicity and endocrine therapy, resulting in non-adherence to follow-up care guidelines, especially if language barriers or lack of a relationship with a provider existed.[2] Another study found that African-American women may not adhere to recommendations concerning breast abnormalities because of a lack of trust with their healthcare providers or lack of a consistent provider due to lower socioeconomic status.[9]

In order to overcome these non-compliance issues, a recent study suggests patients with lower socioeconomic status may need more one-on-one communication about their treatment plans since they tend to have less access to healthcare services.[10] In addition to one-on-one "concierge" interactions, the multidisciplinary breast clinic's consistent messaging and maximized patient engagement and efforts to provide a safe, trusted care environment bolstered patient compliance.

Going Forward

Given the challenge of consistent, reliable follow up of patients with state and federal safety-net funding, the results of this analysis are quite encouraging, with high averages of overall compliance. The authors believe that this study serves as a real-life, practical, consistent community standard that can be achieved by similarly structured patient-centered programs. OI

Melissa Carandang, MD, is a clinical research associate; Wesley Babaran, MD, was a clinical research associate; Lawrence D. Wagman, MD, FACS, is the executive medical director; Lianne Nacpil, MPH, CTR, was the cancer registry manager; Timotea Lara, RN, MSN, NP-C, was a nurse practitioner; Norma Castro is office coordinator and patient navigator; and Shannin Greene is a medical assistant, St. Joseph Hospital, Center for Cancer Prevention and Treatment, Orange, Calif.

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BY CONNIE SAVAGE, LPN

Bridging the Gap from Inpatient to Outpatient Care

In 2014 Cancer & Hematology Centers of Western Michigan looked to improve continuity of care—specifically patient transitions from the hospital inpatient to the outpatient setting. In October of that same year, the practice created the position of inpatient coordinator with an eye towards:

- Improving patient and family satisfaction
- Increasing patient visits by freeing up physician and mid-level provider time
- Reducing no-show appointments
- Decreasing hospital length of stay (LOS) and admissions.

Further, the practice believed an FTE inpatient coordinator would improve the patient discharge experience and facilitate more effective communication between multidisciplinary care teams across care settings.

Key Roles & Responsibilities

Today, the inpatient coordinator works closely with mid-level providers and physicians in the hospital setting. Once patients are ready for discharge, the inpatient coordinator ensures that all outpatient appointments are scheduled, including:

> ...the greatest benefit to adding the inpatient coordinator has been the improvements in patient and provider satisfaction.

- Physician office visits
- Labs
- Imaging appointments
- Referrals and appointments with other physicians
- Referrals and appointments with other providers, for example dietitians or financial advocates.

The inpatient coordinator enters all appointments into the patients' discharge paperwork so that the bedside nurse who goes over the discharge instructions can answer any patient or caregiver questions regarding home or follow-up care. Working in tandem,

Table 1. Inpatient Coordinator Key Roles & Responsibilities
SCHEDULE FOLLOW-UP CARE
• Physician visit(s)
• Lab(s)
• Imaging appointments
• Referrals to other physicians or locations
• Referrals to other specialties (i.e., dietitians, financial advocates)
COORDINATE COMMUNICATION WITH OTHER DEPARTMENTS & OTHER ORGANIZATIONS
• Nursing
• Pharmacy
• Lab
• Reimbursement
• Financial Advocacy
• Social Work
• Behavioral Oncology

the inpatient coordinator and the bedside nurse ensure that patients know exactly what to expect and what they need to do at time of discharge.

The inpatient coordinator has also developed close working relationships with clinic nurses. When a patient is admitted to the hospital, the inpatient coordinator will review the clinic appointment schedule and notify a nurse if an appointment needs to be canceled, thereby opening the slot up for another patient appointment. At discharge, the inpatient coordinator closes the loop by sending discharge information to clinic nurses, including:

- The patient's diagnosis
- Date of discharge
- Reason for the hospital admit
- If chemotherapy was given or held; if medication was held, the inpatient coordinator provides the reasoning behind this decision.

As stated above, the inpatient coordinator also arranges for all follow-up care, keeping the hospital and physician practice informed every step of the way. Table 1, above, identifies the key roles and responsibilities of the inpatient coordinator.

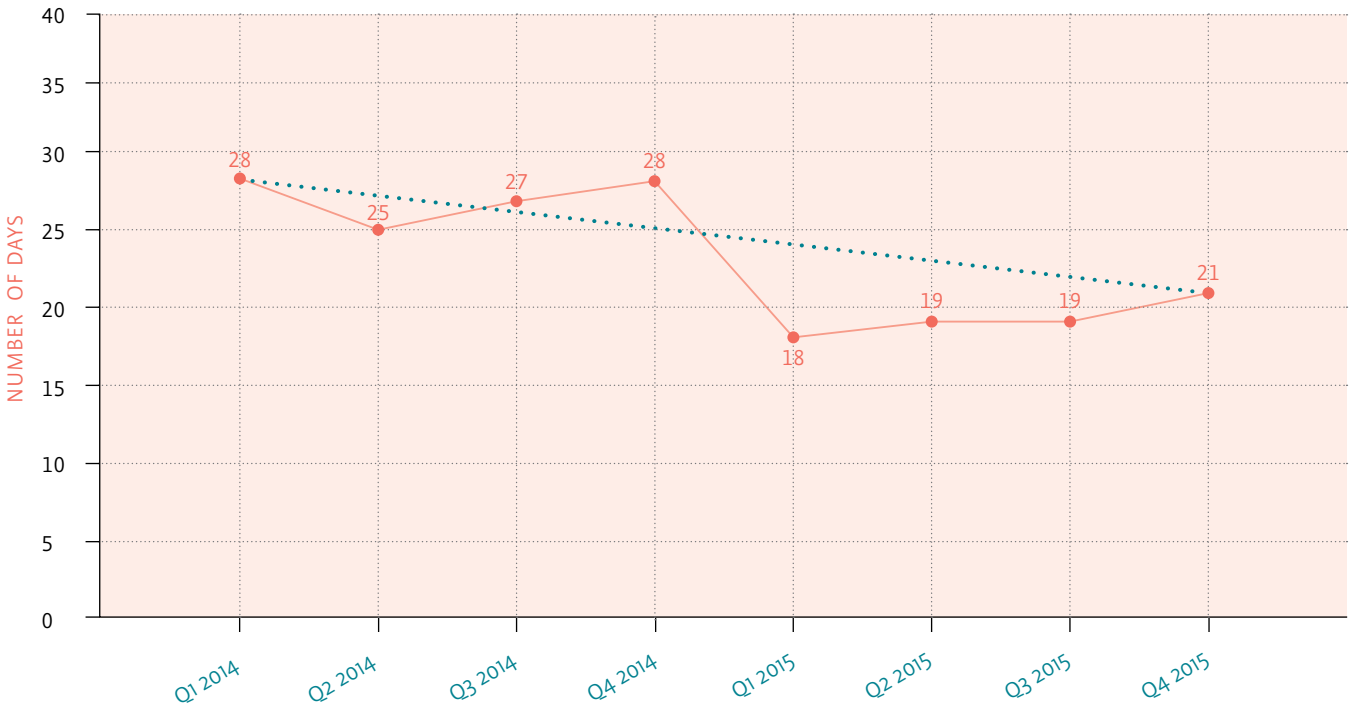
Programmatic Benefits & ROI

Adding this new staff position has resulted in numerous programmatic benefits. In brief, here's how the practice received return on investment (ROI). By giving the inpatient coordinator the responsibility of scheduling appointments and managing follow-up care, mid-level providers and physicians are now able to see more patients each day. This has increased patient volume to the clinic.

