MARCH 2018 • V.12 • N.2

Oncology NURSING NEWS®

cure® EDITION

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LET'S TALK ABOUT

Sex, Fertility, & Intimacy After Cancer

HOW SUSTAINABLE SOLUTIONS CAN CHANGE PATIENTS' LIVES

Jeffrey Albaugh, PhD, APRN, CUCNS

Clinical Insights

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+ Myeloma
+ Hematologic Malignancies
+ Pancreatic Cancer
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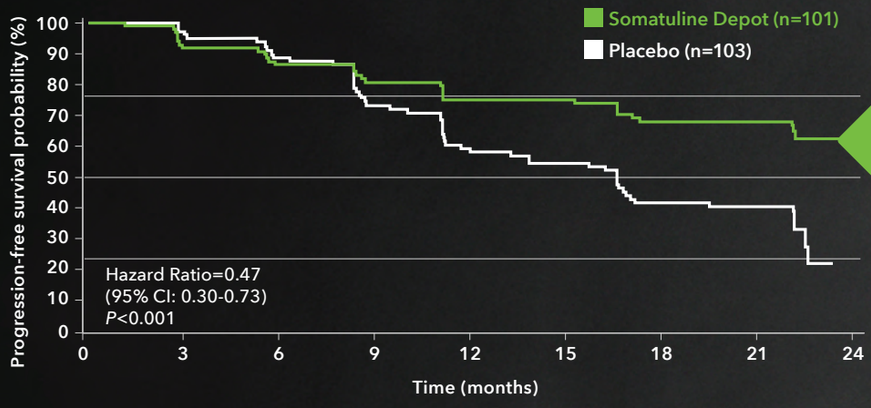
3 REASONS

1 SOMATULINE® DEPOT
(lanreotide) Injection 120 mg

1 PFS IN GEP-NETs

Progression-free Survival (PFS) in Adult Patients With Unresectable, Well- or Moderately-Differentiated, Locally Advanced or Metastatic GEP-NETs[1]

Primary Endpoint: Median PFS for Somatuline Depot vs Placebo[1,2]



53%
reduction in risk of progression or death with Somatuline Depot vs placebo[1]

CLARINET* tested the efficacy of Somatuline Depot in 204 patients with unresectable, well- or moderately-differentiated, metastatic or locally advanced GEP-NETs. Patients received Somatuline Depot 120 mg or placebo every 4 weeks until disease progression, unacceptable toxicity, or a maximum of 96 treatment weeks. Patients were required to have nonfunctioning tumors without hormone-related symptoms. Primary efficacy outcome was PFS, defined as time to either disease progression† or death.[1,2]

- The median PFS for Somatuline Depot was not yet reached at 22 months (95% CI: NE-NE) vs 16.6 months for placebo (95% CI: 11.2-22.1); HR=0.47 (95% CI: 0.30-0.73; *P*<0.001); number of events with Somatuline Depot=32 (31.7%) vs placebo=60 (58.3%)[1]

Adverse Reactions Reported in CLARINET Study

The adverse reactions occurring in ≥5% of Somatuline Depot patients and at a higher rate than placebo were abdominal pain (34%), musculoskeletal pain (19%), vomiting (19%), headache (16%), injection site reaction (15%), hyperglycemia (14%), hypertension (14%), cholelithiasis (14%), dizziness (9%), depression (7%), and dyspnea (6%).[1]

*CLARINET: **C**ontrolled Study of **L**anreotide **A**ntiproliferative **R**esponse **I**n **N**euro**E**ndocrine **T**umors, a randomized, double-blind, placebo-controlled trial.
†Assessed by a central independent radiological review in accordance with the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.0.

IMPORTANT SAFETY INFORMATION

Contraindications

- SOMATULINE DEPOT is contraindicated in patients with hypersensitivity to lanreotide. Allergic reactions (including angioedema and anaphylaxis) have been reported following administration of lanreotide.

Warnings and Precautions

- **Cholelithiasis and Gallbladder Sludge**
  - SOMATULINE DEPOT may reduce gallbladder motility and lead to gallstone formation.
  - Periodic monitoring may be needed.
- **Hypoglycemia or Hyperglycemia**
  - Pharmacological studies show that SOMATULINE DEPOT, like somatostatin and other somatostatin analogs, inhibits the secretion of insulin and glucagon. Patients treated with SOMATULINE DEPOT may experience hypoglycemia or hyperglycemia.
  - Blood glucose levels should be monitored when SOMATULINE DEPOT treatment is initiated, or when the dose is altered, and antidiabetic treatment should be adjusted accordingly.
- **Cardiovascular Abnormalities**
  - SOMATULINE DEPOT may decrease heart rate.
  - In patients in the GEP-NET pivotal trial, 23% of SOMATULINE DEPOT-treated patients had a heart rate of less than 60 bpm compared to 16% of placebo-treated patients. The incidence of bradycardia was similar in the treatment groups. Initiate appropriate medical management in patients with symptomatic bradycardia.
  - In patients without underlying cardiac disease, SOMATULINE DEPOT may lead to a decrease in heart rate without necessarily reaching the threshold of bradycardia. In patients suffering from cardiac disorders prior to treatment, sinus bradycardia may occur. Care should be taken when initiating treatment in patients with bradycardia.

The 1st and Only SSA‡ That Is FDA-approved to Treat Both[1]:

- Adult patients with unresectable, well- or moderately-differentiated, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NETs) to improve progression-free survival; **and**
- Adults with carcinoid syndrome; when used, it reduces the frequency of short-acting somatostatin analog rescue therapy

‡SSA=somatostatin analog.

2 CARCINOID SYNDROME

Reducing the Frequency of Short-acting SSA Rescue Therapy[1]

Somatuline Depot is FDA-approved to treat adults with carcinoid syndrome; when used, it reduces the frequency of short-acting somatostatin analog rescue therapy.

Carcinoid syndrome trial adverse events (AEs) occurring in ≥5% of Somatuline Depot-treated patients and ≥5% more than in placebo-treated patients were headache (12%), dizziness (7%), and muscle spasm (5%); AEs were generally similar to those in the GEP-NETs trial.

3 DELIVERY

Deep Subcutaneous Injection[1]

- Provided in a prefilled, low-volume, single-use syringe
- The recommended dose is 120 mg/0.5 mL, administered by a healthcare provider every 4 weeks
- No reconstitution required
- If your patient is already being treated for GEP-NETs, do not administer an additional dose for the treatment of carcinoid syndrome

Safe'n'Sound® syringe technology

Safe'n'Sound is a registered trademark of *NEMERA LA VERPILLIERE SAS*.

Not actual size.

IMPORTANT SAFETY INFORMATION (continued)

Most Common Adverse Reactions

- **GEP-NETs:** Adverse reactions occurring in greater than 10% of patients who received SOMATULINE DEPOT in the GEP-NET trial were abdominal pain (34%), musculoskeletal pain (19%), vomiting (19%), headache (16%), injection site reaction (15%), hyperglycemia (14%), hypertension (14%), and cholelithiasis (14%).
- **Carcinoid Syndrome:** Adverse reactions occurring in the carcinoid syndrome trial were generally similar to those in the GEP-NET trial. Adverse reactions occurring in greater than 5% of patients who received SOMATULINE DEPOT in the carcinoid syndrome trial and occurring at least 5% greater than placebo were headache (12%), dizziness (7%) and muscle spasm (5%).

Drug Interactions: SOMATULINE DEPOT may decrease the absorption of cyclosporine (dosage adjustment may be needed); increase the absorption of bromocriptine; and require dosage adjustment for bradycardia-inducing drugs (e.g., beta-blockers).

Special Populations

- **Lactation:** Advise women not to breastfeed during treatment and for 6 months after the last dose.

To report SUSPECTED ADVERSE REACTIONS, contact Ipsen Biopharmaceuticals, Inc. at 1-855-463-5127 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see Brief Summary of full Prescribing Information on the following pages.

Learn more at SomatulineDepotHCP.com

IPSEN Innovation for patient care

Somatuline® Depot (lanreotide) Injection 120 mg

SOMATULINE® DEPOT (lanreotide) injection, for subcutaneous use

Brief Summary of full Prescribing Information—GEP-NETs and Carcinoid Syndrome. See full Prescribing Information. Rx Only.

INDICATIONS AND USAGE:

Gastroenteropancreatic Neuroendocrine Tumors: for the treatment of adults with unresectable, well or moderately differentiated, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NETs) to improve progression-free survival.

Carcinoid Syndrome: for the treatment of adults with carcinoid syndrome; when used, it reduces the frequency of short-acting somatostatin analog rescue therapy.

DOSAGE AND ADMINISTRATION

Important Administration Instructions *For deep subcutaneous injection only;* intended for administration by a healthcare provider. The recommended dosage of SOMATULINE DEPOT is 120 mg administered every 4 weeks by deep subcutaneous injection. If patients are already being treated with SOMATULINE DEPOT for GEP-NETs, do not administer an additional dose for the treatment of carcinoid syndrome. For preparation and administration instructions, refer to the full Prescribing Information.

CONTRAINDICATIONS: SOMATULINE DEPOT is contraindicated in patients with history of a hypersensitivity to lanreotide. Allergic reactions (including angioedema and anaphylaxis) have been reported following administration.

WARNINGS AND PRECAUTIONS

Cholelithiasis and Gallbladder Sludge: SOMATULINE DEPOT may reduce gallbladder motility and lead to gallstone formation; therefore, patients may need to be monitored periodically.

Hyperglycemia and Hypoglycemia: Patients treated with SOMATULINE DEPOT may experience hypoglycemia or hyperglycemia. Blood glucose levels should be monitored when lanreotide treatment is initiated, or when the dose is altered, and antidiabetic treatment should be adjusted accordingly.

Cardiovascular Abnormalities: In patients without underlying cardiac disease, SOMATULINE DEPOT may lead to a decrease in heart rate without necessarily reaching the threshold of bradycardia. In patients suffering from cardiac disorders prior to SOMATULINE DEPOT treatment, sinus bradycardia may occur. Care should be taken when initiating treatment with SOMATULINE DEPOT in patients with bradycardia. Cases of hypertension have been reported. In 81 patients with GEP-NETs and baseline heart rates of 60 beats per minute (bpm) or greater treated with SOMATULINE DEPOT, the incidence of heart rate less than 60 bpm was 23% (19/81) as compared to 16% (15/94) of placebo treated patients; 10 patients (12%) had documented heart rates less than 60 bpm on more than one visit. The incidence of documented episodes of heart rate less than 50 bpm as well as the incidence of bradycardia reported as an adverse event was 1% in each treatment group. Initiate appropriate medical management in patients who develop symptomatic bradycardia.

ADVERSE REACTIONS

GEP-NETs: The safety of SOMATULINE DEPOT 120 mg for the treatment of patients with GEP-NETs was evaluated in a double-blind, placebo-controlled trial. Patients were randomized to receive SOMATULINE DEPOT (N=101) or placebo (N=103) administered by deep subcutaneous injection once every 4 weeks. The data below reflect exposure to SOMATULINE DEPOT in 101 patients with GEP-NETs, including 87 patients exposed for at least 6 months and 72 patients exposed for at least 1 year (median duration of exposure 22 months). Patients treated with SOMATULINE DEPOT had a median age of 64 years (range 30 to 83 years), 53% were men and 96% were Caucasian. Eighty-one percent of patients (83/101) in the SOMATULINE DEPOT arm and 82% of patients (82/103) in the placebo arm did not have disease progression within 6 months of enrollment and had not received prior therapy for GEP-NETs. The rates of discontinuation due to treatment-emergent adverse reactions were 5% (5/101 patients) in the SOMATULINE DEPOT arm and 3% (3/103 patients) in the placebo arm. **Adverse reactions occurring in 5% and greater of patients receiving SOMATULINE DEPOT 120 mg (N=101)** rated as either Any or Severe (defined as hazardous to well-being, significant impairment of function or incapacitation) **and at a higher rate than Placebo (N=103)**, also rated as either Any or Severe, respectively, were: **Any Adverse Reactions (88%, 26%, 90%, 31%)**; Abdominal pain: includes upper/lower, abdominal discomfort (34%*, 6%*, 24%*, 4%); Musculoskeletal pain: includes myalgia, musculoskeletal discomfort, musculoskeletal pain, back pain (19%*, 2%*, 13%*, 2%*); Vomiting (19%*, 2%*, 9%*, 2%*); Headache (16%, 0%, 11%, 1%); Injection site reaction: includes infusion site extravasation, injection site discomfort, injection site granuloma, injections site hematoma, injection site hemorrhage, injection site induration, injection site mass, injections site nodule, injection site pain, injection site pruritus, injection site rash, injection site reaction, injection site swelling (15%, 0%, 7%, 0%); Hyperglycemia: includes diabetes mellitus, glucose tolerance impaired, hyperglycemia, type 2 diabetes mellitus (14%*, 0%, 5%, 0%); Hypertension: includes hypertensive crisis (14%*, 1%*, 5%, 0%); Cholelithiasis (14%*, 1%*, 7%, 0%); Dizziness (9%, 0%, 2%*, 0%); Depression: includes depressed mood (7%, 0%, 1%, 0%); Dyspnea (6%, 0%, 1%, 0%). * Includes one or more serious adverse events (SAEs) defined as any event that results in death, is life threatening, results in hospitalization or prolongation of hospitalization, results in persistent or significant disability, results in congenital anomaly/birth defect, or may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed.

Carcinoid Syndrome**:** The safety of SOMATULINE DEPOT 120 mg in patients with histopathologically confirmed neuroendocrine tumors and a history of carcinoid syndrome (flushing and/or diarrhea) was evaluated in a double-blind, placebo-controlled trial. Patients were randomized to receive SOMATULINE DEPOT (N=59) or placebo (N=56) administered by deep subcutaneous injection once every 4 weeks. Patients in both arms had access to subcutaneous octreotide as rescue medication for symptom control. Adverse reactions reported were generally similar to those reported for the GEP-NETs population. Adverse reactions occurring in 5% and greater of SOMATULINE DEPOT-treated patients and occurring at least 5% more than in placebo-treated patients were headache (12% vs 5%, respectively), dizziness (7% vs 0%, respectively), and muscle spasm (5% vs 0%, respectively) by week 16.

Immunogenicity: As with all peptides, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to lanreotide with the incidence of antibodies in other studies or to other products may be misleading. Development of anti-lanreotide antibodies was assessed using a radioimmuno-precipitation assay. In patients with GEP-NETs receiving SOMATULINE DEPOT, the incidence of anti-lanreotide antibodies was 4% (3 of 82) at 24 weeks, 10% (7 of 67) at 48 weeks, 11% (6 of 57) at 72 weeks, and 10% (8 of 84) at 96 weeks. Assessment for neutralizing antibodies was not conducted. Less than 2% (2 of 108) of the carcinoid syndrome patients treated with SOMATULINE DEPOT developed anti-lanreotide antibodies.

Postmarketing Experience: The following adverse reactions have been identified during post-approval use of SOMATULINE DEPOT. 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. *Hepatobiliary:* Steatorrhea, cholecystitis, pancreatitis; *Body as a Whole:* angioedema and anaphylaxis.

DRUG INTERACTIONS

Insulin and Oral Hypoglycemic Drugs: Lanreotide, like somatostatin and other somatostatin analogs, inhibits the secretion of insulin and glucagon. Blood glucose levels should be monitored when SOMATULINE DEPOT treatment is initiated or when the dose is altered, and antidiabetic treatment should be adjusted accordingly.

Cyclosporine: Concomitant administration of cyclosporine with SOMATULINE DEPOT may decrease the absorption of cyclosporine, and therefore, may necessitate adjustment of cyclosporine dose to maintain therapeutic drug concentrations.

Bromocriptine: Limited published data indicate that concomitant administration of a somatostatin analog and bromocriptine may increase the absorption of bromocriptine.

Bradycardia-Inducing Drugs: Concomitant administration of bradycardia-inducing drugs (e.g., beta-blockers) may have an additive effect on the reduction of heart rate associated with lanreotide. Dosage adjustments of concomitant drugs may be necessary.

Drug Metabolism Interactions: The limited published data available indicate that somatostatin analogs may decrease the metabolic clearance of compounds known to be metabolized by cytochrome P450 enzymes, which may be due to the suppression of growth hormone. Since it cannot be excluded that SOMATULINE DEPOT may have this effect, avoid other drugs mainly metabolized by CYP3A4 and which have a low therapeutic index (e.g., quinidine, terfenadine). Drugs metabolized by the liver may be metabolized more slowly during SOMATULINE DEPOT treatment and dose reductions of the concomitantly administered medications should be considered.

USE IN SPECIFIC POPULATIONS

Pregnancy: Limited available data based on postmarketing case reports with SOMATULINE DEPOT use in pregnant women are not sufficient to determine a drug-associated risk of adverse developmental outcomes. In animal reproduction studies, decreased embryo/fetal survival was observed in pregnant rats and rabbits at subcutaneous doses 5- and 2-times the maximum recommended human dose (MRHD) of 120 mg, respectively.

Lactation: There is no information available on the presence of lanreotide in human milk, the effects of the drug on the breastfed infant, or the effects of the drug on milk production. Because of the potential for serious adverse reactions in breastfed infants from SOMATULINE DEPOT, including effects on glucose metabolism and bradycardia, advise women not to breastfeed during treatment with SOMATULINE DEPOT and for 6 months (6 half-lives) following the last dose.

Females and Males of Reproductive Potential: *Infertility (Females)* Based on results from animal studies conducted in female rats, SOMATULINE DEPOT may reduce fertility in females of reproductive potential.

Pediatric Use: The safety and effectiveness of SOMATULINE DEPOT in pediatric patients have not been established.

Geriatric Use: Studies conducted in patients with neuroendocrine tumors, did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Renal Impairment: GEP-NETs No effect was observed in total clearance of lanreotide in patients with mild to moderate renal impairment receiving SOMATULINE DEPOT 120 mg. Patients with severe renal impairment were not studied.

Hepatic Impairment: GEP-NETs SOMATULINE DEPOT has not been studied in patients with GEP-NETs and hepatic impairment.