The inpatient coordinator has also had a positive impact on care coordination. It is well-documented that poor care coordination can result in unnecessary hospital admissions and readmissions, duplicate lab work, and unnecessary imaging, increasing the cost of care for patients and payers. The inpatient coordinator streamlines the discharge process, working in partnership with both inpatient and outpatient providers to improve continuity of care.

These improvements in care have resulted in improvements to the practice's bottom line. For example, Figure 1, right, shows how the time from hospital discharge to charge date was reduced from an average 37 days in 2013 (prior to the creation of the inpatient coordinator role) to an average 27 days in 2014 to an average 19.25 days in 2015. The inpatient coordinator has also helped to reduce hospital LOS (Figure 2, page 46), and the practice expects to see a similar decline in hospital admissions and readmissions.

Figure 1. Inpatient Time Between Date of Service and Charge Date



But perhaps the greatest benefit to adding the inpatient coordinator has been the improvements in patient and provider satisfaction (Table 2, page 46). Cancer patients are easily overwhelmed by the sheer number of clinic visits, tests, labs, and imaging appointments required during treatment, and now these patients have someone on staff to help ease these burdens. The inpatient coordinator manages follow-up care and is readily available to intervene if the need arises or if a patient's situation changes. A Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) survey shows an increase in patient satisfaction; physicians are able to spend more quality time during rounding to communicate with patients and their families. OI

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Cancer & Hematology Centers of Western Michigan At-A-Glance

Established in 1979 as a solo-physician practice, Cancer & Hematology Centers of Western Michigan is currently the largest private oncology/hematology practice in the state. As part of the Texas-based START Midwest Program, the practice has opened the first comprehensive Phase I Oncology Clinical Trials Program in Grand Rapids. Cancer & Hematology Centers of Western Michigan has an on-site CLIA-certified laboratory that offers more than 75 different tests. With 95 percent of the tests drawn on patients run in the in-house lab at the time of draw, the lab supports real-time decision making by its providers. Today, Cancer & Hematology Centers of Western Michigan has 22 physicians, 12 mid-level providers, 4 main clinical sites, 4 infusion pharmacies, 3 specialty pharmacies, an FTE psychologist, and more than 250 employees.

Figure 2. Change in Average Inpatient LOS, Month to Month Comparison 2014 to 2015

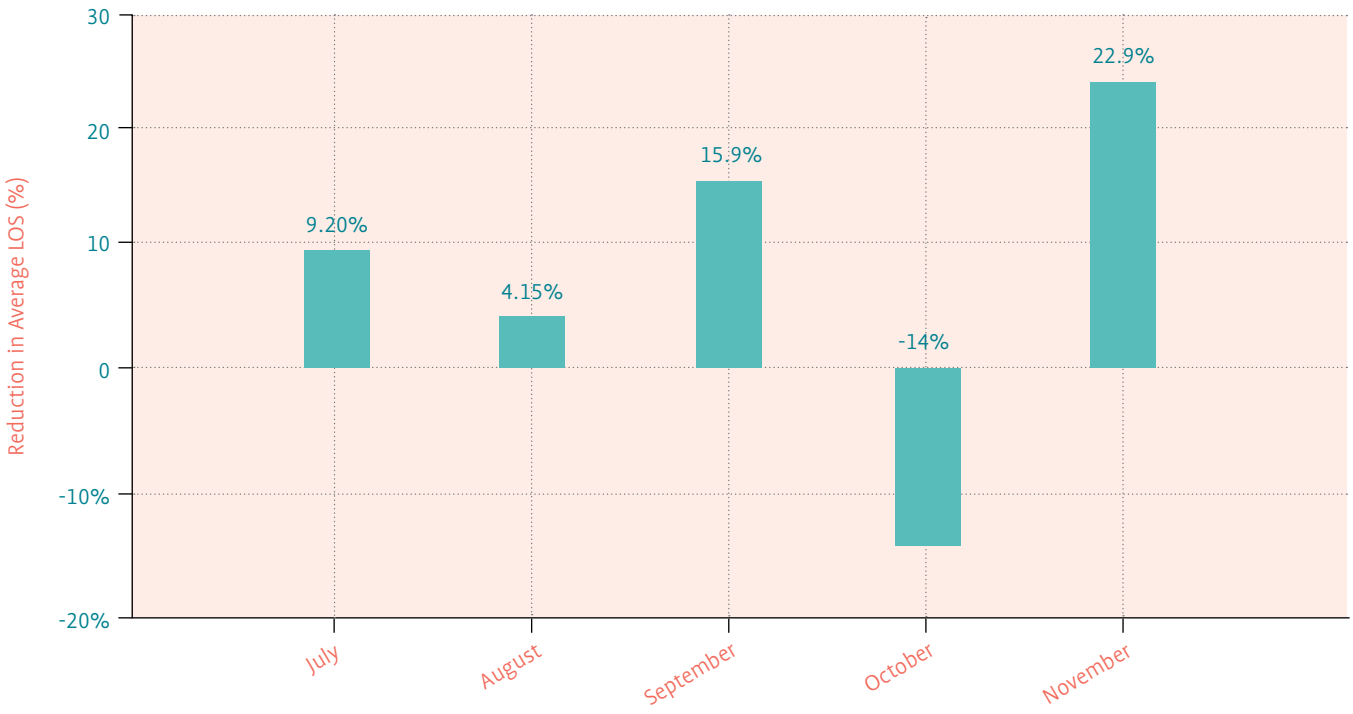

Table 2. HCAHPS Plus Survey Results, a Comparison of September 2014 to September 2015