References: 1. Somatuline Depot (lanreotide) Injection [Prescribing Information]. Basking Ridge, NJ: Ipsen Biopharmaceuticals, Inc.; September 2017. **2.** Caplin ME, Pavel M, Ćwikła JB, et al, for the CLARINET Investigators. Lanreotide in metastatic enteropancreatic neuroendocrine tumors. *N Engl J Med.* 2014;371(3):224-233.

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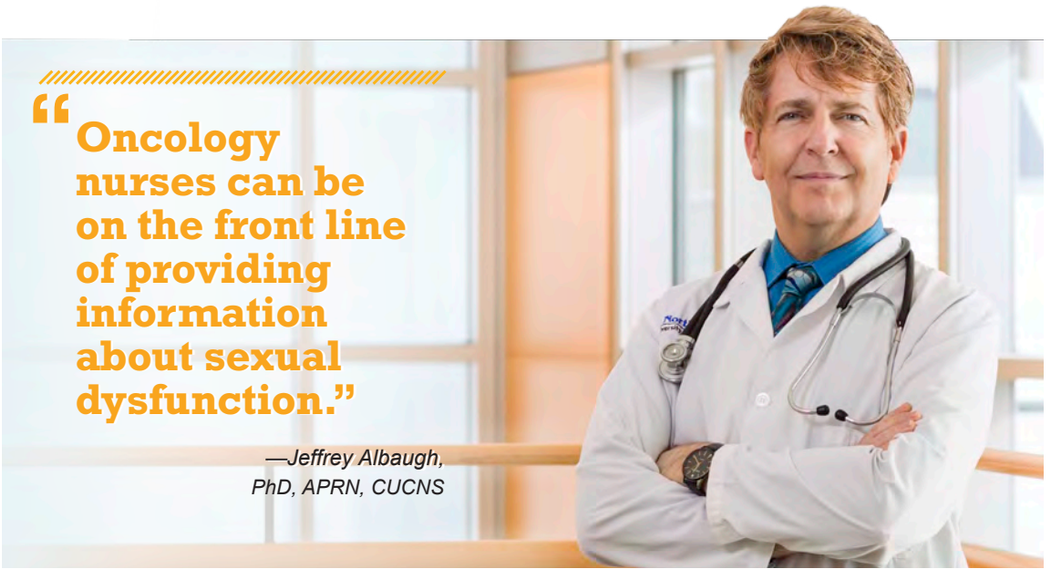

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Editor in Chief

Sex After Cancer: Let Patients Know They Are Not Alone

"Empowering patients with information about sexual dysfunction and fertility can lead to better decision making."

For many patients, one of the most challenging aspects of cancer is the adverse effects that follow disease treatment. They come in different forms, such as nausea, vomiting, diarrhea, hair loss, anemia, and chemo brain. Another unfortunate, and often underreported, adverse effect involves sexual health and fertility.

Although sexual and fertility concerns during and after cancer affect men and women differently, both genders have the same desire for intimacy.

In this issue's cover story, Jeffrey Albaugh, PhD, APRN, CUCNS, director of sexual health at NorthShore University HealthSystem in Evanston, Illinois, walks through the specific issues related to sex that men and women who are cancer survivors face, offering many ways in which oncology nurses can help patients address their concerns.

Albaugh's most crucial piece of advice is to have conversations with patients to let them know they are not alone. A study, discussed by Albaugh in the cover story, found that 62% of internists working with patients with cancer never or rarely address sexual issues. Albaugh understands that sexuality is crucial to being human. Through his nursing experience, he found that empowering patients with information about sexual dysfunction and fertility can lead to better decision making.

This issue of *Oncology Nursing News*® also discusses improving the accuracy of patient identification. Whether it be human or computer error, these mistakes are still happening in cancer care centers across the country despite efforts by the Joint Commission, the American Society of Clinical Oncology, and the Oncology Nursing Society. Our editor in chief dissects a lawsuit that was a result of a wrong-patient error that led to the patient receiving chemotherapy intended for someone else. In these pages, we examine how this could have been avoided and discuss further actions to reduce patient identification mistakes.

Retirement is often dreamed about, but rarely feels like it's within reach. A new book, *Redefining Retirement For Nurses: Finding Meaning After Retirement*, tells the stories of 26 nurses and their journeys to the next phases of life. *Oncology Nursing News*® speaks with one of the authors, who after 45 years of nursing, sold her home and purchased an RV to travel the country. Much like the nurses whose stories she shares, Joanne Evans found it most challenging to not overcommit herself, whether it be for speaking engagements or volunteer work, again in the chapter she likes to call "rewiring" rather than "retiring."

Also in this issue, a new drug to help reduce oral mucositis in patients with head and neck cancer, promoting *BRCA* awareness, and the impact that nurse case managers have on clinical outcomes.

We hope you find these articles informative, and as always, thank you for reading.

Mike Hennessy, Sr
Chairman and CEO


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Cancer Treatment to the Wrong Patient: Why Does This Still Happen?

Although steps have been taken to improve patient safety, patient identification errors can go undetected.

Lisa Schulmeister, MN, RN, FAAN

Editor in Chief
Oncology Nursing News®
Oncology Nursing Consultant

"Patient education and engagement in the identity verification process is crucial."

In 2002, the Joint Commission created its National Patient Safety Goals program, which was effective by the start of the following year. The No. 1 priority: improving the accuracy of patient identification.

To meet this goal, healthcare providers use at least 2 patient identifiers—usually, name and date of birth. However, a medical record number or another identifier can be used, as long as it is not the patient's room or chair number or location. In addition, some facilities check bar-coded identification information on a patient's wristband against information on a medication label or the patient's medical record. A few facilities use biometric patient identification, such as retinal scanning or fingerprint confirmation.

The Joint Commission isn't alone in its efforts to ensure accurate patient identification. American Society of Clinical Oncology (ASCO) and the Oncology Nursing Society collaborated to create chemotherapy administration safety standards to reduce the risk of error when providing adult patients with chemotherapy and give a framework for best practices in cancer care.

Although rare, wrong-patient errors, also called patient identification errors, can cause harm when one patient receives another's cancer treatment. The degree of harm is unknown but may be significant, and even lethal. Consequently, verifying a patient's identity using 2 identifiers is essential to reduce the risk of error.

With these efforts in place, why are wrong-patient errors still happening in cancer treatment facilities?

Consider this real-life example, which led to legal action: In a busy outpatient registration area, a recently hired clerk followed the facility's procedure and entered the name printed on the patient's driver's license. She clicked the first name in the list that appeared on her computer screen and created a wristband, unaware that other patients with the same name existed in the system.

The clerk asked the patient if the information on the band was correct, and he said yes. In court testimony later, he stated that he was not wearing his glasses at the time and was relying on the hospital staff to apply the correct wristband.

The patient was sent to the busy infusion area at noon for his second chemotherapy treatment. A registered nurse asked him if his name was John Jones (name changed here for privacy) and if his birthday was the date that she read from his wristband. He nodded yes.

But an error was made. The patient received the chemotherapy intended for another patient who had the same name but a different birthdate.

In court, the patient said that although the nurse said the correct name but wrong birthdate, he didn't notice, because the nurse had a "heavy accent" and "rattled off numbers." He also stated that the infusion room was loud and busy and that he "didn't hear well." In the nurse's testimony, she said the orders were "unclear" because they were written as "day 1, day 8," and she presumed the patient came in for treatment on the correct day.

praisaeng/ Adobe Stock

Despite receiving the wrong treatment, the patient experienced minimal adverse effects. However, he alleged harm, and a jury agreed.

This case illustrates how a patient identification error can occur and go undetected. With increasingly larger patient databases, it is essential that registration staff select the correct patient from electronic lists. Patients with common names and those who have been registered under multiple names (eg, maiden name and married name) are at a higher risk of identification errors. For instance, "Smith" is the most common surname in the United States—more than 2 million people have it—followed by "Johnson," according to the US Census Bureau. Also, it is not uncommon for patients with the same or similar names also to have the same or similar birthdates. These patients need to be informed that another patient with the same primary identifiers exists in the system. That way, patients can help ensure that their identity is correctly confirmed.

Had the nurse asked for the patient's name and had him state his birthdate, the error might have been avoided. Active confirmation of identity, instead of passive confirmation of identity, is best. The case also illustrates how patients tend to rely on healthcare providers instead of being active participants in the identification process. Patient education and engagement in the identity verification process is crucial.

Identification challenges exist in cases where a patient may be unable to participate in the process for reasons such as cognitive impairment or language barriers. These situations need to be addressed on a case-by-case basis using available resources.

Although a patient's photo should never be used as an identifier, it can be used as an additional verification method. Bar codes, too, should not be relied on but can be an additional identifier.

Electronic systems should allow just 1 patient record to be open at a time; with some older systems, multiple records can be open simultaneously, increasing the risk of errors. Labels containing patient information should be printed and used one patient at a time; batch labeling could result in the wrong label being applied to a blood vial or, worse, a chemotherapy infusion bag. The test result review should include verification of patient identity information. It is not uncommon to find reports, particularly those of tests performed at another facility, scanned or entered into the incorrect electronic medical record. Perhaps most important, patient identification should be verified upon every encounter that requires confirmation, not just at the onset of care delivery that day. For example, patient identity needs to be confirmed before each infusion bag of chemotherapy is administered, even in facilities where nurses feel they "know" their patients. When safety processes, such as verification of patient identity, are performed consistently and attentively, errors can be prevented.

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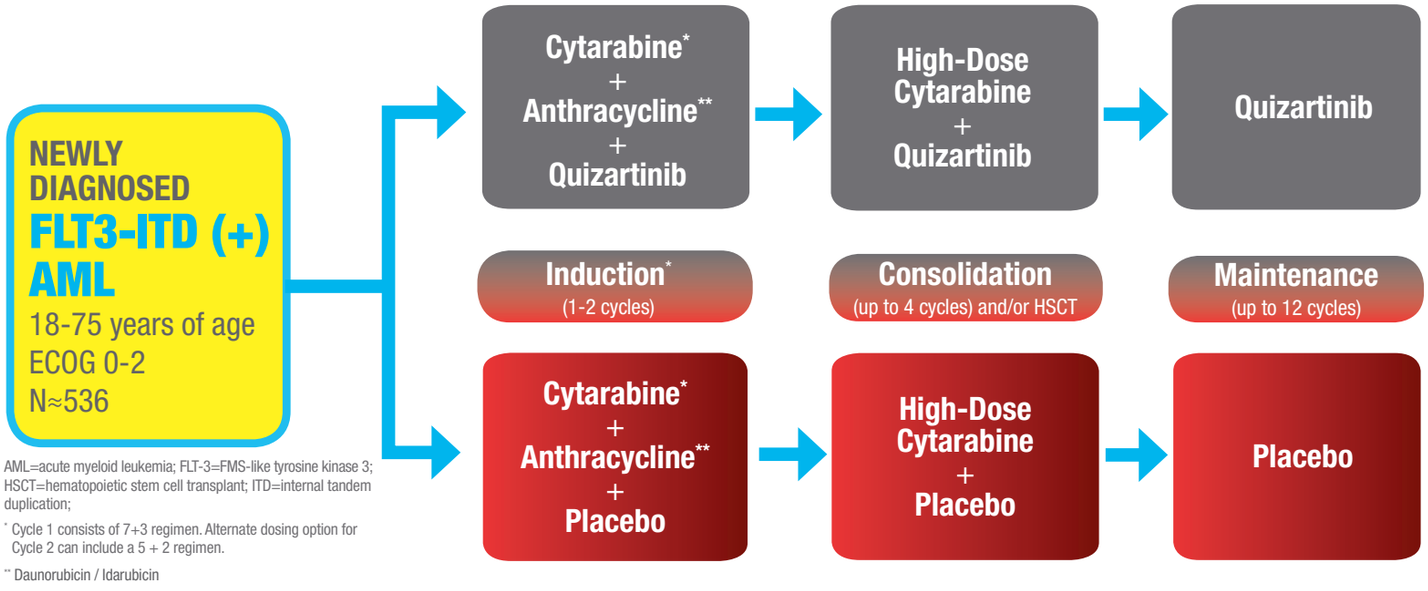

AML=acute myeloid leukemia; FLT-3=FMS-like tyrosine kinase 3; HSCT=hematopoietic stem cell transplant; ITD=internal tandem duplication;

* Cycle 1 consists of 7+3 regimen. Alternate dosing option for Cycle 2 can include a 5 + 2 regimen.

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Primary Endpoint: Event-free Survival (EFS)

Secondary Endpoints:

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Oncology Case Management: Optimizing Care Pathways

Applying 4 philosophies to the nurse case manager role can assist with patient decision making.

Melissa A. Grier, MSN, APRN, ACNS-BC

Melissa Grier is a clinical nurse specialist at Via Christi Health in Wichita, Kansas, where she supports the Via Christi Cancer Institute, as well as the Medical/Surgical Cardiac Department, Resource Pool, Emergency Department, and oncology service line.

"Through communication, resource management, education, and patient advocacy, the case manager coordinates a patient-centered plan of care."

Cancer care starts at prediagnosis. The initial conversation between a patient and the healthcare team helps establish trust.

However, many patients and their loved ones report receiving inadequate information about diagnosis, treatment, and prognosis from the beginning. In a study by Figg et al, 44% of the 437 patients who completed a survey reported that the initial conversation about their cancer diagnosis lasted 10 minutes or less. That can leave a patient feeling confused, angry, and unsupported. However, oncology nurse case managers can help bridge the gap between fear of the unknown and confidence in the healthcare team.

THE MAKING OF AN ONCOLOGY NURSE CASE MANAGER

Oncology nurse case managers optimize quality and cost-effective care in both hospital and community settings. These highly skilled nurses possess specialized training and certification in case management and/or oncology. Case managers may work face-to-face or via telephone with patients.

Nurse case management has been recognized as a successful method for optimizing cancer care pathways, increasing quality of care and achieving cost-effectiveness. These healthcare professionals possess not only an extensive clinical background but also a vast understanding of the healthcare industry, payer sources, and psychosocial care.

Many nurse case managers become certified. The Commission for Case Manager Certification (CCMC) is the largest accrediting body and considered the gold standard in the field. An estimated 50% of employers require the certification for nurse case managers, and 63% of employers offer reimbursement for the exam, according to CCMC. Experience coupled with certification prepares nurse case managers to deliver care in a patient-centric model.

WHAT'S IN A NAME?

Nurse case managers and nurse navigators are often confused and the terms interchanged. Although they may have common responsibilities, such as timely access to care and minimizing healthcare barriers, they are not the same.

Navigation is defined as individualized assistance that helps patients, families, and caregivers overcome healthcare system barriers and facilitates timely access to quality health and psychosocial care, from prediagnosis through all phases of the cancer experience.

Case management involves a collaborative process of assessment, planning, facilitation, care coordination, evaluation, and advocacy for options and services to meet the individual needs of the patient, according to the Case Management Society of America. Through communication, resource management, education, and patient advocacy, the case manager coordinates a patient-centered plan of care.

PHILOSOPHIES OF ONCOLOGY CASE MANAGEMENT

- **Advocacy**. The case manager is tasked with finding the delicate balance between treatment, resource use, evidenced-based medicine, and the patient's ability to make informed decisions. Through education, resource allocation, and support, the case manager advocates for the patient. Further, a case manager advocates for multidisciplinary team members, the hospital, and the payer source. This role of advocacy for the common good and for the patient requires careful balance.
- **Communication**. Case managers are highly skilled in interviewing, reflection, critical thinking, and collaboration. They use techniques such as motivational interviewing to help empower the patient to make individualized decisions and accomplish goals. This approach helps the case manager ensure that all oncology treatment is patient-centered.
- **Resource Management**. Case managers are familiar with available local, state, and national resources. They work with the patient to find the support they need in their own community. For instance, a patient may require transportation, meals, or financial assistance.

A case manager is in a unique role that involves both assisting with the patient's clinical needs and examining interpersonal and psychosocial needs. One of the most challenging aspects of this position involves considering the cost of treatment. Some patients have a realistic outlook on their prognosis; others do not. It is the case manager's job to help the patient find the right resources and treatment that are not only clinically focused but financially sound. This may be the difference between another round of chemotherapy or pursuing palliative or hospice care. These conversations take a great amount of skill, empathy, and compassion.

- **Education**. Nurses educate, and oncology nurse case managers use education as a pillar of their practice. By educating the patient in an open, honest manner, case managers increase adherence to treatment pathways. The case manager ensures that the patient understands the treatment plan, diagnosis, and prognosis. It is the case manager's job to provide the patient with the information needed to make informed self-care decisions.

Case managers are committed to helping patients navigate the highly specialized and fragmented healthcare system. Using the 4 case management philosophies, they ensure that the patient experiences a coherent and individually focused care pathway that is delivered at the right time using the right resources.

Tocome/ Fotolia

■ *Journal Article*

Drug Shows Promise for Reducing Oral Mucositis in Patients with Head and Neck Cancer

sebra/ Fotolia

ORAL MUCOSITIS OCCURS among 70% of patients with head and neck cancer who are being treated with radiation. This adverse effect (AE) can disrupt quality of life, affect the ability to eat, and increase treatment costs due to the need for antibiotics or narcotics or additional or longer hospital stays.

However, GC4419, a new drug created by Galera Therapeutics to reduce severe oral mucositis, may offer much-needed help. The drug candidate is a first-in-class, small molecule enzyme mimetic that converts superoxide to hydrogen peroxide and molecular oxygen.

In a double-blind, placebo-controlled phase IIa trial, researchers randomized 223 patients with head and neck cancer to receive an infusion of either 30 mg or 90 mg of GC4419 or placebo on the days they received radiation treatment. Patients were scheduled to receive 7 weeks of radiation therapy plus cisplatin; therefore, the researchers aimed to determine the duration of severe oral mucositis they experienced in that time frame.

Patients in the placebo arm had severe oral mucositis an average of 19 days, whereas the group of patients who received the 90-mg dose of GC4419 experienced the AE for only about a day and a half—a 92% reduction. Severe oral mucositis occurred in 58% of the placebo arm, but in just 40% of patients who received the 30-mg dose and 37% of those who received 90 mg.