	2014	2015	CHANGE MONTH-TO-MONTH
During this hospital stay, how often did doctors **explain** things in a way you could understand?	66.67%	88.24%	21.57%
During this hospital stay, how often did doctors **listen** carefully to you?	72.22%	94.12%	21.90%
During this hospital stay, how often did doctors **treat** you with courtesy and respect?	77.78%	94.12%	16.34%
Communication with doctors overall?	72.22%	92.16%	19.94%

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Opening up new therapeutic avenues

BY JAMES S. WYSOCK, MD, AND
HERBERT LEPOR, MD

Prostate cancer remains the most common solid tumor diagnosed in American men. Approximately 220,000 men are expected to be diagnosed in 2016, representing approximately 25 percent of all new cancer diagnoses and approximately 9 percent of cancer deaths.[1]

The introduction of serum prostate specific antigen (PSA) screening in the 1990s resulted in a stage migration with most disease being detected at an earlier age, stage, grade, and volume.[2] Most men diagnosed in this fashion traditionally underwent treatment with whole-gland therapies, such as radical prostatectomy and whole-gland radiation, all of which significantly impact quality of life (QOL).[3-5] The paradigm of PSA screening, random prostate biopsy, and aggressive curative intervention of all cancers has resulted in a 40 percent reduction of prostate cancer mortality. While this reduction in prostate mortality is compelling, the lack of PSA specificity and random prostate biopsy to detect "significant disease" has resulted in unnecessary biopsy and treatment. The challenge providers face is to screen and detect "smarter" in order to minimize the burden of unnecessary biopsy and treatment. Ideally, the goal is to identify men who would benefit from aggressive therapy.[6-8]

The challenge providers face is to screen and detect "smarter" in order to minimize the burden of unnecessary biopsy and treatment. Ideally, the goal is to identify men who would benefit from aggressive therapy.[6-8]

Improved Prostate Imaging with MRI

Recently, advancements in prostate cancer imaging using multi-parametric magnetic resonance imaging (mpMRI) have ushered in a paradigm shift for prostate cancer diagnosis.[9] Pelvic mpMRI combines anatomical T2 weighted sequences with diffusion weighted imaging (DWI) and diffusion contrast enhanced (DCE) sequences to localize regions of tumor suspicion within the prostate gland. The use of mpMRI vastly improves upon ultrasound prostate imaging by combining several magnetic resonance (MR) sequences to improve tissue evaluation and differentiation, leading to improved cancer detection and tumor localization within the prostate.[10-12] The sensitivity and specificity for detecting disease with mpMRI ranges from 70 percent to 90 percent and 61 percent to 89 percent respectively, with negative predictive values ranging between 85 percent to 95 percent.[13-18] Incorporating mpMRI into prostate cancer evaluation provides improved disease characterization for detection prior to biopsy, as well as for disease surveillance.[12,19]

Traditionally, prostate cancer is diagnosed through systematic random sampling of the prostate via transrectal ultrasound (TRUS) guidance. Yet TRUS biopsy sampling errors have lead to delayed diagnosis, understaging, and overdetection of low-risk disease.[20] Employing mpMRI prior to biopsy allows for targeting of regions suspicious for cancer.[21] Targeted biopsy can be performed via MR guidance, or via software-assisted MR-US (ultrasound) fusion techniques. Multiple studies have demonstrated improved detection rates for high-risk prostate cancer and decreased detection of low-risk disease when using MR-US fusion biopsy techniques.[22-24]

Improved imaging has opened avenues for image-guided therapies. Using MR-US fusion techniques similar to those used in targeted biopsy, energy ablative technology can now be targeted to lesions as focal therapy. There are many energy sources available to ablate prostate cancer. One such ablative energy source is high-intensity focused ultrasound (or HIFU), which offers novel opportunities for prostate cancer management.

MR-US Fusion Guided Prostate Biopsy

The use of TRUS guidance to sample prostate tissue has been a mainstay of prostate cancer diagnosis since the advent of prostate US imaging. While US imaging adequately defines the boundary

of the prostate, it does not provide accurate differentiation between normal and malignant prostate tissue. Thus, systematic prostate biopsies sample the gland in predefined regions, often using 10 to 12 biopsy core templates in order to sample the entire prostate.[25] Such sampling limitations hinder diagnostic accuracy and result in falsely negative results in up to 40 percent of biopsies. Furthermore, random sampling inadequately characterizes disease, leading to understaging and undergrading in up to 40 percent of men.[26-28]

Translating mpMRI findings to US targets requires specialized software and hardware. Several software and hardware platforms are commercially available.[29,30] Radiologists with expertise in prostate mpMRI interpretation prepare mpMRI imaging through software segmentation and demarcate predefined targets. This segmented mpMRI imaging is then registered to US imaging at the time of prostate biopsy, through a process known as MRI-US fusion. Real-time guidance and tracking of prostate biopsy then allows for targeted tissue sampling of mpMRI.[31]

One example of a commercially available MR-US fusion system is the Eigen Artemis® device. This fusion system uses encoders to track real-time location of prostate biopsies and features a robotic prostate biopsy arm to eliminate operator motion and ensure accurate targeted biopsy. The Artemis device can be easily incorporated into the urologist's usual biopsy workflow. In addition to targeted biopsy, the Artemis also provides spatial distribution of 12 core biopsy samples and tracks location of biopsy for men undergoing active surveillance or repeat biopsy.[32-35] In one of the largest published prospective studies of MRI-US fusion prostate biopsy, researchers at NYU Langone Medical Center reported improved detection of Gleason 7 and higher disease, as well as decreased over detection of Gleason 6 (low-risk) disease through the use of MRI-US fusion targeted biopsy.[23]

The Index Lesion: Defining the Treatment Target

The development of accurate prostate imaging—coupled with precise localization and identification of these image findings—has increased interest in minimally invasive ablative technology to destroy image-visible disease. Focal ablative therapy directs treatment to a precise lesion, otherwise known as lesion-based therapy. Limiting treatment to this lesion can minimize treatment effects to surrounding organs, including the bladder, urethra, rectum, and neurovascular bundles. For focal therapy to succeed, the nature and location of the lesion to be treated must be precisely understood.

Pathology studies confirm that up to 78 percent of prostate cancers on prostatectomy demonstrate multiple tumors and up to 86 percent exhibit bilateral disease.[36] The apparent multi-focal nature of prostate cancer has challenged implementation of focal therapy and serves as the basis for continued use of whole-gland therapy. However, a growing body of research supports the concept of the "index lesion." The index lesion—typically the largest tumor focus—is a single lesion, within the prostate gland that is the site of disease that poses metastatic potential.[37] The index lesion grade and stage predict risk for disease progression.[38] Several studies have demonstrated that the largest tumor by volume on prostatectomy specimen independently predicts biochemical progression.[39-43] Tumors found outside of this index lesion typically represent clinically insignificant disease. Correct identification of this index lesion provides the fundamental basis for focal ablation.[44, 45]

To further support the index lesion hypothesis, recent work by Liu et al. provides evidence that cells from a single disease site serve as the progenitor for metastatic disease.[46] As part of the Project to Eliminate Lethal Prostate Cancer (PELICAN), these researchers evaluated tissues from 30 men who died from metastatic prostate cancer with high-resolution genome wide evaluation of single-nucleotide and copy number polymorphisms. They demonstrated that metastatic sites could be tracked to a single precursor cell within the prostate. The goal of considerable research efforts: to prove that the progenitor metastatic cell stems from an index lesion are visible on mpMRI, further strengthening the oncologic premise of focal ablation.