In addition, patients treated with GC4419 experienced longer delays in the time to onset of oral mucositis, and fewer grade IV AEs occurred. The agent also was well tolerated, and the frequency of treatment-related AEs was comparable across all treatment arms in the trial.

"There are 3 things about this study that are very important for demonstrating that our technology works," Mel Sorensen, chief executive officer of Galera Therapeutics, said. "The first is, we had a very robust result, highly statistically significant and clinically relevant in the primary endpoint. The second is that all of the secondary endpoints pointed in the same direction; they were consistent with the primary endpoint. And third is that the intermediate dose, 30 mg, was also intermediate in results between the 2 arms." The results show promise in reducing the toxicity of radiation, as well as preserving the activity of the chemoradiation, he said.

Galera Therapeutics intends to further investigate GC4419 as an agent to not only reduce the AEs but treat the cancer itself, Sorensen said.

■ *FDA Labeling Changes*

ALIMTA (pemetrexed)

Warnings and Precautions updated:

- Myelosuppression: Pemetrexed can cause severe myelosuppression, resulting in a need for transfusions and potentially leading to neutropenic infection. The risk is higher in patients who do not receive vitamin supplementation.
- Renal failure: Pemetrexed can cause severe, and sometimes fatal, renal toxicity. Incidences of renal failure in clinical studies in which patients received pemetrexed with cisplatin were 2.1% in Study JMDB and 2.2% in Study JMCH. The incidence in studies in which patients received single-agent pemetrexed ranged from 0.4% to 0.6%. Determine creatinine clearance before each dose and periodically monitor renal function during treatment with pemetrexed.
- Skin toxicity: Serious and sometimes fatal bullous, blistering, and exfoliative skin toxicity, including cases suggestive of Stevens-Johnson syndrome/toxic epidermal necrolysis can occur with pemetrexed.
- Interstitial pneumonia: Serious interstitial pneumonitis, including fatal cases, can occur with pemetrexed treatment. Withhold pemetrexed for acute onset of new or progressive unexplained pulmonary symptoms such as dyspnea, cough, or fever pending diagnostic evaluation. If pneumonitis is confirmed, permanently discontinue pemetrexed.
- Radiation recall: Radiation recall can occur with pemetrexed in patients who received radiation weeks to years previously. Monitor patients for inflammation or blistering in areas of previous radiation treatment.
- Concomitant ibuprofen: The risk of adverse reactions is increased in patients with mild to moderate renal impairment who take concomitant ibuprofen while receiving pemetrexed. In patients with creatinine clearances between 45 mL/min and 79 mL/min, avoid administration of ibuprofen for 2 days before, the day of, and 2 days following administration of pemetrexed.
- Embryo-fetal toxicity: Advise females of reproductive potential to use effective contraception during treatment with pemetrexed and for 6 months after the final dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with pemetrexed and for 3 months after the final dose.

LYNPARZA (olaparib)

Drug Interactions updated: renal impairment

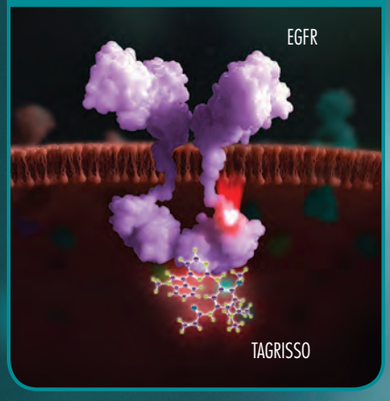
- No adjustment to the starting dose is required in patients with mild renal impairment.
- A 24% increase in mean exposure (area under the curve [AUC]) was observed in patients with mild renal impairment (creatinine clearance rate [CLcr] = 51-80 mL/min) compared with patients with normal renal function (CLcr >80 mL/min). A 44% increase in AUC was observed in patients with moderate renal impairment (CLcr = 31-50 mL/min) compared with patients with normal renal function.
- For patients with moderate renal impairment, reduce the dose of olaparib capsules to 300 mg twice daily. (The recommended dose of olaparib is 400 mg [eight 50-mg capsules] taken orally twice daily with or without food, for a total daily dose of 800 mg. Capsules should not be substituted for tablets).
- There are no data in patients with severe renal impairment or end-stage disease (CLcr ≤30 mL/min).

For full details, visit the FDA's Drug Safety Labeling Changes database at **www.accessdata.fda.gov/scripts/cder/safetylabelingchanges.**

The first and only third-generation EGFR TKI[1]

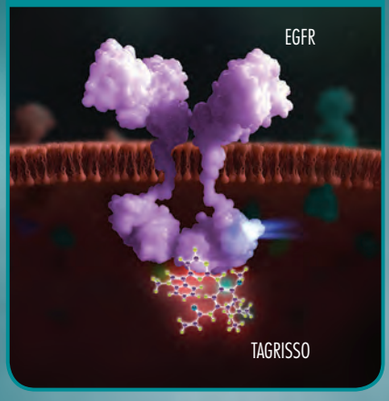
TAGRISSO®—ELEGANT DESIGN MEETS SELECTIVE TARGETING

exon 19



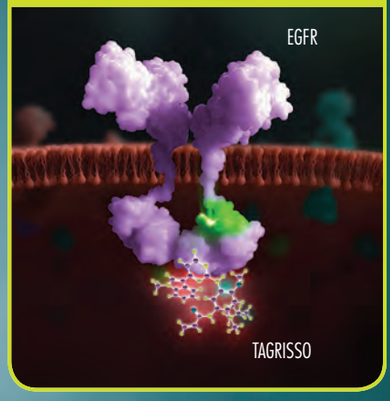
TAGRISSO binds irreversibly to EGFR with **exon 19 deletions**, a mutation seen in approximately 46% of EGFRm metastatic NSCLC[2,3]

exon 21 L858R



TAGRISSO binds irreversibly to EGFR with **exon 21 L858R substitution**, a mutation seen in approximately 39% of EGFRm metastatic NSCLC[2,3]

T790M



TAGRISSO inhibits mutated EGFR with the **T790M** mutation, which is responsible for resistance in more than half of EGFRm metastatic NSCLC cases at progression[2,4]

EGFRm=epidermal growth factor receptor mutation, NSCLC=non-small cell lung cancer, TKI=tyrosine kinase inhibitor.

INDICATION

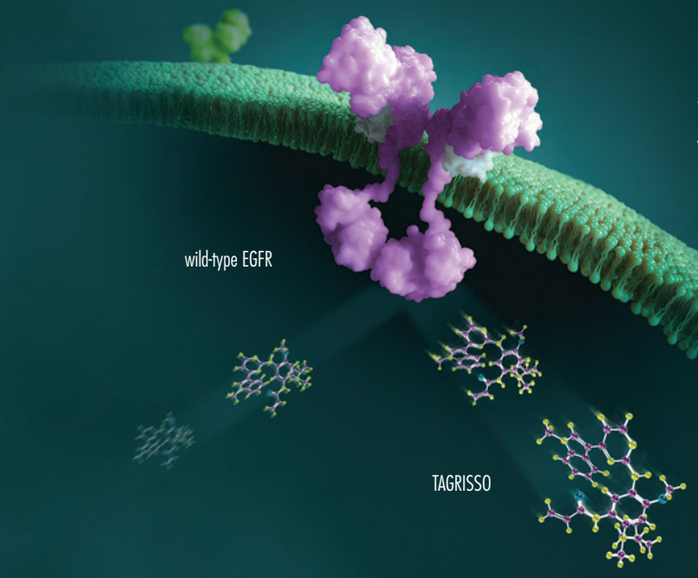
TAGRISSO (osimertinib) is indicated for the treatment of patients with metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive non-small cell lung cancer (NSCLC), as detected by an FDA-approved test, whose disease has progressed on or after EGFR tyrosine kinase inhibitor therapy.

IMPORTANT SAFETY INFORMATION

- There are no contraindications for TAGRISSO
- Interstitial Lung Disease (ILD)/Pneumonitis occurred in 3.5% and was fatal in 0.6% of 833 TAGRISSO-treated patients. Withhold TAGRISSO and promptly investigate for ILD in patients who present with worsening of respiratory symptoms indicative of ILD (eg, dyspnea, cough, and fever). Permanently discontinue TAGRISSO if ILD is confirmed
- Heart rate-corrected QT (QTc) interval prolongation occurred in TAGRISSO-treated patients. Of the 833 TAGRISSO-treated patients, 0.7% of patients were found to have a QTc > 500 msec, and 2.9% of patients had an increase from baseline QTc > 60 msec. No QTc-related arrhythmias were reported. 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

AstraZeneca

TAGRISSO is designed to target EGFR sensitizing mutations and EGFR T790M mutations.[1] TAGRISSO binds irreversibly to these key drivers of disease and resistance while demonstrating a lower affinity for wild-type EGFR[2]



With a lower affinity for **wild-type** EGFR, TAGRISSO binds at approximately 9-fold lower concentrations[2]

- Cardiomyopathy occurred in 1.9% and was fatal in 0.1% of 833 TAGRISSO-treated patients. Left Ventricular Ejection Fraction (LVEF) decline ≥ 10% and a drop to < 50% occurred in 4% of 655 TAGRISSO-treated patients. Conduct cardiac monitoring, including an assessment of LVEF at baseline and during treatment in patients with cardiac risk factors. Assess LVEF in patients who develop relevant cardiac signs or symptoms during treatment. For symptomatic congestive heart failure or persistent, asymptomatic LV dysfunction that does not resolve within 4 weeks, permanently discontinue TAGRISSO
- Keratitis was reported in 0.7% of 833 TAGRISSO-treated patients in clinical trials. Promptly refer patients with signs and symptoms suggestive of keratitis (such as eye inflammation, lacrimation, light sensitivity, blurred vision, eye pain, and/or red eye) to an ophthalmologist
- 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%) in patients treated with TAGRISSO were diarrhea (41%), rash (34%), dry skin (23%), nail toxicity (22%), and fatigue (22%)

Please see accompanying complete Brief Summary of Prescribing Information on adjacent pages.

References: 1. Cross DAE, Ashton SE, Ghiorghiu S, et al. AZD9291, an irreversible EGFR TKI, overcomes T790M-mediated resistance to EGFR inhibitors in lung cancer. *Cancer Discov.* 2014;4: 1046-1061. **2.** TAGRISSO [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2017. **3.** Shigematsu H, Lin L, Takahashi T, et al. Clinical and biological features associated with epidermal growth factor receptor gene mutations in lung cancers. *J Natl Cancer Inst.* 2005;97(5): 339-346. **4.** Yu HA, Arcila ME, Rekhtman N, et al. Analysis of tumor specimens at the time of acquired resistance to EGFR-TKI therapy in 155 patients with *EGFR*-mutant lung cancers. *Clin Cancer Res.* 2013;19:2240-2247.

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, whose disease has progressed on or after EGFR tyrosine kinase inhibitor (TKI) therapy.

DOSAGE AND ADMINISTRATION

Patient Selection

Confirm the presence of a T790M EGFR mutation in tumor or plasma specimens prior to initiation of treatment with TAGRISSO *[see Indications and Usage (1) and Clinical Studies (14) in full Prescribing Information]*. Testing for the presence of the mutation in plasma specimens is recommended only in patients for whom a tumor biopsy cannot be obtained. If this mutation is not detected in a plasma specimen, re-evaluate the feasibility of biopsy for tumor tissue testing. 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 nasogastric tube is required, disperse the tablet as above in 15 mL of non-carbonated 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.
	Symptomatic congestive heart failure or asymptomatic left ventricular dysfunction that persists ≥ 4 weeks	Permanently discontinue TAGRISSO.
Other	Adverse reaction of Grade 3 or greater severity	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
[†] 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

The following information for ILD/ Pneumonitis, QTc Interval Prolongation, Cardiomyopathy and Keratitis reflects exposure to TAGRISSO in 833 patients with EGFR T790M mutation-positive non-small cell lung cancer (NSCLC) who received TAGRISSO at the recommended dose of 80 mg once daily in AURA3 (n=279), AURA Extension (n=201), AURA2 (n=210), and an expansion cohort in the first-in-human trial of osimertinib (AURA1, n=143).

Interstitial Lung Disease/Pneumonitis

Interstitial lung disease (ILD)/pneumonitis occurred in 3.5% (n=29) of TAGRISSO-treated patients (n=833); 0.6% (n=5) of cases were fatal.

Withhold TAGRISSO and promptly investigate for ILD in patients who present 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

Heart rate-corrected QT (QTc) interval prolongation occurs in patients treated with TAGRISSO. Of the 833 patients treated with TAGRISSO in clinical trials, 0.7% (n=6) were found to have a QTc greater than 500 msec, and 2.9% of patients (n=24) had an increase from baseline QTc greater than 60 msec *[see Clinical Pharmacology (12.2) in full Prescribing Information]*. No QTc-related arrhythmias were reported.

Clinical trials of TAGRISSO did not enroll patients with baseline QTc of greater than 470 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 *[see Dosage and Administration (2.4) in full Prescribing Information]*.

Cardiomyopathy

Across clinical trials, cardiomyopathy (defined as cardiac failure, congestive heart failure, pulmonary edema or decreased ejection fraction) occurred in 1.9% (n=16) of 833 TAGRISSO-treated patients: 0.1% (n=1) of cases were fatal.

Left Ventricular Ejection Fraction (LVEF) decline greater than or equal to 10% and a drop to less than 50% occurred in 4.0% (26/655) of patients who had baseline and at least one follow-up LVEF assessment.

Conduct cardiac monitoring, including an assessment of LVEF at baseline and during treatment in patients with cardiac risk factors. Assess LVEF in patients who develop relevant cardiac signs or symptoms during treatment. 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]*.

Keratitis

Keratitis was reported in 0.7% (n=6) of 833 patients treated with TAGRISSO in clinical trials. Promptly refer patients with signs and symptoms suggestive of keratitis (such as eye inflammation, lacrimation, light sensitivity, blurred vision, eye pain and/or red eye) to an ophthalmologist.

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]*

Cardiomyopathy *[see Warnings and Precautions (5.3) in full Prescribing Information]*

Keratitis *[see Warnings and Precautions (5.4) 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 patients with EGFR T790M mutation-positive metastatic NSCLC in an open-label, randomized, active-controlled trial (AURA3, n=279) and in two single arm trials, AURA Extension (n=201) and AURA2 (n=210). Patients with a history of interstitial lung disease, drug induced interstitial disease or radiation pneumonitis that required: steroid treatment, serious arrhythmia or baseline QTc interval greater than 470 msec on electrocardiogram were excluded from trial enrollment.

AURA3 Trial

The safety of TAGRISSO was evaluated in AURA3, a multicenter international open label randomized (2:1) controlled trial conducted in 419 patients with unresectable or metastatic EGFR T790M mutation-positive NSCLC who had progressive disease following first line EGFR TKI treatment. A total of 279 patients received TAGRISSO 80 mg orally once daily until intolerance to therapy, disease progression, or investigator determination that the patient was no longer benefiting from treatment. A total of 136 patients received pemetrexed plus either carboplatin or cisplatin every three weeks for up to 6 cycles; patients without disease progression after 4 cycles of chemotherapy could continue maintenance pemetrexed until disease progression, unacceptable toxicity, or investigator determination that the patient was no longer benefiting from treatment. Left Ventricular Ejection Fraction (LVEF) was evaluated at screening and every 12 weeks. The median duration of treatment was 8.1 months for patients treated with TAGRISSO and 4.2 months for chemotherapy-treated patients. The trial population characteristics were: median age 62 years, age less than 65 (58%), female (64%), Asian (65%), never smokers (68%), and ECOG PS 0 or 1 (100%).

The most common adverse reactions (≥20%) in patients treated with TAGRISSO were diarrhea (41%), rash (34%), dry skin (23%), nail toxicity (22%), and fatigue (22%). Serious adverse reactions were reported in 18% of patients treated with TAGRISSO and 26% in the chemotherapy group. No single serious adverse reaction was reported in 2% or more patients treated with TAGRISSO. One patient (0.4%) treated with TAGRISSO experienced a fatal adverse reaction (ILD/pneumonitis).

Dose reductions occurred in 2.9% of patients treated with TAGRISSO. The most frequent adverse reactions leading to dose reductions or interruptions were prolongation of the QT interval as assessed by ECG (1.8%), neutropenia (1.1%), and diarrhea (1.1%). Adverse reactions resulting in permanent discontinuation of TAGRISSO occurred in 7% of patients treated with TAGRISSO. The most frequent adverse reaction leading to discontinuation of TAGRISSO was ILD/pneumonitis (3%).

Tables 2 and 3 summarize common adverse reactions and laboratory abnormalities which occurred in TAGRISSO-treated patients in AURA3. AURA3 was not designed to demonstrate a

statistically significant reduction in adverse reaction rates for TAGRISSO, or for the control arm, for any adverse reaction listed in Tables 2 and 3.

Table 2. Adverse Reactions Occurring in ≥10% of Patients Receiving TAGRISSO in AURA3

Adverse Reaction	TAGRISSO (N=279)		Chemotherapy (Pemetrexed/Cisplatin or Pemetrexed/Carboplatin) (N=136)	
	All Grades[a] (%)	Grade 3/4[a] (%)	All Grades[a] (%)	Grade 3/4[a] (%)
Gastrointestinal disorders				
Diarrhea	41	1.1	11	1.5
Nausea	16	0.7	49	3.7
Stomatitis	15	0	15	1.5
Constipation	14	0	35	0
Vomiting	11	0.4	20	2.2
Skin disorders				
Rash[b]	34	0.7	5.9	0
Dry skin[c]	23	0	4.4	0
Nail toxicity[d]	22	0	1.5	0
Pruritus[e]	13	0	5.1	0
Metabolism and Nutrition Disorders				
Decreased appetite	18	1.1	36	2.9
Respiratory, Thoracic and Mediastinal Disorders				
Cough	17	0	14	0
Musculoskeletal and Connective Tissue Disorders				
Back pain	10	0.4	9	0.7
General Disorders and Administration Site Conditions				
Fatigue[f]	22	1.8	40	5.1

* NCI CTCAE v4.0.

[a] No grade 4 events were reported.

[b] Includes rash, rash generalized, rash erythematous, rash macular, rash maculo-papular, rash papular, rash pustular, erythema, folliculitis, acne, dermatitis and acneform dermatitis.

[c] Includes dry skin, eczema, skin fissures, xerosis.

[d] Includes nail disorders, nail bed disorders, nail bed inflammation, nail bed tenderness, nail discoloration, nail disorder, nail dystrophy, nail infection, nail ridging, nail toxicity, onychoclasis, onycholysis, onychomadesis, paronychia.

[e] Includes pruritus, pruritus generalized, eyelid pruritus.

[f] Includes fatigue, asthenia.

Table 3. Common Laboratory Abnormalities (>20% for all NCI CTCAE Grades) in AURA3

Laboratory Abnormality	TAGRISSO (N=279)		Chemotherapy (Pemetrexed/Cisplatin or Pemetrexed/Carboplatin) (N=131[a])	
	Change from Baseline All Grades (%)	Change from Baseline to Grade 3 or Grade 4 (%)	Change from Baseline All Grades (%)	Change from Baseline to Grade 3 or Grade 4 (%)
Leukopenia	61	1.1	75	5.3
Lymphopenia	63	8.2	61	9.9
Thrombocytopenia	46	0.7	48	7.4
Neutropenia	27	2.2	49	12

[a] Based on the number of patients with available follow-up laboratory data

AURA Extension and AURA2 Trials

The safety of TAGRISSO was evaluated in two single arm trials, AURA Extension (n=201) and AURA2 (n=210). A total of 411 patients with EGFR 790M mutation-positive NSLC who received one or more prior EGFR therapies including an EGFR TKI were treated with TAGRISSO (80 mg daily). The majority of patients were heavily pretreated. Prior to enrollment, 68% of patients had received at least 2 prior treatment regimens, 46% had received 3 or more prior lines of therapy, and 63% had received prior platinum-based chemotherapy.

Median duration of exposure to TAGRISSO was 7.7 months (range: <0.1 to 11.6 months). The toxicity profile of TAGRISSO observed in the AURA Extension and AURA2 trials was generally consistent with the toxicity profile observed in the AURA3 trial. Four patients (1%) treated with TAGRISSO developed fatal adverse reactions of ILD/pneumonitis. 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.

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

Three hundred and forty-six (42%) of the 833 patients in AURA3 (n=279), AURA Extension (n=201), AURA2 (n=210), and an expansion cohort in the first-in-human trial of osimertinib (AURA1, n=143) were 65 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 (9.8% versus 6.8%) and more frequent dose modifications for adverse reactions (10.1% versus 6.0%) 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)] moderate, (CLcr 30-59 mL/min, as estimated by C-G) or severe (CLcr 15-29 mL/min) renal impairment. There is no recommended dose of TAGRISSO for patients with 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] or moderate hepatic impairment (total bilirubin between 1.5 to 3 times ULN and any AST). There is no recommended dose for TAGRISSO for patients with severe hepatic impairment *[see Clinical Pharmacology (12.3) in full Prescribing Information]*.

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Medical World News®

▼ Clinical Trials in Progress

Novel Antibody Tested in First-Line Diffuse Large B-Cell Lymphoma Therapy

INVESTIGATORS ARE STUDYING the value of polatuzumab vedotin (RG7596) in patients with intermediate- or high-risk diffuse large B-cell lymphoma (DLBCL). Polatuzumab vedotin is a CD79b-specific antibody conjugated to a microtubule disrupting agent, monomethyl auristatin E (MMAE), with a stable linker. The novel antibody–drug conjugate is being combined with R-CHP (rituximab, cyclophosphamide, doxorubicin, and prednisone) as a first-line treatment in the phase III, randomized, multicenter POLARIX clinical trial (NCT03274492).

RATIONALE

This combination is being compared with R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone), the current first-line standard of care for patients with DLBCL. Although many patients with DLBCL treated with R-CHOP are cured, "following standard R-CHOP, 30% to 40% of patients with DLBCL relapse, [and] patients who experience early relapse have a poor prognosis," said Christopher R. Flowers, MD, MS, professor of hematology and medical oncology at Emory University School of Medicine in Atlanta, Georgia. "The trial aims to address these problems by evaluating a new approach for first-line treatment of DLBCL that may improve upon [outcomes with] R-CHOP." Flowers also is director of the Emory Lymphoma Program and scientific director of the Winship Research Informatics shared resource at the university's Winship Cancer Institute. He is the principal investigator for POLARIX at Emory and a member of the trial's international steering committee.

TRIAL DESIGN

The investigators will assess the safety and efficacy of polatuzumab vedotin using investigator-assessed progression-free survival as the primary endpoint. They also will evaluate potential biomarkers to predict improved outcomes and as a means for devising new therapeutic approaches, according to Flowers.

Polatuzumab vedotin consists of a CD79b-specific monoclonal antibody conjugated to a potent cytotoxin that is selectively delivered to tumor cells.1 This combination delivers highly potent cytotoxins directly to tumor cells, which then absorb the cytotoxin.2

WHO IS ELIGIBLE?

The study will enroll patients with any subtype of CD20-positive DLBCL with an ECOG performance status of 0 to 2; a cardiac ejection fraction of at least 50%; and an International Prognostic Index (IPI) score of 2 to 5, which indicates intermediate- to high-risk disease. Patients with an IPI score of 2 to 5 have a greater risk of relapse and worse survival with standard R-CHOP than the general group of patients with DLBCL. Participants cannot have had prior treatment for DLBCL.

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FGFR Inhibitor Tested in Hard-to-Treat GI Cancer

GIVEN THE FEW OPTIONS available for intrahepatic cholangiocarcinoma (ICC), investigators are excited about a phase III trial of the multikinase inhibitor derazantinib (ARQ 087) as a second-line treatment for patients with inoperable or advanced disease. Current options are particularly limited for patients who experience disease progression after standard-of-care first-line chemotherapy. In the single-arm trial (NCT03230318), derazantinib is being tested in patients who have a genetic aberration in the fibroblast growth factor receptor 2 (*FGFR2*) gene.

RATIONALE

With this oral small-molecule inhibitor, investigators hope to treat what is currently considered an orphan disease. "Ten to 15% of patients with ICC may be effectively targeted with a specific FGFR inhibitor," said Milind Javle, MD, a professor in the Department of Gastrointestinal Medical Oncology at The University of Texas MD Anderson Cancer Center in Houston. Javle is the trial's principal investigator.

Among gastrointestinal cancers, *FGFR2* fusions occur most commonly in ICC and are believed to be drivers in oncogenesis. Cancer triggered by *FGFR2* fusions tends to persist despite FGFR-directed therapy, according to Javle. Also, mutations associated with a poor prognosis, such as *KRAS* and *IDH1*, are rarely seen in the presence of an *FGFR2* fusion, which makes it important to treat specifically for *FGFR2*-related cancer. "One interesting factor about *FGFR* fusions is that the patients are often younger, often women, and have a relatively indolent, slow-growth cholangiocarcinoma compared with the *FGFR* wild-type," Javle said.

Selective FGFR inhibitors have been very effective in ICC. A study of the FGFR inhibitor BGJ398 showed that patients with *FGFR2* genetic fusions responded well, achieving partial responses or stable disease.[1] Derazantinib inhibits FGFR kinases. Fibroblast growth factors and their receptors tightly regulate cell proliferation, differentiation, migration, survival, and angiogenesis. In cancer, *FGFR* genes have been found to be dysregulated by multiple mechanisms, including aberrant expression, mutations, chromosomal rearrangements, and amplifications.[2] Activation of an FGFR kinase, as with many tyrosine kinases, requires autophosphorylation, a process that the drug inhibits. Additionally, derazantinib binds to the unphosphorylated protein, delaying its activation or phosphorylation.

TRIAL DESIGN

The phase III trial of derazantinib, which is currently enrolling, will test the agent's anticancer activity in approximately 100 patients with an *FGFR2* fusion. Objective response rate is the primary endpoint.

WHO IS ELIGIBLE?

Eligible patients will have histologically or cytologically confirmed locally advanced, inoperable, or metastatic ICC with *FGFR2* gene fusion status confirmed by next-generation sequencing or fluorescence in situ hybridization testing. Participants must have received at least 1 regimen of prior systemic therapy, with evidence of radiographic progression. Patients who were not able to tolerate prior systemic therapy may also be enrolled.

Participants also cannot have evidence of corneal or retinal disorders. FGFR inhibitors have ocular toxicities, according to Javle, so patients will undergo ophthalmologic examination before going on the study and be regularly monitored throughout it.

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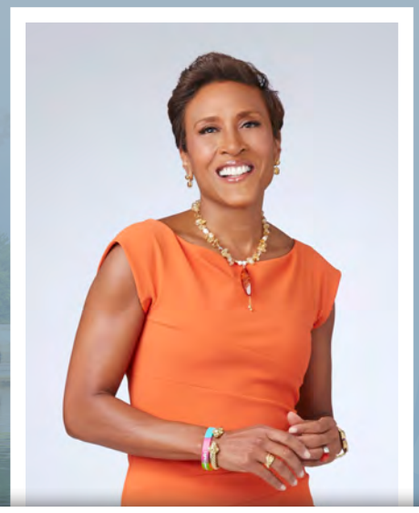

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> **"Let patients know that sexual issues are not uncommon, and resources are available to help them understand and address the problems. Simply normalizing the situation opens the door for further discussion or information seeking."**
>
> —Jeffrey Albaugh, PhD, APRN, CUCNS

Let's Talk About Sex, Fertility, and Intimacy After Cancer

A sexual health expert and oncology nurse hopes to empower patients to make informed decisions.

By Jeffrey Albaugh, PhD, APRN, CUCNS, director of sexual health at NorthShore University HealthSystem in Evanston, Illinois

In the United States, 38.5% of men and women will receive a cancer diagnosis at some point.[1] Many of these patients will suffer in silence with sexual and fertility problems because of the stigma associated with them. Patients wait for their trusted healthcare professionals to bring up the subject, which often doesn't happen. A study by Park et al found that 62% of internists working with patients with cancer never or rarely address sexual issues.[2] Patients need to know that it is OK to ask about and address sexual health issues.

Findings from several studies show that sexual issues are common among many patients. For instance, in a Livestrong Foundation study, investigators determined that sexual dysfunction was among the top 3 physical concerns reported by 43% of the men and women with cancer.[3]

ADVERSE EFFECTS EXPERIENCED BY PATIENTS

Cancer treatment can affect sex and intimacy in terms of functional changes, physical disfigurement, and/or alterations in relationship dynamics with partners. Sexual dysfunction can involve loss of sexual desire, lack of arousal, and/or orgasm problems in both genders. For women, it could also involve pain with sex, lack of lubrication and vaginal dryness, atrophy, and/or stenosis. Specific issues for men include erectile dysfunction (ED), ejaculatory dysfunction, and/or hypogonadism (low testosterone accompanied by symptoms).

Treatments involving surgery, chemotherapy, and radiation can affect reproductive organs, leading to sexual dysfunction or infertility. Chemotherapy, specifically, can alter hormones such as estrogen and testosterone, leading to a multitude of sexual problems, including decreased desire, dryness, pain with penetration, or ED.

Although fertility may not be a concern for all patients, assumptions should be put aside and fertility information should be addressed and offered to anyone who might be interested in childbearing. In a study of 3129 patients with cancer, fertility was a concern for about 60%, of whom 70% said they did not receive information about options for preserving fertility.[3] Cancers, such as prostate, colon, testicular, ovarian, uterine, and cervical, often occur in the pelvic area, which contains the reproductive organs—ovaries, uterus, fallopian tubes, testicles, and prostate. Surgical excision of or radiation therapy to these organs can lead to infertility.

ADDRESSING SEXUAL CONCERNS

As patients perceive sexual dysfunction as a problem—a bother—they often feel embarrassment and shame that

JEFF ALBAUGH BY ALISSA PAGELS-MINOR

negatively affect quality of life.[4-6] However, healthcare professionals can help prevent that by taking immediate actions following a patient's cancer diagnosis. For instance, patients should receive pamphlets and other educational materials about sexual health and fertility issues—they all will need this information. Most important, let patients know that sexual issues are not uncommon, and resources are available to help them understand and address the problems. Simply normalizing the situation opens the door for further discussion or information seeking.

Treatment of fertility and sexual problems is directed and driven by the patient's goals and desires. Because sexual dysfunction is multifactorial, assessment and treatment can be time intensive and complex. Referral to an appropriate trained expert, such as through the Sexual Medicine Society of North America (statusplus.net/smsna/healthcare-provider-search/index.php) or the American Society of Sexual Educators, Counselors and Therapists (aasect.org/referral-directory), is significant, but the most critical step is to let patients know that they are not alone and there are treatment options.

For many women with cancer, vaginal dryness occurs. Treatment may include local intravaginal estrogen therapy, nonhormonal moisturizers used regularly, hyaluronic acid, ospemifene, and/or lubricants to reduce friction during sex.[7] Penetrative pain also can be related to pelvic floor muscle hypertonicity or stenosis. This can be treated with pelvic floor physical therapy, vaginal dilators, and intravaginal muscle relaxants.

ED is an adverse effect seen in men following cancer treatment but can be treated with phosphodiesterase type 5 inhibitors—eg, sildenafil (Viagra), vardenafil (Levitra), and tadalafil (Cialis)—a vacuum constriction device, intraurethral suppository, intracavernosal injections, or a penile implant.[8,9] Premature ejaculation can be treated with cognitive behavioral therapies (eg, stop/start, positioning, and squeeze technique), layered condoms to decrease sensation, desensitizing sprays or gels, and/or off-label use of antidepressants.[10] Hypogonadism in men involves a low testosterone blood level combined with symptoms such as decreased sex drive, energy, or mood; fatty weight gain; and decreased ability to concentrate. The syndrome is typically treated with testosterone (eg, transdermal or buccal patch, injection, pellets, or nasal spray). Because testosterone is a steroid, proceeding with such therapy after cancer diagnosis and treatment may be controversial and even contraindicated—specifically in the case of prostate cancer, because steroids may increase or contribute to cancer growth. Experts in replacement therapy should handle this with care and caution, collaborating with the oncology team.

Diminished ability to climax affects both men and women. Identifying and resolving the underlying cause, such as use of antidepressants and/or pain medications, can improve the ability to orgasm. In some cases, consulting a sex therapist and/or adding vibration to stimulation may help a patient orgasm.

Sexual issues often involve a psychogenic component, which can negatively affect intimacy and sexual encounters. Concerns about ED or pain during penetration, for example, can affect self-confidence, self-esteem, and quality of life. It may be beneficial for men and women to address body image issues, function loss, or relationship problems through sex or relationship therapy.

In terms of fertility, it is critical that patients are offered the option of retrieving and preserving gametes prior to cancer treatment that may permanently compromise their ability to produce their own sperm or oocytes (eggs). Some treatments, such as chemotherapy and radiation, may temporarily halt sperm or egg production. Removal of the sex organs, which produce gametes, may permanently impair a patient's ability to bear children. Although cancers of the reproductive system would more likely lead to infertility issues, chemotherapy for other types of cancers may also affect the hormonal system and possibly lead to infertility. All these factors must be considered.

One option is cryopreservation of sperm or oocytes, which requires planning on the patient's part. Men who have reached puberty can donate sperm (ideally, several samples, not just 1) prior to cancer treatment. Assistive methods for ejaculation can also be engaged when needed for sperm extraction. If sperm donation is not an option or a male has not reached puberty, testicular gonadal tissue can be cryopreserved. Women can preserve oocytes or embryos, which requires 10 days of ovarian stimulation with gonadotropins, followed by transvaginal needle aspiration of mature oocytes while under sedation. The challenging thing about preserving embryos is that women must choose a sperm donor to fertilize the egg before cryopreservation. Ovarian tissue also can be cryopreserved. Assistive reproductive methods can also be helpful, including insemination and in vitro fertilization; other, more advanced implantation options continue to become available.

EMPOWERING PATIENTS

Sexuality is a vital part of the human experience. Therefore, identifying and helping patients address fertility and sexual issues is an essential part of cancer care. Oncology nurses can be on the front line of providing information about sexual dysfunction, which should be available to patients before, during, and after treatment. Empowering patients with information about fertility and sexual dysfunction treatment options allows men and women to make their own informed decisions about treatment. As cancer survival rates increase and patients live longer, addressing long-term adverse effects such as sexual dysfunction becomes increasingly paramount. That can be as simple as providing a list of some of the excellent resources available or letting the patient know that sexual issues are common after cancer.

References available at OncNursingNews.com.

RESOURCES FOR PATIENTS WITH SEXUAL CONCERNS

American Cancer Society
The American Cancer Society resource discusses sexual feelings and attitudes during cancer, as well as fertility. Within this page, additional online resources are listed for specific needs of men and women.
bit.ly/cancerandsexlife

MiddlesexMD
Targeted to women with breast cancer, MiddlesexMD provides sexual health information and products that can help women of any age
middlesexmd.com

National Cancer Institute
The National Cancer Institute gives an overview of treatments and the sexual health issues they may cause, as well as ways to manage them.

For men: bit.ly/sexualhealth-men
For women: bit.ly/sexualhealth-women

Northshore University HealthSystem
A series of free videos tackles topics ranging from arousal disorder to penile implants.
bit.ly/sexualhealth-videos

Reclaiming Sex and Intimacy After Prostate Cancer
The free online book is a guide for men and their partners following a cancer diagnosis. It is written by Jeffrey Albaugh, PhD, APRN, CUCNS.
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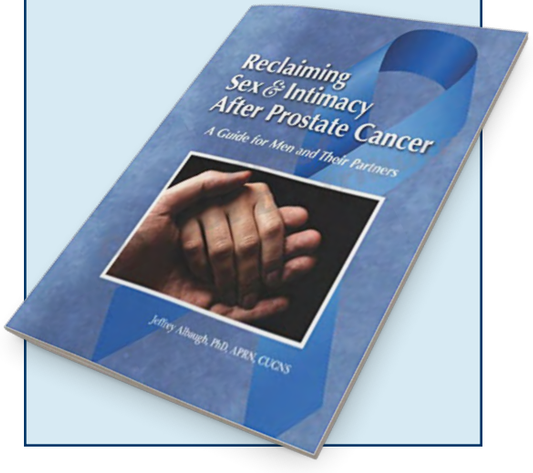

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Gynecologic Cancers

Cotesting Unlikely to Detect More Cervical Cancers Than HPV Testing Alone

By Jason Harris

Use of both a Pap smear and a human papillomavirus (HPV) test did not identify more cervical cancers than HPV testing alone, according to results from a study of more than 1.2 million women screened since 2003.