HIFU: Focal Ablation of Prostate Tissue

Sound waves generated with a frequency greater than those perceptible by the human ear (frequency over 16 kHz) are considered ultrasound waves. These ultrasound waves can be projected into tissue and the measurement and display of the interaction of these ultrasound waves with biologic tissue provide the basis for diagnostic ultrasound imaging. As the ultrasound wave energy is increased, the energy imparted into tissue can result in biologic changes. When the energy is raised to greater than five Watts of power, the ultrasound becomes high intensity. High-intensity focused ultrasound, or HIFU, uses a dual-purpose transrectal ultrasound probe that allows for diagnostic imaging, but also allows for ultrasound energy to be imparted into tissue.[47] The energy ablation mode of the HIFU probe focuses ultrasound energy to a fixed point. Focused ultrasound energy consequently results in tissue absorption of the ultrasound energy, which is converted into heat. Temperatures exceeding 60 ºC can be obtained in a well-defined treatment zone, resulting in protein denaturation, coagulative necrosis, and cellular disruption. Secondarily, ultrasound energy absorption results in oscillation of micro-bubbles within tissue and leads to cavitation of these bubbles within tissue, resulting in further cellular destruction.[48]

The HIFU probe provides US imaging for localization of the target regions within the prostate and contains software to monitor local temperature effects on target tissue as well as surrounding tissue, such as the rectal wall. Through real-time treatment effect

monitoring and accurate image-guided planning, HIFU minimizes damage to surrounding tissue while achieving desired treatment effect to target tissue.

Currently one example of a platform available for HIFU in the United States is the Sonablate® 500 device. This device uses a dual ultrasound transducer (3 and 4 MHz) for both imaging and treatment. The procedure can be performed in an outpatient setting under general anesthesia and treatment is achieved entirely through a transrectal approach. The treatment is typically made in several zones, applying ultrasound energy in an anterior to posterior sequence. The urologist performing HIFU monitors treatment effects in real time and adjusts the treatment based on observations of the effects on tissue, such as cavitation and rectal wall temperature.

HIFU has been available in Europe and Japan for more than a decade and typically has been employed to ablate the entire prostate gland. Most studies evaluating whole-gland ablation report complications such as urethral stricture (19.7%), erectile dysfunction (34.9%) epididymitis (6.2%), incontinence (2.3%), and rectourethral fistula (0.1%).[49] In many cases, the morbidity of whole-gland HIFU ablation exceeded that of radical prostatectomy. Focal targeted HIFU promises to provide the ability to destroy a well-defined zone of the prostate harboring cancer with minimal impact on surrounding tissue, thus potentially decreasing side effects such as incontinence and erectile dysfunction.

As treatment zones become more precise and focused, morbidity decreases. In a recent study of men undergoing HIFU prostate hemiablation (ablation of half of the prostate), the 12 month pad-free continence rate was reported as 97 percent and 78 percent reported preservation of erectile function. While the cancer control results from this study suggest adequate treatment effects—89 percent of treated men undergoing surveillance prostate biopsy demonstrated absence of significant disease—these results remain immature and require further follow up as well as validation in larger studies.[50]

Combining MRI-US Fusion with HIFU: Improved Focal Targeting

Because of limitations in accurately targeting the site and the extent of prostate cancer, early studies of focal HIFU prostate ablation involved hemiablation treatment strategies. In order to minimize the complications associated with focal therapy, it is possible to target and treat only the cancer, with only a minimal margin of normal tissue included within the ablation zone. In this fashion, collateral damage to the neighboring structures is minimized. Such precise treatment requires an accurate definition of the location and extent of the index lesion needing ablation. The ablation must then be accurately targeted to this region with precise pre-planned treatment margins.

Current studies on mpMRI demonstrate that the index lesion is visible in up to 80 percent of cases.[51] Visible lesions can provide targets for MR-US fusion biopsy, allowing for reliable tissue sampling and disease mapping. The Artemis MR-US fusion platform then stores the location of targeted biopsies within the Profuse® software platform. The biopsy sites can then be mapped to the pathology results and a precise record of the exact tumor locations is created. This software also allows prior biopsy locations to be re-sampled on future biopsies, enabling re-examination of sites of disease and tracking of treatment efficacy. This feature allows for improved disease monitoring for men on active surveillance and also treatment effect monitoring for men undergoing focal ablation. With this software, the index lesion on mpMRI can be thoroughly sampled and surrounding tissue can be mapped.

The Profuse software is included with both the Artemis fusion biopsy devices and the Sonablate platform. Bridging the gap between biopsy and treatment, the software allows exportation of biopsy sites and fused mpMRI zones to the Sonablate 500 software, translating disease targeting to the treatment platform. At the time of focal HIFU ablation, the Sonablate 500 software can then perform MR-US fusion using real-time HIFU US imaging to fuse the index lesion location to treatment zones for targeted ablation.

NYU Langone Medical Center was the second tertiary center in the U.S. to offer focal HIFU ablation using the Sonablate 500. The combination of accurate mpMRI imaging with precise disease mapping via MR-US fusion biopsy requires multidisciplinary expertise in radiology and urology. Long-term data regarding cancer control through focal image-guided HIFU is being accrued; however, early data has demonstrated that the treatment does not impact sexual function or urinary control.

Future Challenges

While initial results are promising and providers gain experience with focal HIFU prostate ablation, challenges remain for improving focal therapy treatments. First, the current Sonablate 500 device is unable to accurately image and consequently map prostate glands much greater than 40 cm^3. In addition, index tumor location in the midline or anterior zone may present technical challenges for focal HIFU ablation. Also, the treatment margin needed to ensure complete index lesion ablation remains undetermined. While mpMRI appears to accurately visualize the index lesion, whole-mount pathology studies indicate that mpMRI imaging underestimates tumor volume.[52]

As focal therapy technologies advance, different ablative technologies may be required to optimally target and treat different lesions based upon size, location, clinical features, and proximity to critical surrounding structures, such as the apex, urethra, neurovascular bundles, or bladder neck. For example, bilateral HIFU prostate ablation may result in urethral sloughing and may pose a higher risk to urethral scarring and damage to the apex

as compared to focal cryotherapy, which uses a urethral warming catheter. Conversely, focal HIFU offers more precise treatment to peripheral zone tissue near the neurovascular bundler or rectal wall, while cryotherapy may result in less effective treatment in these zones given concerns over local treatment side effects.