The Pap test detected only a small percentage of precancers (3.5%) and cancers (5.9%) missed on the HPV test. Investigators observed that these cancers were more likely to be regional or distant stage.

Given the relative rarity of cervical cancer—the Centers for Disease Control and Prevention says roughly 12,000 women receive a diagnosis annually—investigators concluded that adding the Pap test to HPV screening translated to earlier detection of at most 5 cases per million women per year. Cotesting is "unlikely to detect cancer cases that wouldn't be found using HPV testing alone," the investigators said.

"The choice between the two strategies and the screening interval chosen, whether 3 years or 5 years or more, depends on societal judgments (eg, cancer prevention benefits vs resource allocation) and not scientific facts," first author Mark Schiffman, MD, MPH, division of cancer epidemiology and genetics, National Cancer Institute, et al wrote. "Nevertheless, even using cotesting at 3-year intervals (the most aggressive strategy in common use), cervical cancer continues to occur rarely (albeit typically at a curable stage). Excessive screening in an attempt to prevent every case could have minimal cancer prevention benefits while increasing the harms of screening."

HPV testing is more sensitive than the Pap test for detecting precancer. The HPV test captures the known cancer-causing viruses, but some gynecologists conduct cotesting because of reports of rare HPV-negative, Pap test–positive cancers, even though using both tests is more expensive.

Investigators quantified the detection of cervical precancer and cancer by cotesting compared with HPV testing alone at Kaiser Permanente, where 1,208,710 women have undergone cervical cotesting every 3 years since 2003. Investigators reviewed screening histories preceding cervical cancers in 623 women and precancers in 5369 women to assess the relative contributions of the Pap test and HPV test components in identifying patients.

Overall, prediagnostic HPV testing was more clinically sensitive than cytology (76.7% vesus 59.1%; $P<.001$ for paired comparison). About 82% of all prediagnostic cotests were positive by HPV and/or cytology. Stratified by histopathology, the differences in positivity between HPV and cytology were smaller for squamous cell carcinoma (75.0% vesus 69.6%; $P = .03$) than for adenocarcinoma (79.0% vesus 45.4%; $P<.001$).

Among those with cancer, women diagnosed with microinvasive cancer tended to be younger than women with other cancers (40 vesus 57 years). The median age for women diagnosed with squamous cell carcinomas or adenocarcinomas was 47 years. Women diagnosed with precancer had a median age of 38 years. Investigators noted that this analysis excluded women younger than age 30, elevating the average age of patients with precancer.

HPV testing identified more women who subsequently received a diagnosis of cancer and precancer than the Pap test. Overall, prediagnostic HPV testing was more likely to be positive than cytology (83.8% vesus 61.9%; $P<.001$). Almost 9 in 10 prediagnostic cotests (87.3%) were positive by HPV and/or cytology. HPV testing was more likely to be positive than cytology prior to both cervical intraepithelial neoplasia grade 3 (83.9% vesus 62.8%; $P<.001$) and adenocarcinoma in situ (82.2% vesus 53.2%; $P<.001$).

Cotests done within 12 months of diagnosis were more likely to be HPV and/or cytology positive than cotests done ≥12 months before the diagnosis. HPV was statistically significantly more likely to be positive than cytology less than 12 months prior to a precancer diagnosis (96.2% vesus 89.8%; $P<.001$) but not immediately prior to a cancer diagnosis (89.2% vesus 86.3%; $P = .1$).

At ≥12 months, HPV was statistically significantly more likely to be positive than cytology for both a precancer diagnosis (70.6% vesus 32.4%; $P<.001$) and a cancer diagnosis (62.8% vesus 28.7%; $P<.001$).

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Myeloma

Timely Hospice Use Increases Among Patients With Myeloma

By Kristie L. Kahl

Hospice use has significantly increased over time among patients with myeloma, which in turn hopefully highlights the need for timely enrollment, according to a retrospective analysis published in the journal *Blood*.

Timely hospice enrollment helps quality end-of-life care. However, previous research has shown an increase in "late" enrollment, which is defined as 3 or more days before death, among patients with blood cancers. "Late hospice enrollment limits the ability of patients and their families to receive the full palliative and supportive benefits of hospice services," said Oreofe O. Odejide, MD, of Dana-Farber Cancer Institute in Boston, Massachusetts.

Therefore, the investigators characterized hospice use among 12,803 patients, in particular on prevalence and predictors of late enrollment. Patients were 65 years of age or older, had a primary diagnosis of myeloma between 2000 and 2013, and lived for at least 30 days after their diagnosis.

The investigators chose myeloma because of the distinct features associated with the disease compared with other blood cancers, Odejide said.

"For example, myeloma is incurable at diagnosis, there is a very high prevalence of pain among patients with myeloma because of bony involvement by their disease, and there is a high likelihood of renal involvement with possible need for dialysis," he said. "We felt that these characteristics could potentially impact hospice use and, thus, sought to characterize patterns of hospice use and barriers to timely enrollment in this unique population."

Overall, 47.9% of patients enrolled in hospice, with the majority using outpatient/home hospice services (80.5%), for approximately 12 days. Among those enrolled, 17.8% of patients spent 3 days or more in hospice.

The investigators found a significant trend toward increased hospice use from 18.6% in 2000 to 56.4% in 2013; however, they saw no significant increase in late enrollment (from 12% to 16.7%, respectively). "This suggests that there have been meaningful changes in hospice use for patients with myeloma," said Odejide. "Distinct features of myeloma such as incurability and high prevalence of pain may make the need for hospice services clearer and encourage timely use."

In particular, transfusion-dependent patients (37.9%) and patients on dialysis (32.9%) were more likely to experience late enrollment. Odejide acknowledged that this finding suggests that transfusion dependence is a key barrier to timely enrollment. "The current reimbursement pattern for hospices precludes many hospices from being able to provide transfusions even though they are palliative," he said. "Policy changes and reimbursement reform that will enable provision of palliative transfusions while enrolled in hospice are thus likely to promote even more timely enrollment for patients with myeloma."

Odejide commended the fact that meaningful progress in hospice use among patients with myeloma has been made. However, more work can be done. "Even though the majority enrolled by 2013, there is still room for additional improvement," he said. "Accordingly, it is important for healthcare teams to engage in timely goals-of-care discussions with patients and families in order to understand and honor preferences regarding hospice care."

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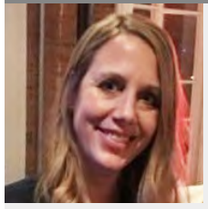
NURSE PERSPECTIVE



Kate Carlson Wrammert, MSN, ANP-BC, WHNP-BC, AOCNP
Nurse Practitioner
McKelvey Lung Transplant Program
Emory University Hospital
Atlanta, GA

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Patients with multiple myeloma, an advanced neoplasm of the plasma cells with a limited survival, generally carry a high symptom burden including anemia, bone pain, and renal failure. For patients who become transfusion dependent or require hemodialysis, reimbursement limitations may postpone enrollment in hospice services.

As defined by Medicare, hospice care is appropriate for any individual with a life expectancy of less than 6 months, yet many people misunderstand hospice care to be applicable only when a patient is in the last days to weeks of life. Often, patients who enroll late spend their final days hospitalized—possibly in an intensive care unit—rather than at home, leading to poorly controlled symptoms and prolonged grief for the family. By using hospice care earlier in the disease process, the patient and family can experience an improved quality of life and reduced symptom burden, as demonstrated by extensive research.

According to the American Society of Clinical Oncology, concurrent use of oncologic care with palliative care with eventual transition to hospice care demonstrates reduced symptom burden, better outcomes for caregivers, and equal or better survival in some patients. Perhaps, if this were available in the community, transfusion-dependent and/or dialysis-dependent patients could benefit from enrolling in aggressive care with palliative care before developing a high symptom burden. Given the known prognosis of myeloma, early referral to an outpatient palliative care program could facilitate conversations and further educate the patient and family regarding the appropriate timing of hospice care. Patients would be enabled to make informed decisions regarding earlier enrollment, thus reducing the percentage of late referrals in this population.

Hematologic Malignancies

Understanding Predictors Can Decrease Unplanned Hospital Readmissions

By Kristie L. Kahl

Patients with blood cancers are at an increased risk of multiple hospital readmissions. However, multidisciplinary teams and patients can work together to identify predictors and avoid these occurrences.

Newly diagnosed, hospitalized patients with hematologic malignancies tend to have high symptom burdens from the diagnosis itself. This population also needs prolonged courses of chemotherapy and consequent transfusion support. Therefore, they are predisposed to unplanned readmissions to the hospital.

Investigators from the Taussig Cancer Institute at the Cleveland Clinic evaluated 30-day unplanned readmissions, defined as hospitalization within 30 days of original admission for any reason other than planned chemotherapy, that occurred at their institution from January 2011 to February 2016.

"We specifically looked at how we can predict a readmission after the first readmission," said Girish Kunapareddy, MD, of the Leukemia Program.

Hematologic malignancies included acute leukemias, myelodysplastic syndromes and aggressive lymphomas. To evaluate associated predictors, the investigators collected information regarding demographics, clinical characteristics, disease status, body mass index at discharge, absolute neutrophil count at discharge/readmission, reason for readmission, length of stay at original admission/readmission, and discharge characteristics.

The investigators observed 259 thirty-day unplanned readmissions in 157 patients, including 107 patients who had a single occurrence, and 50 with more than 2.

The majority of patients were men (59%), with a median age of 66 years, and had acute myeloid leukemia (44%), including half with relapsed or refractory disease. Median income was approximately $51,000, and 86% of patients had more than a high school education, according to census tract–based data. In addition, 49% of patients were covered by Medicare, 21% by Medicaid, and 36% by private insurance.

Following unplanned readmission discharges, patients were sent home (50%), sent home with home health (32%), sent to a nursing facility (15%), or received hospice care (3%). Among these readmission discharges, 10% of patients were sent home on intravenous antibiotics, 44% on opioids, and 48% on psychotropic drugs.

Neutropenic fever appeared to be the primary diagnosis (61%) at readmission, with 59% demonstrating symptoms at presentation of readmission.

At discharge from unplanned readmissions, median absolute neutrophil count was 870 mL and increased to 940 mL at the time of readmission. Patients stayed for a median of 5 days and were readmitted approximately 11 days later. Unplanned readmissions originated from visits to outpatient clinics, emergency departments or patients' homes (46%), and non-healthcare facilities (27%) or outside hospital transfers (22%).

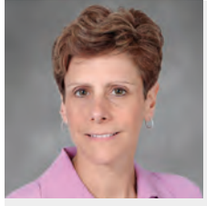
The investigators found 30-day readmissions were associated with absolute neutrophil counts of more than 2000 mL at last discharge; constitutional symptoms, such as fevers, chills, sweats, and severe fatigue, at admission presentation; gastrointestinal symptoms; whether patients were transferred from an outside facility; febrile neutropenia; relapsed or refractory disease; and higher education.

Of note, Kunapareddy and colleagues were most surprised by higher education having an association with increased 30-day unplanned readmissions. "Maybe having higher education means these patients are more likely to follow instructions or know what symptoms to look for to come in to the hospital," he said. "Or it may be other reasons for socioeconomic status, like having good transportation, having good access to care, being able to miss work, or having family who can take off to bring you to the hospital, or if you are more financially stable."

To address high hospital readmissions rates, Kunapareddy recommends that physicians create individualized care plans and follow up more closely with patients. "It is better to create individualized plans for each patient. The only way you can do that is if you have a multidisciplinary team—social work, case management, care coordinators, physician assistants, palliative medicine oncology—that sits around a round table and discusses this particular patient's issues and figures out things we can do to help."

Patients should also be their own advocates, utilize additional resources at institutions, and, most important, not wait to see their physicians at the onset of symptoms, Kunapareddy added. "Reporting these findings earlier to the doctor, even if patients think it seems minor, helps with better symptom control early on."

NURSE PERSPECTIVE



Phyllis McKiernan, MSN, APN, OCN
Blood & Marrow Transplant Program
John Theurer Cancer Center, Hackensack, NJ

Unplanned hospital readmissions for patients with hematologic malignancies create stress for those patients and their families as well as for the healthcare system. Patients lose time with family members and friends and at work or school. The financial burden includes not only lost wages but also insurance co-payments for hospitalizations. The emergency room, hospital or physician clinic, and medical transportation are all used. The on-call medical team needs to evaluate and admit the patient, and the hospital staff on the unit will need to tap resources for the admission.

In addition, hospital beds used for unplanned admissions are subsequently not available for planned admissions.

Understanding predictors for unplanned readmissions is the first step in developing strategies to mitigate risk for these occurrences. The most common diagnosis leading to unplanned readmission was, not surprisingly, neutropenic fever. Risk reduction methods include patient education regarding precautions, antimicrobial prophylaxis, and the use of growth factor support. Patients receiving regimens most commonly associated with neutropenic fever could be followed more closely as outpatients in an attempt to recognize signs of impending fever or infection. Early identification of symptoms may allow a patient with uncomplicated neutropenic fever to be treated as an outpatient and avoid readmission.

Interestingly, patients with higher education had an increased incidence of unplanned readmissions. Providing all patients with education regarding signs and symptoms to report to the physician and team may help bridge the education gap. Keeping open communication with patients and using technology, such as e-mail and online chart access, will allow patients to have real-time contact with the healthcare team and may lead to early symptom control. Addressing social issues proactively could prevent delays in access to care. As mentioned above, a multidisciplinary team approach may decrease the incidence of unplanned hospital readmissions, thus alleviating strain on the patients and the healthcare system.

Pancreatic Cancer

Nab-Paclitaxel/Gemcitabine Effective for Locally Advanced Pancreatic Cancer

By Silas Inman

Induction treatment with nab-paclitaxel (Abraxane) plus gemcitabine demonstrated a time to treatment failure (TTF) of 8.8 months (90% CI, 6.67-9.82) for patients with newly diagnosed locally advanced pancreatic cancer, according to updated findings from the phase II LAPACT trial presented at the 2018 Gastrointestinal Cancers Symposium.

In the single-arm, international trial, the nab-paclitaxel regimen elicited an objective response rate of 32%. The overall disease control rate (DCR) was 77.6%. The median progression-free survival was 10.8 months (90% CI, 9.26-11.63) with the combination, and the 12-month overall survival (OS) rate was 72% (90% CI, 64.5%-78.9%).

"Disease control is key in our patients with locally advanced disease, as it may lead to opportunities for additional treatment interventions, including radiotherapy, or even, in some favorable cases, surgical resection," lead study author Pascal Hammel, MD, PhD, Gastroenterologist/Oncologist, Hôpital Beaujon, Clichy, France, said in a statement. "The results from this study are encouraging, as it shows that induction therapy has the potential to help us achieve disease control in these locally advanced patients."

The study enrolled 106 patients at a median age of 65 years with locally advanced pancreatic cancer. Induction therapy was administered with nab-paclitaxel at 125 mg/m^2 plus gemcitabine at 1000 mg/m^2 on days 1, 8, and 15 of a 28-day cycle for 6 total cycles. All patients had not received prior therapy for pancreatic cancer and were classified as unresectable. Following the induction phase, patients were offered continuation of nab-paclitaxel/gemcitabine or a switch to another treatment.

The primary endpoint of the study was TTF, with a goal of achieving a median of 6.6 months. All responses in the study were partial responses. The stable disease rate for ≥16 weeks was 44.9%, and 32.7% of patients had stable disease for ≥24 weeks. The DCR for ≥16 weeks was 77.6%, and the DCR for ≥24 weeks was 65.4%.

All 6 cycles of induction therapy were completed by 57.5% of patients in the trial. Overall, 15% of patients went on to subsequent surgical resection following treatment with the regimen. Those who completed induction but did not receive surgery went on to chemoradiation (16%) or continued nab-paclitaxel and gemcitabine (11%).

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Of those who did not complete induction therapy, the most common causes for treatment discontinuation were adverse events (AEs; n = 20), progressive disease (n = 8), protocol noncompliance (n = 5), physician decision (n = 6), death (n = 2), and other reasons (n = 4).

The most frequently observed grade ≥3 treatment-emergent AEs were neutropenia (42%), anemia (11%), fatigue (10%), thrombocytopenia (7.5%), peripheral sensory neuropathy (3.8%), diarrhea (3.8%), and febrile neutropenia (3.8%).

"Pancreatic cancer remains an extremely challenging disease to treat because it is often diagnosed at the metastatic stage, and even those diagnosed with locally advanced disease typically have a poor prognosis," noted Hammel.

The combination of nab-paclitaxel and gemcitabine was approved for patients with metastatic pancreatic cancer in 2013, based on findings from the phase III MPACT trial. In this trial, the median OS was 8.5 months with nab-paclitaxel plus gemcitabine compared with 6.7 months for patients treated with gemcitabine alone (HR, 0.72; 95% CI, 0.62-0.84; $P<.0001$).

"Since its approval to treat metastatic pancreatic cancer in 2013, the Abraxane-plus-gemcitabine regimen has become a standard of care in first-line metastatic pancreatic cancer," Nadim Ahmed, president, Hematology and Oncology, at Celgene, the company developing the regimen, said in a statement. "The findings from LAPACT offer insight into the potential of Abraxane-based treatment for locally advanced pancreatic cancer patients, and it's encouraging to see a nearly 9-month time to treatment failure in these patients treated with an Abraxane regimen."

Several trials continue to assess nab-paclitaxel for patients with pancreatic cancer. In this setting, the agent is being explored in combination with more than 50 other agents across 130 clinical trials, according to Celgene. Most notably, the phase III APACT trial exploring adjuvant nab-paclitaxel/gemcitabine compared with gemcitabine alone recently completed enrollment of 866 participants. Initial findings from this open-label trial are anticipated in early 2019 (NCT01964430).

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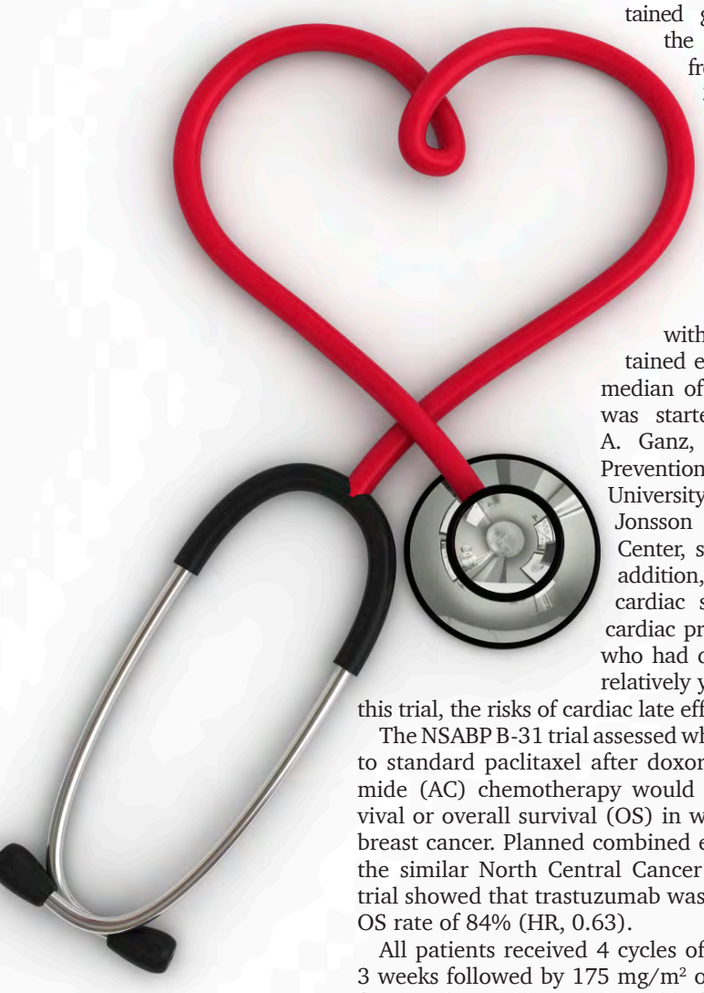
Breast Cancer

Study Finds No Cardiac Toxicity Increase With Trastuzumab in Patients With HER2+ Breast Cancer

By Jason Harris

Trastuzumab (Herceptin) did not reduce cardiac function in women with node-positive, HER2-positive, early-stage breast cancer, according to long-term follow-up (LTF) results from the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-31 trial published in the *Journal of Clinical Oncology*.

Investigators reported that both women who received trastuzumab along with adjuvant chemotherapy and those who received chemotherapy alone maintained good cardiac function. At the LTF, only 4.5% of patients from the control group and 3.4% from the trastuzumab group had a >10% decline in left ventricular ejection fraction (LVEF) from baseline to a value <50%.



"Breast cancer patients who received anthracycline and taxane-based chemotherapy, with or without trastuzumab , maintained excellent cardiac function a median of 8.8 years after treatment was started," lead author Patricia A. Ganz, MD, director of Cancer Prevention and Control Research, University of California, Los Angeles, Jonsson Comprehensive Cancer Center, said in a press release. "In addition, patient reports of greater cardiac symptoms indicated more cardiac problems in the small group who had difficulties. Overall, for the relatively young women who entered this trial, the risks of cardiac late effects were minimal."

The NSABP B-31 trial assessed whether adding trastuzumab to standard paclitaxel after doxorubicin and cyclophosphamide (AC) chemotherapy would improve disease-free survival or overall survival (OS) in women with HER2-positive breast cancer. Planned combined efficacy joint analysis with the similar North Central Cancer Treatment Group N9831 trial showed that trastuzumab was associated with a 10-year OS rate of 84% (HR, 0.63).

All patients received 4 cycles of 60/600 mg/m^2 AC every 3 weeks followed by 175 mg/m^2 of paclitaxel every 3 weeks for 4 cycles or 80 mg/m^2 weekly for 12 weeks. Patients randomly assigned to the investigational group also received trastuzumab at 4 mg/kg concurrently with the first dose of paclitaxel followed by 2 mg/kg weekly for a total of 52 weeks.

A total of 128 patients in the control group and 313 in the experimental group agreed to participate in the LTF assessments of cardiac function, patient-reported outcomes (PROs) related to health-related quality of life (HR QoL), and cardiac-related symptoms and morbidity.

Investigators monitored cardiac function using LVEF measured by multigated acquisition (MUGA) scans at 3, 6, 9, and 18 months after random assignment. In the control group, 110 patients completed the MUGA scans and 98 completed HR QoL questionnaires compared with 297 and 268 in the trastuzumab group, respectively.

At 18 months, the mean decline from baseline was 3.2% in the control group and 3.9% in the trastuzumab group. At the LTF assessments, the mean decline from baseline was 3.9% versus 2.8%, respectively.

Three (2.7%) control group LTF participants had a reported decline of ≥10% to <50% at their 18-month assessment compared with 23 patients (7.7%) in the trastuzumab group. At the LTF assessment, 5 patients (4.5%) in the control group experienced a decline versus 10 (3.4%) in the trastuzumab group. One patient in the control group and 2 in the trastuzumab group with LVEF measurements >50% at 18 months had LTF measurements that declined to <40% at LTF.

Nearly 90% of LTF participants completed PRO surveys. The median time from random assignment to questionnaire completion was 8.7 years (range, 5.5-14.0). Investigators found high scores on the mental component scale (MCS) and physical component scale (PCS) of the 36-Item Short Form Medical Outcomes Study and the Duke Activity Status Index (DASI), "reflecting higher-than-expected physical and mental functioning compared with reference populations of the same age."

The mean PCS score for all patients was 49.7 (SD, 9.1), and the mean MCS score was 52.9 (SD, 9.4). The mean DASI score was 45.6 (SD, 13.8; range, 7.2-58.2) for the total sample. Investigators said lower DASI scores were linked with age and use of certain medications but did not correlate with the addition of trastuzumab.

"Our study improved the 10-year survival for women with this type of aggressive breast cancer to 84%, and now our long-term follow-up of how these women are doing provides positive and encouraging data specifically about their cardiac function and health," coauthor Edward Romond, MD, professor, University of Kentucky Markey Cancer Center, said in a press release.

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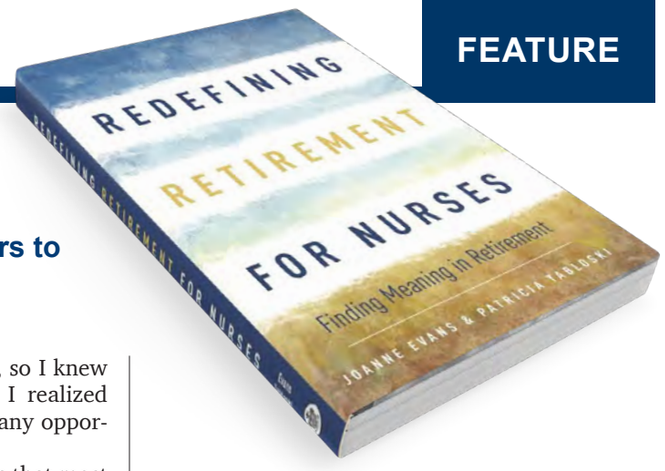

Creating a New Beginning

A recent book shares the stories of 26 retired nurses to inspire others to continue to find meaning in retirement.

By Katie Kosko

Joanne Evans' new beginning—as she likes to call it—began after she retired from her 45-year nursing career. Evans, who holds a string of credentials—MEd, RN, PMHCNS-BC—sold her house, bought an RV, and put 9000 miles on it in 7 months. Besides traveling throughout the United States, she continues to write and speak at nursing conferences on plant-based nutrition—another one of her passions.

But for some retired nurses, as Evans learned, figuring out what to do with their newfound free time isn't as easy as they anticipated. So, along with Patricia A. Tabloski, PhD, GNP-BC, FGSA, FAAN, she wrote a book to help. *Redefining Retirement for Nurses: Finding Meaning in Retirement* delves into re-creating life after leaving a career. In an interview with *Oncology Nursing News*®, Evans discussed what they learned from their interviews with 26 nurses.

What can readers expect from *Redefining Retirement*?

Most of us grew up with 1 concept of retirement, and nowadays it's really different. There are so many more opportunities. Retirement is almost like a whole new phase of life, because you most likely have another 20 years. The book looks at how 26 nurses continued to bring meaning to their lives after leaving a full-time nursing position. These nurses have spent their whole careers taking care of other people and making decisions—whether in research, education, management, or clinical areas—and now, how can they take all this knowledge and continue to bring meaning to their lives in this next phase? Do they do it in nursing or another area?

The book explores areas such as healthy aging, being active, eating healthy food, financial management, spending time with family and friends, getting adequate sleep, and reducing stress. It also discusses how to decide on a good time to retire, whether to move or stay put, and about volunteer activities, as well as how to deal with the unexpected life challenges.

What inspired you to write on this subject?

For me, I was 65, and when I enter new beginnings, I tend to talk with other people. Pat and I were sitting at her beach house on Cape Cod, and I said, "Pat, what do people really do in their next phase? And, what do nurses do?"

We started talking, and then I began to speak with other nurses. I lived in the Washington, DC, area for 42 years, and I didn't know if I wanted to stay there or if I wanted to move. I didn't know if I wanted to keep my house or rent it out. I wanted to travel and buy an RV, but I had never traveled in an RV. I met with a financial adviser, so I knew where I was financially. That's when I realized how broad retirement was and how many opportunities I might consider.

I learned upon doing these interviews that most people weren't even calling it retirement. They preferred "rewiring," "repurposing," "new beginning," or "transitioning."

Of the 26 personal stories, did any related to oncology stand out to you?

One nurse had spent a lot of time focused on planning retirement, but then she retired and received a cancer diagnosis. Her whole plan went out the window. The book examines how she dealt with it, replanned, and regrouped. Other nurses have experienced health challenges, and they also shared how they navigated the unexpected.

A section of the book is titled "The New Realities of Retirement." What are those realities?

Many people underestimate the number of opportunities available. Retirement is a time to focus on yourself, as well as family, friends, and the community. As nurses, we don't do this.

Nurses should take a look at their health. Do they have chronic or genetic health problems now or that may be coming down the road?

As far as money, all the nurses interviewed said it's crucial to talk with a financial adviser or someone knowledgeable in this area.

Regarding family, some nurses spent their retirement taking care of their grandchildren or even a parent or friend who had health problems.

Where did the nurses you spoke with end up?

Some continued in nursing but moved to part-time positions or taught classes and workshops. Some started new businesses. Other people decided they didn't want to do anything related to nursing but wanted to volunteer. One nurse recommended that nurses "speed date" the organizations they are interested in. Once organizations know that nurses are willing to volunteer, everybody wants them.

If nurses want to do volunteer work, it's best to figure out how much time they actually have available. Do they want to do ongoing work or specific projects?

All the nurses agreed that they wanted to declutter, have less stress, and not overcommit themselves again. They all said that they have no concept of boredom and loved having the option to say no.

What nursing-related roles can be taken on in retirement?

I have done medical missions in the Dominican Republic and Ecuador. There are a lot of international volunteering opportunities. Nurses also can stay local and participate on boards, mentor new graduates, talk with high school students about nursing, or speak at community colleges. In oncology, they can teach about healthcare and prevention, as well as lead workshops with different community organizations that focus on their expertise. They may also be interested in writing that could eventually be published in a local newspaper.

You mentioned earlier that nurses are used to putting others' needs ahead of their own. Do you feel this makes the retirement transition more difficult?

It's more of a challenge that you don't get overcommitted. All of us have been in positions where we easily put in 40, 60 hours a week. You can also do that in retirement with not much trouble.

Everyone said they love having choices. They can pick and choose what they want to do. Additionally, nurses we interviewed said they looked forward to sleeping in, no longer dealing with morning or night meetings, and not having to worry about shifts on holidays or weekends or even bad weather and staffing patterns.

We live in a world that is very fast-paced, so 1 of the challenges is learning to slow down. Retirement is the time to practice this.

What retirement advice would you offer a new nurse, and what would you tell one who is nearing the end of a career?

When just starting out, the biggest item is finances. It's good to meet with a financial adviser or someone who is astute about finance, so they can look at long-term goals.

Those close to retirement should figure out how much money they will need 5, 10, 20 years out. It's important to be knowledgeable about that.

Is there anything else that you would like to add?

The only thing that holds you back is your health, time, creativity, and money—otherwise, opportunities are wide open. ●

To get a copy of *Redefining Retirement for Nurses: Finding Meaning in Retirement*, visit Amazon.com.

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- An increased risk of bleeding may occur following NEXAVAR administration. In the HCC study, the following bleeding adverse reactions were reported in the NEXAVAR-treated vs. placebo-treated patients, respectively: bleeding from esophageal varices (2.4% vs. 4%) and bleeding with fatal outcome at any site (2.4% vs. 4%). If bleeding necessitates medical intervention, consider permanent discontinuation of NEXAVAR
- Monitor blood pressure weekly during the first 6 weeks and periodically thereafter, and treat, if required. In the HCC study, hypertension was reported in approximately 9.4% of NEXAVAR-treated patients and 4.3% of patients in the placebo-treated group. Hypertension was usually mild to moderate, occurred early in the course of treatment, and was managed with standard antihypertensive therapy. In cases of severe or persistent hypertension despite institution of antihypertensive therapy, consider temporary or permanent discontinuation of NEXAVAR
- Hand-foot skin reaction and rash are the most common adverse reactions attributed to NEXAVAR. Management may include topical therapies for symptomatic relief. In cases of any severe or persistent adverse reactions, temporary treatment interruption, dose modification, or permanent discontinuation of NEXAVAR should be considered. There have been reports of severe dermatologic toxicities, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). These cases may be life-threatening. Discontinue NEXAVAR if SJS or TEN are suspected
- Gastrointestinal perforation was an uncommon adverse reaction and has been reported in less than 1% of patients taking NEXAVAR. Discontinue NEXAVAR in the event of a gastrointestinal perforation
- Infrequent bleeding or elevations in the International Normalized Ratio (INR) have been reported in some patients taking warfarin while on NEXAVAR. Monitor patients taking concomitant warfarin regularly for changes in prothrombin time (PT), INR, or clinical bleeding episodes
- Temporary interruption of NEXAVAR therapy is recommended in patients undergoing major surgical procedures
- In a subset analysis of two randomized controlled trials in chemo-naïve patients with Stage IIIB-IV non-small cell lung cancer, patients with squamous cell carcinoma experienced higher mortality with the addition of NEXAVAR compared to those treated with carboplatin/paclitaxel alone (HR 1.81, 95% CI 1.19–2.74) and gemcitabine/cisplatin alone (HR 1.22, 95% CI 0.82-1.80). NEXAVAR, in combination with gemcitabine/cisplatin, is not recommended in patients with squamous cell lung cancer. The safety and effectiveness of NEXAVAR has not been established in patients with non-small cell lung cancer

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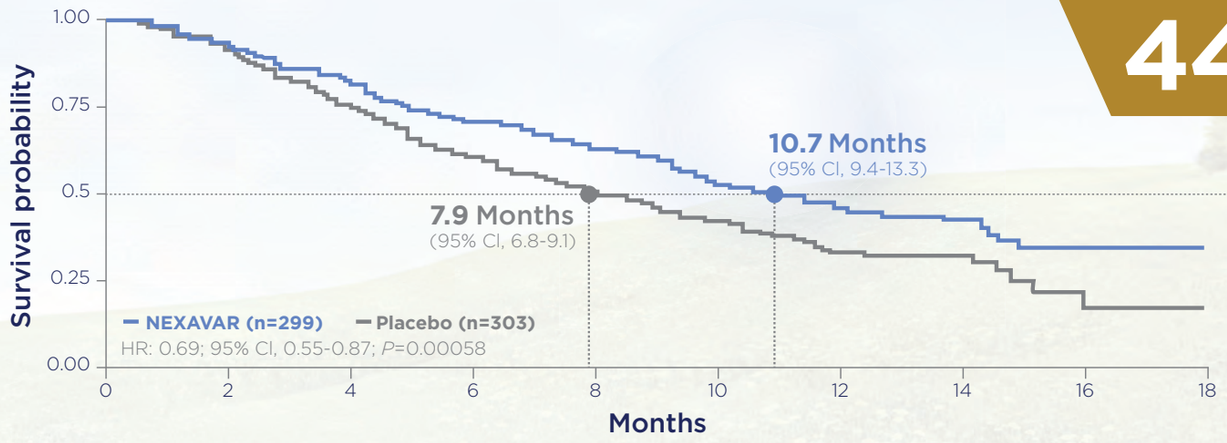

*SHARP (**S**orafenib **H**CC **A**ssessment **R**andomized **P**rotocol): a randomized, double-blind, placebo-controlled, international, multicenter, phase III study in patients with unresectable HCC (N=602).[1]

IMPORTANT SAFETY CONSIDERATIONS (continued)

- NEXAVAR can prolong the QT/QTc interval and increase the risk for ventricular arrhythmias. Avoid use in patients with congenital long QT syndrome and monitor electrolytes and electrocardiograms in patients with congestive heart failure, bradyarrhythmias, drugs known to prolong the QT interval, including Class Ia and III antiarrhythmics, and electrolyte abnormalities. Correct electrolyte abnormalities (magnesium, potassium, calcium). Interrupt NEXAVAR if QTc interval is greater than 500 milliseconds or for an increase from baseline of 60 milliseconds or greater
- Sorafenib-induced hepatitis is characterized by a hepatocellular pattern of liver damage with significant increases of transaminases which may result in hepatic failure and death. Increases in bilirubin and INR may also occur. Liver function tests should be monitored regularly and in cases of increased transaminases without alternative explanation, NEXAVAR should be discontinued
- NEXAVAR may cause fetal harm when administered to a pregnant woman. Women of child-bearing potential should be advised to avoid becoming pregnant while on NEXAVAR
- Female patients should be advised against breastfeeding while receiving NEXAVAR
- In the HCC study, the most common laboratory abnormalities observed in the NEXAVAR arm versus the placebo arm, respectively, were hypoalbuminemia (59% vs. 47%), lymphopenia (47% vs. 42%), thrombocytopenia (46% vs. 41%), elevations in INR (42% vs. 34%), elevated lipase (40% vs. 37%), hypophosphatemia (35% vs. 11%), elevated amylase (34% vs. 29%), hypocalcemia (27% vs. 15%), and hypokalemia (9.5% vs. 5.9%)
- Avoid concomitant use of strong CYP3A4 inducers, when possible, because inducers can decrease the systemic exposure of sorafenib. NEXAVAR exposure decreases when co-administered with oral neomycin. Effects of other antibiotics on NEXAVAR pharmacokinetics have not been studied
- Most common adverse reactions reported for NEXAVAR-treated patients vs. placebo-treated patients in unresectable HCC, respectively, were: diarrhea (55% vs. 25%), fatigue (46% vs. 45%), abdominal pain (31% vs. 26%), weight loss (30% vs. 10%), anorexia (29% vs. 18%), nausea (24% vs. 20%), and hand-foot skin reaction (21% vs. 3%). Grade 3/4 adverse reactions were 45% vs. 32%

Reference: 1. NEXAVAR Prescribing Information. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc; November 2015.