Conclusions

More than 200,000 men will be diagnosed with prostate cancer this year. The majority of these men will be diagnosed with low- to intermediate-risk disease on systematic TRUS prostate biopsy using 10 to 12 randomly placed needles. These men face a complex and difficult decision regarding disease management. A properly performed multi-parametric MRI of the prostate will drastically improve the disease characterization for many of these men and can assist with proper treatment choice. Furthermore, including mpMRI prior to biopsy in the diagnostic pathway would further allow many men to avoid the inherent shortcomings of random systematic biopsy.

As access to quality mpMRI becomes more widely available, the prevalence of clinically localized and MR-visible disease will increase. Broader use of MR-US fusion targeted prostate biopsy will more accurately identify the index lesion in these prostates. Evolving from the foundation of accurate disease localization through imaging, and precise disease characterization via targeted sampling, focal ablation offers a promising next stage in prostate cancer management.

While many facets of this improved paradigm for prostate cancer detection, diagnosis, and treatment have yet to gain widespread availability, only a few centers of excellence currently offer expertise in mpMRI, targeted biopsy, and focal therapy, including focal HIFU. Through evidence-based application of these principles, focal therapy currently offers an attractive new option for men who meet proper selection criteria and are committed to rigorous follow up. As provider experience with these techniques and treatment options matures, we believe focal therapy will ultimately gain acceptance as an attractive, safe, and effective outpatient treatment option for a subset of men diagnosed with localized prostate cancer. OI

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Strategic Planning for Oncology

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Lessons learned from the trenches

Whether chosen or imposed, the amount and pace of change that we are asked to navigate daily in our personal, professional, and organizational environments is a significant challenge for each of us. In the midst of this "controlled chaos" is the call by our hospital and practice leadership for a deliberate, thoughtful, directed, measured, monitored, and wisely executed strategic plan for our respective departments and/or service lines.

Of course, developing and executing a strategic plan within dynamic environments—both internal and external—is a daunting challenge. In addition to multiple operational and financial requirements, we must also address the uncertain future of oncology care delivery, specifically regulatory, legal, and political ramifications as we attempt to establish a clear vision, develop an actionable pathway, and generate a successful outcome for our program. We must also fulfill these expectations while simultaneously meeting ever-increasing demands to generate additional revenue, reduce overall costs, eliminate denials, and produce a contribution margin that supports not only the growth of our own program but also non-reimbursable services, such as navigation and survivorship. Despite potential roadblocks, such as organizational restructuring, competitive pressure from external markets, and increased data demands from both public and private payers, it is possible to establish creative and attainable goals within a strategic plan.

Despite potential roadblocks, such as organizational restructuring, competitive pressure from external markets, and increased data demands from both public and private payers, it is possible to establish creative and attainable goals within a strategic plan.

Several factors need to be considered prior to launching such an endeavor. First, know your audience; it is imperative to know those who will be receiving, interpreting, and supporting your strategic plan. This knowledge will inform format and content. Second, make sure that you have a reliable source for data collection. You must be able to explain and sometimes defend the methodology, as well as the data on which your strategic plan rests. And third, give careful consideration to the composition of your strategic planning team—who will both help develop the plan and champion its implementation. Next, complete a SWOT (strengths, weaknesses, opportunities, threats) analysis with your key stakeholders to help hone in on the types of strategic initiatives to develop for your program. Finally, establish timeframes and mile markers, avoiding potential sinkholes along the way.

The Planning Team

The composition of the team to bring to the table for the initial phase of developing a strategic plan is critical for success. Including a broad spectrum of interdisciplinary perspectives will strengthen both input and outcomes. Each participant brings a unique opinion and vantage point, enriching the conversation and contributing to the overall success of the process.

Historically, there has existed a diametric and sometimes challenging chasm in perspectives between administration and

medical staff. In today's world, efforts are being made to bring these viewpoints into alignment so that the gap, if not narrowing, is at least resulting in improved collaboration. Physician representation in the strategic planning process is imperative. However, keep in mind that physician colleagues will likely use the same skill set in the strategic planning as they do in their daily clinic. From the patient perspective, we want physicians to apply a laser-like focus on reviewing the data to quickly assess anomalies, identify potential causes, and create a plan to treat the abnormality. When we invite physicians into the strategic planning process, we suddenly expect them to adopt an open-ended, collaborative approach, which may not happen. The expectations, however, should be to invite, accept, and harness critically minded, data-focused perspectives to the project at hand, understanding and appreciating that this skill set will keep the group on track and push the members beyond a placid planning process. And, when inviting clinically-minded colleagues into the planning session, make sure to include those who may have an indirect influence on the plan. Gaining the perspective of staff who will be referring patients (PCPs, surgeons, etc.) or staff who will be providing supportive services (imaging, pathology, etc.) is beneficial.

In addition to the physician leaders, be deliberate about bringing an array of both formal and informal leaders into the process. Obviously, your organization has delineated roles and responsibilities with titles and job descriptions that will identify the formal leaders who should be involved in the strategic planning process. There are also long-term and charismatic leaders among your staff whose input, influence, and support will serve to propel your plan forward and whose disapproval may seriously inhibit or stall the overall success. Don't hesitate to ask for the participation and input from your most influential—formal or informal—leaders.

A third group to have represented during the strategic planning process is the front-line staff; those who will ultimately bear the responsibility for initiating and sustaining progress. Initially, you may need to encourage these staff to express their opinions, but if allowed to find their voice within the larger group, their insights will be both practical and foundational to a successful implementation process. Front-line staff bring both the technical expertise as well as a real-world perspective when it comes to actually applying tactics and altering processes.

And finally, don't forget to involve representatives from supporting service lines or departments, such as Finance, Marketing, or Recruitment. We often develop strategies that necessitate the collection of data and the delivery of supporting materials, such as brochures, pamphlets, or website upgrades, without thought or consideration for the current workload, priorities, or assignments already in the queue for these departments. Having these representatives seated at the table initially will allow for the development of reasonable expectations when it comes to delivering on agreed upon timelines.

Laying the Ground Work

In general, it is best to begin with a market analysis to understand where your cancer program stands compared to your competitors. This analysis is two-pronged, encompassing both "soft" and "hard" data. Soft data requires taking a long, hard look at your own program, setting aside any preconceived notions. While you may believe that your program is fantastic, others likely have their own impressions and opinions. If your "star" breast surgeon is not seen as a star by the primary care physicians, patients will not be referred. If you think your marketing activities are strong but your community or physicians are unaware of those messages, then your marketing is in need of revamping. To know how your program is perceived, you must ask your customers (patients, physicians, and even payers) for their honest opinions and then listen to them.