Please see brief summary of full Prescribing Information on the following pages.

Nexavar® (sorafenib) tablets

NEXAVAR (sorafenib) tablets, oral
Initial U.S. Approval: 2005

BRIEF SUMMARY OF PRESCRIBING INFORMATION
CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

INDICATIONS AND USAGE

Hepatocellular Carcinoma

NEXAVAR® is indicated for the treatment of patients with unresectable hepatocellular carcinoma (HCC).

Renal Cell Carcinoma

NEXAVAR is indicated for the treatment of patients with advanced renal cell carcinoma (RCC).

Differentiated Thyroid Carcinoma

NEXAVAR is indicated for the treatment of patients with locally recurrent or metastatic, progressive, differentiated thyroid carcinoma (DTC) that is refractory to radioactive iodine treatment.

CONTRAINDICATIONS

- NEXAVAR is contraindicated in patients with known severe hypersensitivity to sorafenib or any other component of NEXAVAR.
- NEXAVAR in combination with carboplatin and paclitaxel is contraindicated in patients with squamous cell lung cancer.

WARNINGS AND PRECAUTIONS

Risk of Cardiac Ischemia and/or Infarction In the HCC study, the incidence of cardiac ischemia/infarction was 2.7% in NEXAVAR-treated patients compared with 1.3% in the placebo-treated group, in RCC Study 1, the incidence of cardiac ischemia/infarction was higher in the NEXAVAR-treated group (2.9%) compared with the placebo-treated group (0.4%), and in the DTC study, the incidence of cardiac ischemia/infarction was 1.9% in the NEXAVAR-treated group compared with 0% in the placebo-treated group. Patients with unstable coronary artery disease or recent myocardial infarction were excluded from this study. Temporary or permanent discontinuation of NEXAVAR should be considered in patients who develop cardiac ischemia and/or infarction.

Risk of Hemorrhage An increased risk of bleeding may occur following NEXAVAR administration. In the HCC study, an excess of bleeding regardless of causality was not apparent and the rate of bleeding from esophageal varices was 2.4% in NEXAVAR-treated patients and 4% in placebo-treated patients. Bleeding with a fatal outcome from any site was reported in 2.4% of NEXAVAR-treated patients and 4% in placebo-treated patients. In RCC Study 1, bleeding regardless of causality was reported in 15.3% of patients in the NEXAVAR-treated group and 8.2% of patients in the placebo-treated group. The incidence of CTCAE Grade 3 and 4 bleeding was 2% and 0%, respectively, in NEXAVAR-treated patients, and 1.3% and 0.2%, respectively, in placebo-treated patients. There was one fatal hemorrhage in each treatment group in RCC Study 1. In the DTC study, bleeding was reported in 17.4% of NEXAVAR-treated patients and 9.6% of placebo-treated patients; however the incidence of CTCAE Grade 3 bleeding was 1% in NEXAVAR-treated patients and 1.4% in placebo-treated patients. There was no Grade 4 bleeding reported and there was one fatal hemorrhage in a placebo-treated patient. If any bleeding necessitates medical intervention, permanent discontinuation of NEXAVAR should be considered. Due to the potential risk of bleeding, tracheal, bronchial, and esophageal infiltration should be treated with local therapy prior to administering NEXAVAR in patients with DTC.

Risk of Hypertension Monitor blood pressure weekly during the first 6 weeks of NEXAVAR. Thereafter, monitor blood pressure and treat hypertension, if required, in accordance with standard medical practice. In the HCC study, hypertension was reported in approximately 9.4% of NEXAVAR-treated patients and 4.3% of patients in the placebo-treated group. In RCC Study 1, hypertension was reported in approximately 16.9% of NEXAVAR-treated patients and 1.8% of patients in the placebo-treated group. In the DTC study, hypertension was reported in 40.6% of NEXAVAR-treated patients and 12.4% of placebo-treated patients. Hypertension was usually mild to moderate, occurred early in the course of treatment, and was managed with standard antihypertensive therapy. In cases of severe or persistent hypertension despite institution of antihypertensive therapy, consider temporary or permanent discontinuation of NEXAVAR. Permanent discontinuation due to hypertension occurred in 1 of 297 NEXAVAR-treated patients in the HCC study, 1 of 451 NEXAVAR-treated patients in RCC Study 1, and 1 of 207 NEXAVAR-treated patients in the DTC study.

Risk of Dermatologic Toxicities Hand-foot skin reaction and rash represent the most common adverse reactions attributed to NEXAVAR. Rash and hand-foot skin reaction are usually CTCAE Grade 1 and 2 and generally appear during the first six weeks of treatment with NEXAVAR. Management of dermatologic toxicities may include topical therapies for symptomatic relief, temporary treatment interruption and/or dose modification of NEXAVAR, or in severe or persistent cases, permanent discontinuation of NEXAVAR. Permanent discontinuation of therapy due to hand-foot skin reaction occurred in 4 (1.3%) of 297 NEXAVAR-treated patients with HCC, 3 (0.7%) of 451 NEXAVAR-treated patients with RCC, and 11 (5.3%) of 207 NEXAVAR-treated patients with DTC.

There have been reports of severe dermatologic toxicities, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). These cases may be life-threatening. Discontinue NEXAVAR if SJS or TEN are suspected.

Risk of Gastrointestinal Perforation Gastrointestinal perforation is an uncommon adverse reaction and has been reported in less than 1% of patients taking NEXAVAR. In some cases this was not associated with apparent intra-abdominal tumor. In the event of a gastrointestinal perforation, discontinue NEXAVAR.

Warfarin Infrequent bleeding or elevations in the International Normalized Ratio (INR) have been reported in some patients taking warfarin while on NEXAVAR. Monitor patients taking concomitant warfarin regularly for changes in prothrombin time (PT), INR or clinical bleeding episodes.

Wound Healing Complications No formal studies of the effect of NEXAVAR on wound healing have been conducted. Temporary interruption of NEXAVAR is recommended in patients undergoing major surgical procedures. There is limited clinical experience regarding the timing of reinitiation of NEXAVAR following major surgical intervention. Therefore, the decision to resume NEXAVAR following a major surgical intervention should be based on clinical judgment of adequate wound healing.

Increased Mortality Observed with NEXAVAR Administered in Combination with Carboplatin/Paclitaxel and Gemcitabine/Cisplatin in Squamous Cell Lung Cancer In a subset analysis of two randomized controlled trials in chemo-naive patients with Stage IIIB-IV non-small cell lung cancer, patients with squamous cell carcinoma experienced higher mortality with the addition of NEXAVAR compared to those treated with carboplatin/paclitaxel alone (HR 1.81, 95% CI 1.19–2.74) and gemcitabine/cisplatin alone (HR 1.22, 95% CI 0.82-1.80). The use of NEXAVAR in combination with carboplatin/paclitaxel is contraindicated in patients with squamous cell lung cancer. NEXAVAR in combination with gemcitabine/cisplatin is not recommended in patients with squamous cell lung cancer. The safety and effectiveness of NEXAVAR has not been established in patients with non-small cell lung cancer.

Risk of QT Interval Prolongation NEXAVAR can prolong the QT/QTc interval. QT/QTc interval prolongation increases the risk for ventricular arrhythmias. Avoid NEXAVAR in patients with congenital long QT syndrome. Monitor electrolytes and electrocardiograms in patients with congestive heart failure, bradyarrhythmias, drugs known to prolong the QT interval, including Class Ia and III antiarrhythmics. Correct electrolyte abnormalities (magnesium, potassium, calcium). Interrupt NEXAVAR if QTc interval is greater than 500 milliseconds or for an increase from baseline of 60 milliseconds or greater.

Drug-Induced Hepatitis Sorafenib-induced hepatitis is characterized by a hepatocellular pattern of liver damage with significant increases of transaminases which may result in hepatic failure and death. Increases in bilirubin and INR may also occur. The incidence of severe drug-induced liver injury, defined as elevated transaminase levels above 20 times the upper limit of normal or transaminase elevations with significant clinical sequelae (for example, elevated INR, ascites, fatal, or transplantation), was two of 3,357 patients (0.06%) in a global monotherapy database. Monitor liver function tests regularly. In case of significantly increased transaminases without alternative explanation, such as viral hepatitis or progressing underlying malignancy, discontinue NEXAVAR.

Embryofetal Risk Based on its mechanism of action and findings in animals, NEXAVAR may cause fetal harm when administered to a pregnant woman. Sorafenib caused embryo-fetal toxicities in animals at maternal exposures that were significantly lower than the human exposures at the recommended dose of 400 mg twice daily. Advise women of childbearing potential to avoid becoming pregnant while on NEXAVAR because of the potential hazard to the fetus.

Impairment of Thyroid Stimulating Hormone Suppression in Differentiated Thyroid Carcinoma NEXAVAR impairs exogenous thyroid suppression. In the DTC study, 99% of patients had a baseline thyroid stimulating hormone (TSH) level less than 0.5 mU/L. Elevation of TSH level above 0.5 mU/L was observed in 41% of NEXAVAR-treated patients as compared with 16% of placebo-treated patients. For patients with impaired TSH suppression while receiving NEXAVAR, the median maximal TSH was 1.6 mU/L and 25% had TSH levels greater than 4.4 mU/L.

Monitor TSH levels monthly and adjust thyroid replacement medication as needed in patients with DTC.

ADVERSE REACTIONS

The following serious adverse reactions are discussed elsewhere in the labeling:

- Cardiac ischemia, infarction
- Hemorrhage
- Hypertension
- Hand-foot skin reaction, rash, Stevens-Johnson syndrome, and toxic epidermal necrolysis
- Gastrointestinal perforation
- QT Interval Prolongation
- Drug-Induced Hepatitis
- Impairment of TSH suppresion in DTC

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 in the Adverse Reactions section reflect exposure to NEXAVAR in 955 patients who participated in placebo controlled studies in hepatocellular carcinoma (N=297), advanced renal cell carcinoma (N=451), or differentiated thyroid carcinoma (N = 207).

The most common adverse reactions (≥20%), which were considered to be related to NEXAVAR, in patients with HCC, RCC or DTC are diarrhea, fatigue, infection, alopecia, hand-foot skin reaction, rash, weight loss, decreased appetite, nausea, gastrointestinal and abdominal pains, hypertension, and hemorrhage.

Adverse Reactions in HCC Study Table 4 shows the percentage of patients with HCC experiencing adverse reactions that were reported in at least 10% of patients and at a higher rate in the NEXAVAR arm than the placebo arm. CTCAE Grade 3 adverse reactions were reported in 39% of patients receiving NEXAVAR compared to 24% of patients receiving placebo. CTCAE Grade 4 adverse reactions were reported in 6% of patients receiving NEXAVAR compared to 8% of patients receiving placebo.

Table 4: Adverse Reactions Reported in at Least 10% of Patients and at a Higher Rate in NEXAVAR Arm than the Placebo Arm – HCC Study

	NEXAVAR N=297			Placebo N=302		
Adverse Reaction NCI- CTCAE v3 Category/Term	All Grades %	Grade 3 %	Grade 4 %	All Grades %	Grade 3 %	Grade 4 %
Any Adverse Reaction	98	39	6	96	24	8
Constitutional symptoms						
Fatigue	46	9	1	45	12	2
Weight loss	30	2	0	10	1	0
Dermatology/skin						
Rash/desquamation	19	1	0	14	0	0
Pruritus	14	<1	0	11	<1	0
Hand-foot skin reaction	21	8	0	3	<1	0
Dry skin	10	0	0	6	0	0
Alopecia	14	0	0	2	0	0
Gastrointestinal						
Diarrhea	55	10	<1	25	2	0
Anorexia	29	3	0	18	3	<1
Nausea	24	1	0	20	3	0
Vomiting	15	2	0	11	2	0
Constipation	14	0	0	10	0	0
Hepatobiliary/pancreas						
Liver dysfunction	11	2	1	8	2	1
Pain						
Pain, abdomen	31	9	0	26	5	1

Hypertension was reported in 9% of patients treated with NEXAVAR and 4% of those treated with placebo. CTCAE Grade 3 hypertension was reported in 4% of NEXAVAR-treated patients and 1% of placebo-treated patients. No patients were reported with CTCAE Grade 4 reactions in either treatment group.

Hemorrhage/bleeding was reported in 18% of those receiving NEXAVAR and 20% of placebo-treated patients. The rates of CTCAE Grade 3 and 4 bleeding were also higher in the placebo-treated group (CTCAE Grade 3 – 3% NEXAVAR and 5% placebo and CTCAE Grade 4 – 2% NEXAVAR and 4% placebo). Bleeding from esophageal varices was reported in 2.4% in NEXAVAR-treated patients and 4% of placebo-treated patients.

Renal failure was reported in <1% of patients treated with NEXAVAR and 3% of placebo-treated patients. The rate of adverse reactions (including those associated with progressive disease) resulting in permanent discontinuation was similar in both the NEXAVAR and placebo-treated groups (32% of NEXAVAR-treated patients and 35% of placebo-treated patients).

Laboratory Abnormalities

The following laboratory abnormalities were observed in patients with HCC:

Hypophosphatemia was a common laboratory finding observed in 35% of NEXAVAR-treated patients compared to 11% of placebo-treated patients; CTCAE Grade 3 hypophosphatemia (1–2 mg/dL) occurred in 11% of NEXAVAR-treated patients and 2% of patients in the placebo-treated group; there was 1 case of CTCAE Grade 4 hypophosphatemia (<1 mg/dL) reported in the placebo-treated group. The etiology of hypophosphatemia associated with NEXAVAR is not known.

Elevated lipase was observed in 40% of patients treated with NEXAVAR compared to 37% of patients in the placebo-treated group. CTCAE Grade 3 or 4 lipase elevations occurred in 9% of patients in each group. Elevated amylase was observed in 34% of patients treated with NEXAVAR compared to 29% of patients in the placebo-treated group. CTCAE Grade 3 or 4 amylase elevations were reported in 2% of patients in each group. Many of the lipase and amylase elevations were transient, and in the majority of cases NEXAVAR treatment was not interrupted. Clinical pancreatitis was reported in 1 of 297 NEXAVAR-treated patients (CTCAE Grade 2).

Elevations in liver function tests were comparable between the 2 arms of the study. Hypoalbuminemia was observed in 59% of NEXAVAR-treated patients and 47% of placebo-treated patients; no CTCAE Grade 3 or 4 hypoalbuminemia was observed in either group.

INR elevations were observed in 42% of NEXAVAR-treated patients and 34% of placebo-treated patients; CTCAE Grade 3 INR elevations were reported in 4% of NEXAVAR-treated patients and 2% of placebo-treated patients; there was no CTCAE Grade 4 INR elevation in either group.

Lymphopenia was observed in 47% of NEXAVAR-treated patients and 42% of placebo-treated patients.

Thrombocytopenia was observed in 46% of NEXAVAR-treated patients and 41% of placebo-treated patients; CTCAE Grade 3 or 4 thrombocytopenia was reported in 4% of NEXAVAR-treated patients and less than 1% of placebo-treated patients.

Hypocalcemia was reported in 27% of NEXAVAR-treated patients and 15% of placebo-treated patients. CTCAE Grade 3 hypocalcemia (6–7 mg /dL) occurred in 2% of NEXAVAR-treated patients and 1% of placebo-treated patients. CTCAE Grade 4 hypocalcemia (<6 mg/dL) occurred in 0.4% of NEXAVAR-treated patients and in no placebo-treated patients.

Hypokalemia was reported in 9.5% of NEXAVAR- treated patients compared to 5.9% of placebo-treated patients. Most reports of hypokalemia were low grade (CTCAE Grade 1). CTCAE Grade 3 hypokalemia occurred in 0.4% of NEXAVAR-treated patients and 0.7% of placebo-treated patients. There were no reports of Grade 4 hypokalemia.

Adverse Reactions in RCC Study 1 Table 5 shows the percentage of patients with RCC experiencing adverse reactions that were reported in at least 10% of patients and at a higher rate in the NEXAVAR arm than the placebo arm. CTCAE Grade 3 adverse reactions were reported in 31% of patients receiving NEXAVAR compared to 22% of patients receiving placebo. CTCAE Grade 4 adverse reactions were reported in 7% of patients receiving NEXAVAR compared to 6% of patients receiving placebo.