Take an inventory of your services and those services your competitors offer, including:

- Physician specialties and subspecialties
- Equipment and clinical services
- Supportive services and programs.

Look for gaps in both; those gaps are your potential strategic initiatives. MEDPAR (Medicare Provider Analysis and Review) data is also useful in this analysis.

Market Share

Market demand and market share are, for oncology, very difficult to calculate accurately. This is partly because the vast majority of hard data available is hospital discharge data. However, on average, an oncology patient experiences between 1.6 and 2.1 hospital admissions for cancer-related care over his or her entire lifetime, according to the American College of Surgeons CoC Cancer Datalinks. The remainder of care is delivered in the outpatient setting. Accordingly, cancer programs must use a more complicated approach to calculate market share.

First, using a data source such as the U.S. Census Bureau, estimate the population in your market. Granted, these data are somewhat old and may need to be projected to current and/or future years. Next, from a source such as the American Cancer Society (ACS) or the Centers for Disease Control (CDC), calculate the expected cancer incidence in your market. Again, the data is not completely accurate, but it provides the most reasonable estimate possible—unless your state cancer registry has something more current and more specific.

From the above data, you now have a useful view of the demand in your market. To calculate your share, compare the expected incident cases to your cancer registry data, using Class

of Case to identify those patients who migrated in or out of your health system and those whom you captured and kept.

Financial analysis is a key component in eventually prioritizing strategic initiatives, particularly in terms of identifying specific disease sites to focus on. To accomplish this, run reports by department and diagnosis: charges, costs, and reimbursement for all patients with a cancer-related diagnosis as defined by ICD-10 codes. This will help identify disease types that are generating positive margins across all departments. In addition to learning that, for example, brain cancers generate high margins across all hospital departments (e.g., imaging, lab, pharmacy, and others as well as infusion and/or radiation), an initiative to grow your neuro-oncology services may be a good choice if there is sufficient patient demand not being captured. Conversely, some cancers generate negative margins so investing funds to grow these programs may not be a wise choice.

All of this data and information allows the strategic planning team to build a list of initiatives that have potential for growth and success. Added to those are initiatives to address issues like changes in reimbursement models, such as Accountable Care Organizations and the Oncology Care Model, as well as various bundled, episode-of-care, and "value-based" models. Some recent initiatives that cancer programs have undertaken include:

- Hospital/physician alignment and integration
- Strategies to improve patient and community awareness of service distinctions
- Multidisciplinary clinics
- Service line restructuring
- Physician leadership development
- Facility expansion
- Academic affiliations.

Below we offer two specific case studies of successful strategic initiatives.

Hospital/Physician Initiative

One healthcare system identified integration with the medical oncology practice as a strategic initiative in 2010. At that time, the comprehensive cancer program, established in 1990, had services situated in various locations throughout the hospital. In 2010—through a multi-million dollar donation—the hospital formalized a vision for a comprehensive cancer center on the hospital campus. The oncology medical staff at the time consisted of one employed hematologist/oncologist and two private free-standing physician-owned oncology groups offering chemotherapy and infusion at their clinic locations. The hospital contracted with a private group to offer radiation oncology services, which were provided at the hospital.

The hospital engaged oncology specialized consultants in 2011 to develop strategies for the new comprehensive cancer program, center location, and center design. In 2012 the design process was interrupted for a change in architects and then moved forward without the consulting group. After engaging a second consultant group to work with the physician practices and the hospital, professional service agreements (PSAs) and co-management agreements between all groups were signed. The integration of hospital and oncologists was the first true hospital/physician integration and leadership model for this healthcare system.

With building design and construction complete in 2013, radiation therapy services were moved into the new location in December of that year. All other services, including three physician clinic practices, were phased into the new location over the next four months. Today, nine providers practice under a unified name with the anticipated addition of two more providers during the next few months.

The growth of this cancer program has been phenomenal. Over the first year of operation there was a monthly growth of six percent in infusion services and three percent in average daily radiation treatments. Hospital leadership supported the new cancer center and its physicians by investing in staff, including chemotherapy certified registered nurses, support staff, a genetic counselor, nurse navigators, a phone triage nurse, a dietitian, a social worker, and pharmacists—all dedicated solely to the cancer center.

What went well in the process? The building site has proven to be an excellent selection, and even though the building design got off to a slow start, the end result was a beautiful and functional facility with a healing environment. The relationships between the physicians, cancer program leadership, and hospital administration have proven to be very successful with a level of trust and transparency at the foundation. These stakeholders regularly engage in honest and crucial conversations regarding the operational and financial aspects of the cancer center.

As with most strategic plans, some decisions and actions might have been done differently. For example, strategic planning and growth strategies should have included how to handle "growing at a faster than predicted rate." The cancer center is now experiencing the dilemma of adapting the new building model and the growth rate without any service disruption. The merger of two freestanding physician practices into an unfamiliar clinic design, and the merger of different practice patterns can be huge disruptors unless the communication is flowing uninterrupted between cancer program leadership and physicians. A comprehensive cancer center operation is very hard to fit into a hospital unit model, and when one maintains hospital-based status, it can be very difficult to walk the fine line between what is the best for the cancer center and what is best according to the hospital system's C-suite. The fast track of preparing the PSA model was difficult; reporting of CMS (Centers for Medicare & Medicaid Services) quality measures continues to be challenging.

In short, even when all of the key stakeholders are able to

develop mutual trust and shared incentives, there will always be challenges in bringing physician practices and hospital-based programs together. However, these challenges can be overcome as long as the trust and aligned interests remain.

Improving Community Awareness of Cancer Services

While much focus is placed on addressing more complex and somewhat sophisticated processes, the tactics that emanate from a strategic plan can be quite simple and straightforward. For instance, a rural facility with a history of financial fluctuations located in a bedroom community had developed a reputation for being a "Band-Aid" station amongst the commuting crowd. The facility was considered to be adequate for the treatment of minor injuries or simple procedures, but if residents required more complex healthcare, many made the decision to travel an hour north to the nearest metropolitan area.

Unbeknownst to the commuters, a group of physicians from a metropolitan practice were actually providing services in their local facility.

To raise awareness of this medical expertise provided in the community, the hospital arranged for a short-term lease of several billboards along key routes to and from the greater metropolitan area. The first billboard in the series asked the question, "What is the difference in care between (here) and (there)?" The next billboard provided the answer—50 miles. The final billboard in the series featured the practice logo and the names of those physicians providing care at the facility right within their community.

The response from the community was immediate, with commuting residents flooding the facility operators with calls inquiring about the cancer services and providers.

While the utilization of billboards may be seem a bit outdated for today's marketing departments, this demonstrates that strategic goals can be executed and achieved with creative and relatively low-cost initiatives. Amidst the lessons learned from this exercise was the importance of including physicians in the conversation. Although the metropolitan-based physician practice was aware that its physicians were treating patients from the rural community, their assumption was that patients were coming to their practice because they worked in the metro area.

Another lesson learned through this endeavor was the importance of internal marketing and communication. While the commuting residents of the area were exposed to the billboards, those who worked within the community, including hospital staff, were not immediately aware of this initiative. As a result, many employees were taken by surprise when informed by their commuting spouse or approached by inquisitive neighbors, fellow church members, and other school parents. In hindsight, providing more comprehensive internal communication would have prepared employees and prevented these uninformed and somewhat embarrassing encounters. This is another reason to include support services, such as Marketing and Communications representatives, on the initial planning team.

Closing Thoughts

Strategic planning can be an exhausting effort, and the nature of the strategic initiatives chosen, as illustrated above, can range from seemingly small and easy goals to very broad-reaching endeavors. The involvement of key stakeholders is vital to success. Whether the initiative is small or large, clinical or programmatic, quick or drawn-out, clear communication and transparency are undoubtedly two of the most important common threads. OI

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action

ACCC Welcomes its Newest Members

Hardin Memorial Health, Cancer Care Center
Elizabethtown, Kentucky
Delegate Rep: Nancy Bowles, MSN
Website: hmh.net

New ACCC Health System Member
UnityPoint Health
Website: unitypoint.org

St. Luke's Cancer Care
Cedar Rapids, Iowa
Delegate Rep: Kimberly Ivester, MS, BSN, RN, OCN
Website: unitypoint.org/cedarrapids

Trinity Cancer Center
Moline, Illinois
Delegate Rep: Leanne Hullett
Website: unitypoint.org/quadcities

Waterloo Community Cancer Center
Waterloo, Iowa
Delegate Rep: Cathy Wilson-Sands, MSN
Website: unitypoint.org/waterloo

Oncology Pharmacy Education Network (OPEN) Regional Meetings

December 14, 2016
Costa Mesa, Calif.
Hilton Orange County/Costa Mesa

March 1, 2017
Austin, Tex.
The Driskill Hotel

Register online at: accc-cancer.org/OPEN

SAVE THE DATES!
Oncology Reimbursement Meetings

December 13, 2016
Costa Mesa, Calif.
Hilton Orange County/Costa Mesa

April 13, 2017
Minneapolis, Minn.
Hyatt Regency Minneapolis

April 25, 2017
Tampa, Fla.
The Westin Tampa Harbour Island

May 18, 2017
Omaha, Nebr.
Embassy Suites by Hilton Omaha Downtown Old Market

Register for these free meetings at: accc-cancer.org/reimbursementmeeting.

Rooms That Rock 4 Chemo

BY NANCY BALLARD

In May 2011, at the age of 60, I was happily retired, living the dream as a successful artist, author, wife, mother, and Nana. It was then I saw my first chemotherapy room "by mistake." Simply by taking a right turn instead of a left turn, a nurse who admired my botanical art showed me a chemo room that needed some tender loving care. I wondered aloud how anyone could heal in a room that was so sad and drab; that lacked any interest, joy, or beauty. I knew just a single piece of art wasn't going to make the difference, more significant re-design was needed. Contacting volunteer designers and local vendors and using a 100 percent volunteer work force, we "rocked" our first room.

This experience led to the creation of Rooms That Rock 4 Chemo, a non-profit organization that updates and beautifies spaces where cancer patients—and those who care for them—spend the many hours the treatment requires. Five years later, our rooms host more than 880,000 patient visits per year in 18 facilities in the U.S. and 2 in San Salvador.

My Calling

Rooms That Rock 4 Chemo (RTR4C) has been called an "accidental non-profit," as I was not looking for a project—let alone a 24/7 volunteer job. I cannot exactly say why I was so moved in this direction or why I took it on so personally. Maybe it was a reaction to the blessing that I and my family are physically well. Maybe it was the artist in me that was literally shocked that an environment could look so hopeless.

I recognized a very real need to reach out to those who are often marginalized because of cancer and who—because of their urgent health needs—must endure lengthy treatments. I saw firsthand that those receiving chemotherapy in hopes of saving their lives were often subjected to dismal, dark, and non-healing environments without thought or consideration for comfort, rest, and tranquility. Patients and family members sought to get through the grueling ordeal of cancer while in rooms that often did not support their human dignity or struggle. Ours is the first organization to acknowledge the very real problem of drab chemo room environments and work to find a solution.

My vision is that every patient receiving chemotherapy treatment is provided with a concrete sign of care and concern, bringing awareness to the fact that these patients and their families are so much more than just numbers in a complex healthcare system. We do this by providing lovely, hopeful, and soothing environments. And for the kids—fun!

It Takes a Village

Rooms That Rock 4 Chemo would not be possible without the passionate donation of talent, time, and money from thousands of volunteers, and local and national businesses that donate supplies and provide sponsorships. All of these volunteers and donors have responded with enthusiasm and gratitude for the opportunity to be involved.

Our "rocked rooms" have brought an increased awareness to healthcare providers and local community leaders, highlighting the non-medical needs of this patient population. RTR4C has also brought gratitude and appreciation from those who have benefited from the healing and soothing effects, and has given the community volunteers a sense of accomplishment and a deeper appreciation of the plight of cancer patients. Our volunteers want to keep on giving, allowing RTR4C to make this a long-term and possibly world-wide project. As an added bonus, we are improving the daily lives of those who by profession serve this population, and we are challenging other communities to do likewise.

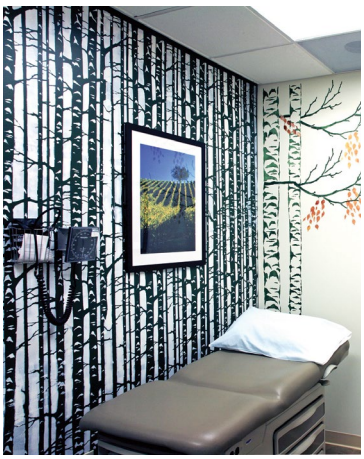
Rock with Us...A Patient Story

Three times. Three times diagnosed. Three times sitting in a chemotherapy chair hoping for the best. Hoping this third time would be the charm.

Fighting for her life in drab and uninspiring surroundings. This patient is in the twilight of her years and wants to give up. No one could blame her.

Friday afternoon: Her chemotherapy session is over. Finally. The kind-faced nurses say good-bye and wish her a good weekend. They promise to see her Monday bright and early. Everyone is tired. Yet another Monday looming in her future with the fear and difficulty of chemotherapy.

For the past six months we have planned and designed the transformation of these treatment rooms with a fabulous group of volunteers. Our team today numbers 90 volunteers—all there to make a difference in the lives of those receiving chemotherapy. We don't all know each other but we all



agree, together we will make a difference. Our work must be completed in one short weekend; we don't have the luxury of time.

On Your Mark, Get Set, Go!

It is now Friday night. We stay until midnight, looking over the site, checking our inventory, paint, and supplies, and outdoor building space. Is food arranged for all volunteers? Check.

Do we have the new lighting supplies? Nope. (Put that on the list for Saturday and make a note to send someone out shopping). Make sure the wall art and volunteer T-shirts have arrived.

Saturday is a whirlwind of painting and stenciling.

It is now Sunday near midnight: Eight rooms are completed and restored. The wall art is hung. Decorator touches are in place. The environment is abuzz with hope and new beginnings.

Monday morning and our patient arrives for her appointment. She shuffles actually, shoulders sagging, head down. No hurry. She looks up to sign in at the front desk to find it, well, unrecognizable! The walls have been painted in soothing colors, beautiful artwork, murals, and stencils are placed perfectly between the new privacy curtains and the chemotherapy chairs. Even the waiting room is inviting and fresh.

She can feel the brilliance, the kindness coming out of each nook and cranny. She wonders who would do such a thing? How did this happen?

It is then she sees the ribbon cutting ceremony and hears the many "oh's and ah's" from staff and patients alike. She hears the story of RTR4C and its wonderful volunteers.

With tears streaming down her face, the patient sits in a new chemotherapy chair facing the party, taking it all in. Her eyes twinkle; the room sparkles. Asked her opinion of the transformation, she almost jumps out of her chair with a spryness not seen lately by staff or fellow chemo buddies. She smiles wide and says, "Oh my, this is great. I'm gonna beat it. Yes, I'm gonna beat it this time. It is bea-u-ti-ful!"

Fingers crossed for the patient, and my team moves on to the next project! OI

Artist Nancy Ballard founded Rooms That Rock 4 Chemo in 2011. Learn more about Nancy and RTR4C at: roomsthatrock4chemo.org.

Xtandi® (enzalutamide) 40 mg capsules

XTANDI® (enzalutamide) capsules for oral use
Initial U.S. Approval: 2012
BRIEF SUMMARY OF PRESCRIBING INFORMATION

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

INDICATIONS AND USAGE

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

CONTRAINDICATIONS

Pregnancy

XTANDI can cause fetal harm when administered to a pregnant woman based on its mechanism of action and findings in animals. XTANDI is not indicated for use in women. XTANDI is contraindicated in women who are or may become pregnant. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, apprise the patient of the potential hazard to the fetus and the potential risk for pregnancy loss.

WARNINGS AND PRECAUTIONS

Seizure

In Study 1, which enrolled 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 Study 2, 1 of 871 (0.1%) chemotherapy-naive patients treated with XTANDI and 1 of 844 (0.1%) patients treated with placebo 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.

Two 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. In both studies, patients received XTANDI 160 mg orally once daily in the active treatment arm or placebo in the control arm. 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 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: Metastatic Castration-Resistant Prostate Cancer 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: Chemotherapy-naive Metastatic Castration-Resistant Prostate Cancer

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

Table 2. Adverse Reactions in Study 2 (cont.)

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.

Laboratory Abnormalities

In the two randomized 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 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 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– Pregnancy Category X.

Risk Summary

XTANDI can cause fetal harm when administered to a pregnant woman based on its mechanism of action and findings in animals. While there are no human data on the use of XTANDI in pregnancy and XTANDI is not indicated for use in women, it is important to know that maternal use of an androgen receptor inhibitor could affect development of the fetus. Enzalutamide caused embryo-fetal toxicity in mice at exposures that were lower than in patients receiving the recommended dose. XTANDI is contraindicated in women who are or may become pregnant while receiving the drug. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, apprise the patient of the potential hazard to the fetus and the potential risk for pregnancy loss. Advise females of reproductive potential to avoid becoming pregnant during treatment with XTANDI.

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).

Nursing Mothers

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

Pediatric Use

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

Geriatric Use

Of 1671 patients who received XTANDI in the two randomized 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).

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

Marketed by:
Astellas Pharma US, Inc., Northbrook, IL 60062
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Revised: October 2015

15C018-XTA

Rx Only

astellas MEDIVATION

076-1200-PM

Indication and Important Safety Information

Indication

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

Important Safety Information

Contraindications

XTANDI is not indicated for women and is contraindicated in women who are or may become pregnant. XTANDI can cause fetal harm when administered to a pregnant woman.

Warnings and Precautions

Seizure In Study 1, conducted in patients with metastatic castration-resistant prostate cancer (CRPC) who previously received docetaxel, seizure occurred in 0.9% of XTANDI patients and 0% of placebo patients. In Study 2, conducted in patients with chemotherapy-naive metastatic CRPC, seizure occurred in 0.1% of XTANDI patients and 0.1% of placebo patients. There is no clinical trial experience re-administering XTANDI to patients who experienced a seizure, and limited safety data are available in patients with predisposing factors for seizure. Study 1 excluded the use of concomitant medications that may lower threshold; 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 during which 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) 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%) reported from two combined clinical studies that occurred more commonly (≥ 2% over placebo) in XTANDI patients 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 Study 1, 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 Study 2, 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.

- Lab Abnormalities: 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 Study 1, 1% of XTANDI patients compared to 0.3% of placebo patients died from infections or sepsis. In Study 2, 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. 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. No patients experienced hypertensive crisis. Medical history of hypertension was balanced between arms. Hypertension led to study discontinuation in < 1% of all patients.

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 Pharma US, Inc. **2.** 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):424-433.

astellas MEDIVATION

Xtandi® (enzalutamide) 40 mg capsules

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

TO EXTEND SURVIVAL[1]

23% reduction in risk of death with XTANDI + GnRH therapy vs placebo + GnRH therapy†‡[1]

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

Co-primary endpoint, radiographic progression or death: (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**

Select Safety Information

XTANDI is not indicated for use in women. XTANDI is contraindicated in women who are or may become pregnant.

Seizure occurred in 0.9% of patients receiving XTANDI who previously received docetaxel and in 0.1% of patients who were chemotherapy-naive. Permanently discontinue XTANDI in patients who develop a seizure during treatment.

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

CI, confidence interval; HR, hazard ratio; NR, not reached.

***Or after bilateral orchiectomy.[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.[1,2]

‡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®
(enzalutamide)
40 mg capsules