Table 5: Adverse Reactions Reported in at Least 10% of Patients and at a Higher Rate in NEXAVAR Arm than the Placebo Arm – RCC Study 1

	NEXAVAR N=451			Placebo N=451		
Adverse Reactions NCI- CTCAE v3 Category/Term	All Grades %	Grade 3 %	Grade 4 %	All Grades %	Grade 3 %	Grade 4 %
Any Adverse Reactions	95	31	7	86	22	6
Cardiovascular, General						
Hypertension	17	3	<1	2	<1	0
Constitutional symptoms						
Fatigue	37	5	<1	28	3	<1
Weight loss	10	<1	0	6	0	0
Dermatology/skin						
Rash/desquamation	40	<1	0	16	<1	0
Hand-foot skin reaction	30	6	0	7	0	0
Alopecia	27	<1	0	3	0	0
Pruritus	19	<1	0	6	0	0
Dry skin	11	0	0	4	0	0
Gastrointestinal symptoms						
Diarrhea	43	2	0	13	<1	0
Nausea	23	<1	0	19	<1	0
Anorexia	16	<1	0	13	1	0
Vomiting	16	<1	0	12	1	0
Constipation	15	<1	0	11	<1	0
Hemorrhage/bleeding						
Hemorrhage – all sites	15	2	0	8	1	<1
Neurology						
Neuropathy-sensory	13	<1	0	6	<1	0
Pain						
Pain, abdomen	11	2	0	9	2	0
Pain, joint	10	2	0	6	<1	0
Pain, headache	10	<1	0	6	<1	0
Pulmonary						
Dyspnea	14	3	<1	12	2	<1

The rate of adverse reactions (including those associated with progressive disease) resulting in permanent discontinuation was similar in both the NEXAVAR and placebo-treated groups (10% of NEXAVAR-treated patients and 8% of placebo-treated patients).

Laboratory Abnormalities

The following laboratory abnormalities were observed in patients with RCC in Study 1:

Hypophosphatemia was a common laboratory finding observed in 45% of NEXAVAR-treated patients compared to 11% of placebo-treated patients. CTCAE Grade 3 hypophosphatemia (1–2 mg/dL) occurred in 13% of NEXAVAR-treated patients and 3% of patients in the placebo-treated group. There were no cases of CTCAE Grade 4 hypophosphatemia (<1 mg/dL) reported in either NEXAVAR or placebo-treated patients. The etiology of hypophosphatemia associated with NEXAVAR is not known.

Elevated lipase was observed in 41% of patients treated with NEXAVAR compared to 30% of patients in the placebo-treated group. CTCAE Grade 3 or 4 lipase elevations occurred in 12% of patients in the NEXAVAR-treated group compared to 7% of patients in the placebo-treated group. Elevated amylase was observed in 30% of patients treated with NEXAVAR compared to 23% of patients in the placebo-treated group. CTCAE Grade 3 or 4 amylase elevations were reported in 1% of patients in the NEXAVAR-treated group compared to 3% of patients in the placebo-treated group. Many of the lipase and amylase elevations were transient, and in the majority of cases NEXAVAR treatment was not interrupted. Clinical pancreatitis was reported in 3 of 451 NEXAVAR-treated patients (one CTCAE Grade 2 and two Grade 4) and 1 of 451 patients (CTCAE Grade 2) in the placebo-treated group.

Lymphopenia was observed in 23% of NEXAVAR-treated patients and 13% of placebo-treated patients. CTCAE Grade 3 or 4 lymphopenia was reported in 13% of NEXAVAR-treated patients and 7% of placebo-treated patients. Neutropenia was observed in 18% of NEXAVAR-treated patients and 10% of placebo-treated patients. CTCAE Grade 3 or 4 neutropenia was reported in 5% of NEXAVAR-treated patients and 2% of placebo-treated patients.

Anemia was observed in 44% of NEXAVAR-treated patients and 49% of placebo-treated patients. CTCAE Grade 3 or 4 anemia was reported in 2% of NEXAVAR-treated patients and 4% of placebo-treated patients.

Thrombocytopenia was observed in 12% of NEXAVAR-treated patients and 5% of placebo-treated patients. CTCAE Grade 3 or 4 thrombocytopenia was reported in 1% of NEXAVAR-treated patients and in no placebo-treated patients.

Hypocalcemia was reported in 12% of NEXAVAR-treated patients and 8% of placebo-treated patients. CTCAE Grade 3 hypocalcemia (6–7 mg/dL) occurred in 1% of NEXAVAR-treated patients and 0.2% of placebo-treated patients, and CTCAE Grade 4 hypocalcemia (<6 mg/dL) occurred in 1% of NEXAVAR-treated patients and 0.5% of placebo-treated patients.

Hypokalemia was reported in 5.4% of NEXAVAR-treated patients compared to 0.7% of placebo-treated patients. Most reports of hypokalemia were low grade (CTCAE Grade 1). CTCAE Grade 3 hypokalemia occurred in 1.1% of NEXAVAR-treated patients and 0.2% of placebo-treated patients. There were no reports of Grade 4 hypokalemia.

Adverse Reactions in DTC Study The safety of NEXAVAR was evaluated in 416 patients with locally recurrent or metastatic, progressive differentiated thyroid carcinoma (DTC) refractory to radioactive iodine (RAI) treatment randomized to receive 400 mg twice daily NEXAVAR (n=207) or matching placebo (n=209) until disease progression or intolerable toxicity in a double-blind trial *[see Clinical Studies (14.3)]*. The data described below reflect a median exposure to NEXAVAR for 46 weeks (range 0.3 to 135). The population exposed to NEXAVAR was 50% male, and had a median age of 63 years.

Dose interruptions for adverse reactions were required in 66% of patients receiving NEXAVAR and 64% of patients had their dose reduced. Drug-related adverse reactions that resulted in treatment discontinuation were reported in 14% of NEXAVAR-treated patients compared to 1.4% of placebo-treated patients.

Table 6 shows the percentage of DTC patients experiencing adverse reactions at a higher rate in NEXAVAR-treated patients than placebo-treated patients in the double-blind phase of the DTC study. CTCAE Grade 3 adverse reactions occurred in 53% of NEXAVAR-treated patients compared to 23% of placebo-treated patients. CTCAE Grade 4 adverse reactions occurred in 12% of NEXAVAR-treated patients compared to 7% of placebo-treated patients.

Table 6: Per-Patient Incidence of Selected Adverse Reactions Occurring at a Higher Incidence in NEXAVAR-Treated Patients [Between Arm Difference of ≥ 5% (All Grades)[1] or ≥ 2% (Grades 3 and 4)]

MedDRA Primary System Organ Class & Preferred Term	NEXAVAR N = 207		Placebo N = 209	
	All Grades (%)	Grades 3 and 4 (%)	All Grades (%)	Grades 3 and 4 (%)
Gastrointestinal disorders				
Diarrhea	68	6	15	1
Nausea	21	0	12	0
Abdominal pain[2]	20	1	7	1
Constipation	16	0	8	0.5
Stomatitis[3]	24	2	3	0
Vomiting	11	0.5	6	0
Oral pain[4]	14	0	3	0
General disorders and administration site conditions				
Fatigue	41	5	20	1
Asthenia	12	0	7	0
Pyrexia	11	1	5	0
Investigations				
Weight loss	49	6	14	1
Metabolism and nutrition disorders				
Decreased appetite	30	2	5	0
Musculoskeletal and connective tissue disorders				
Pain in extremity	15	1	7	0
Muscle spasms	10	0	3	0
Neoplasms benign, malignant and unspecified				
Squamous cell carcinoma of skin	3	3	0	0
Nervous system disorders				
Headache	17	0	6	0
Dysgeusia	6	0	0	0

Table 6: Per-Patient Incidence of Selected Adverse Reactions Occurring at a Higher Incidence in NEXAVAR-Treated Patients [Between Arm Difference of ≥ 5% (All Grades)[1] or ≥ 2% (Grades 3 and 4)] (continued)

MedDRA Primary System Organ Class & Preferred Term	NEXAVAR N = 207		Placebo N = 209	
	All Grades (%)	Grades 3 and 4 (%)	All Grades (%)	Grades 3 and 4 (%)
Respiratory, thoracic and mediastinal disorders				
Dysphonia	13	0.5	3	0
Epistaxis	7	0	1	0
Skin and subcutaneous tissue disorders				
PPES[5]	69	19	8	0
Alopecia	67	0	8	0
Rash	35	5	7	0
Pruritus	20	0.5	11	0
Dry skin	13	0.5	5	0
Erythema	10	0	0.5	0
Hyperkeratosis	7	0	0	0
Vascular disorders				
Hypertension[6]	41	10	12	2

[1] National Cancer Institute Common Terminology Criteria for Adverse Events Version 3.0
[2] Includes the following terms: abdominal pain, abdominal discomfort, hepatic pain, esophageal pain, esophageal discomfort, abdominal pain lower, abdominal pain upper, abdominal tenderness, abdominal rigidity
[3] Includes the following terms: stomatitis, aphthous stomatitis, mouth ulceration, mucosal inflammation
[4] Includes the following terms: oral pain, oropharyngeal discomfort, glossitis, burning mouth syndrome, glossodynia
[5] Palmar-plantar erythrodysesthesia syndrome (Hand-foot skin reaction)
[6] Includes the following terms: hypertension, blood pressure increased, blood pressure systolic increased

Laboratory Abnormalities

Elevated TSH levels are discussed elsewhere in the labeling *[see Warnings and Precautions (5.12)]*. The relative increase for the following laboratory abnormalities observed in NEXAVAR-treated DTC patients as compared to placebo-treated patients is similar to that observed in the RCC and HCC studies: lipase, amylase, hypokalemia, hypophosphatemia, neutropenia, lymphopenia, anemia, and thrombocytopenia *[see Adverse Reactions (6.1, 6.2)]*.

Serum ALT and AST elevations were observed in 59% and 54% of the NEXAVAR-treated patients as compared to 24% and 15% of placebo-treated patients, respectively. High grade (≥ 3) ALT and AST elevations were observed in 4% and 2%, respectively, in the NEXAVAR-treated patients as compared to none of the placebo-treated patients.

Hypocalcemia was more frequent and more severe in patients with DTC, especially those with a history of hypoparathyroidism, compared to patients with RCC or HCC. Hypocalcemia was observed in 36% of DTC patients receiving NEXAVAR (with 10% ≥ Grade 3) as compared with 11% of placebo-treated patients (3% ≥ Grade 3). In the DTC study, serum calcium levels were monitored monthly.

Additional Data from Multiple Clinical Trials The following additional drug-related adverse reactions and laboratory abnormalities were reported from clinical trials of NEXAVAR (*very common* 10% or greater, *common* 1 to less than 10%, *uncommon* 0.1% to less than 1%, *rare* less than 0.1 %):

Cardiovascular: *Common*: congestive heart failure*†, myocardial ischemia and/or infarction *Uncommon:* hypertensive crisis* *Rare:* QT prolongation*

Dermatologic: *Very common:* erythema *Common:* exfoliative dermatitis, acne, flushing, folliculitis, hyperkeratosis *Uncommon:* eczema, erythema multiforme

Digestive: *Very common:* increased lipase, increased amylase *Common:* mucositis, stomatitis (including dry mouth and glossodynia), dyspepsia, dysphagia, gastrointestinal reflux *Uncommon:* pancreatitis, gastritis, gastrointestinal perforations*, cholecystitis, cholangitis

Note that elevations in lipase are very common (41%, see below); a diagnosis of pancreatitis should not be made solely on the basis of abnormal laboratory values

General Disorders: *Very common:* infection, hemorrhage (including gastrointestinal* and respiratory tract* and uncommon cases of cerebral hemorrhage*), asthenia, pain (including mouth, bone, and tumor pain), pyrexia, decreased appetite *Common:* influenza-like illness

Hematologic: *Very common:* leukopenia, lymphopenia *Common:* anemia, neutropenia, thrombocytopenia *Uncommon:* INR abnormal

Hepatobiliary disorders: *Rare:* drug-induced hepatitis (including hepatic failure and death)

Hypersensitivity: *Uncommon:* hypersensitivity reactions (including skin reactions and urticaria), anaphylactic reaction

Metabolic and Nutritional: *Very common:* hypophosphatemia *Common:* transient increases in transaminases, hypocalcemia, hypokalemia, hyponatremia, hypothyroidism *Uncommon:* dehydration, transient increases in alkaline phosphatase, increased bilirubin (including jaundice), hyperthyroidism

Musculoskeletal: *Very common:* arthralgia *Common:* myalgia, muscle spasms

Nervous System and Psychiatric: *Common:* depression, dysgeusia *Uncommon:* tinnitus, reversible posterior leukoencephalopathy*

Renal and Genitourinary: *Common*: renal failure, proteinuria *Rare:* nephrotic syndrome

Reproductive: *Common:* erectile dysfunction *Uncommon:* gynecomastia

Respiratory: *Common:* rhinorrhea *Uncommon:* interstitial lung disease-like events (includes reports of pneumonitis, radiation pneumonitis, acute respiratory distress, interstitial pneumonia, pulmonitis and lung inflammation)

In addition, the following medically significant adverse reactions were uncommon during clinical trials of NEXAVAR: transient ischemic attack, arrhythmia, and thromboembolism. For these adverse reactions, the causal relationship to NEXAVAR has not been established.

*adverse reactions may have a life-threatening or fatal outcome.

†reported in 1.9% of patients treated with NEXAVAR (N= 2276).

Postmarketing Experience The following adverse drug reactions have been identified during post-approval use of NEXAVAR. 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.

Dermatologic: Stevens-Johnson syndrome and toxic epidermal necrolysis (TEN)

Hypersensitivity: Angioedema

Musculoskeletal: Rhabdomyolysis, osteonecrosis of the jaw

Respiratory: Interstitial lung disease-like events (which may have a life-threatening or fatal outcome)

DRUG INTERACTIONS

Effect of Strong CYP3A4 Inducers on Sorafenib Rifampin, a strong CYP3A4 inducer, administered at a dose of 600 mg once daily for 5 days with a single oral dose of NEXAVAR 400 mg in healthy volunteers resulted in a 37% decrease in the mean AUC of sorafenib. Avoid concomitant use of strong CYP3A4 inducers (such as, carbamazepine, dexamethasone, phenobarbital, phenytoin, rifampin, rifabutin, St. John's wort), when possible, because these drugs can decrease the systemic exposure to sorafenib.

Effect of Strong CYP3A4 Inhibitors on Sorafenib Ketoconazole, a strong inhibitor of CYP3A4 and P-glycoprotein, administered at a dose of 400 mg once daily for 7 days did not alter the mean AUC of a single oral dose of NEXAVAR 50 mg in healthy volunteers.

Effect of Sorafenib on Other Drugs NEXAVAR 400 mg twice daily for 28 days did not increase the systemic exposure of concomitantly administered midazolam (CYP3A4 substrate), dextromethorphan (CYP2D6 substrate), and omeprazole (CYP2C19 substrate).

Neomycin Neomycin administered as an oral dose of 1 g three times daily for 5 days decreased the mean AUC of sorafenib by 54% in healthy volunteers administered a single oral dose of NEXAVAR 400 mg. The effects of other antibiotics on the pharmacokinetics of sorafenib have not been studied.

Drugs that Increase Gastric pH The aqueous solubility of sorafenib is pH dependent, with higher pH resulting in lower solubility. However, omeprazole, a proton pump inhibitor, administered at a dose of 40 mg once daily for 5 days, did not result in a clinically meaningful change in sorafenib single dose exposure. No dose adjustment for NEXAVAR is necessary.

USE IN SPECIFIC POPULATIONS

Pregnancy Pregnancy Category D. Based on its mechanism of action and findings in animals, NEXAVAR may cause fetal harm when administered to a pregnant woman. Sorafenib caused embryo-fetal toxicities in animals at maternal exposures that were significantly lower than the human exposures at the recommended dose of 400 mg twice daily. There are no adequate and well-controlled studies in pregnant women using NEXAVAR. Inform patients of childbearing potential that NEXAVAR can cause birth defects or fetal loss. Instruct both men and women of childbearing potential to use effective birth control during treatment with NEXAVAR and for at least 2 weeks after stopping treatment. Counsel female patients to contact their healthcare provider if they become pregnant while taking NEXAVAR.

When administered to rats and rabbits during the period of organogenesis, sorafenib was teratogenic and induced embryo-fetal toxicity (including increased post-implantation loss, resorptions, skeletal retardations, and retarded fetal weight). The effects occurred at doses considerably below the recommended human dose of 400 mg twice daily (approximately 500 mg/m^2/day on a body surface area basis). Adverse intrauterine development effects were seen at doses ≥0.2 mg/kg/day (1.2 mg/m^2/day) in rats and 0.3 mg/kg/day (3.6 mg/m^2/day) in rabbits. These doses result in exposures (AUC) approximately 0.008 times the AUC seen in patients at the recommended human dose. A NOAEL (no observed adverse effect level) was not defined for either species, since lower doses were not tested.

Nursing Mothers It is not known whether sorafenib 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 NEXAVAR, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Following administration of radiolabeled sorafenib to lactating Wistar rats, approximately 27% of the radioactivity was secreted into the milk. The milk to plasma AUC ratio was approximately 5:1.

Pediatric Use The safety and effectiveness of NEXAVAR in pediatric patients have not been studied.

Repeat dosing of sorafenib to young and growing dogs resulted in irregular thickening of the femoral growth plate at daily sorafenib doses ≥ 600 mg/m^2 (approximately 0.3 times the AUC at the recommended human dose), hypocellularity of the bone marrow adjoining the growth plate at 200 mg/m^2/day (approximately 0.1 times the AUC at the recommended human dose), and alterations of the dentin composition at 600 mg/m^2/day. Similar effects were not observed in adult dogs when dosed for 4 weeks or less.

Geriatric Use In total, 59% of HCC patients treated with NEXAVAR were age 65 years or older and 19% were 75 and older. In total, 32% of RCC patients treated with NEXAVAR were age 65 years or older and 4% were 75 and older. No differences in safety or efficacy were observed between older and younger patients, and 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 Hepatic Impairment In a trial of HCC patients with mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment, the systemic exposure (AUC) of sorafenib was within the range observed in patients without hepatic impairment. In another trial in subjects without HCC, the mean AUC was similar for subjects with mild (n=15) and moderate (n=14) hepatic impairment compared to subjects (n=15) with normal hepatic function. No dose adjustment is necessary for patients with mild or moderate hepatic impairment. The pharmacokinetics of sorafenib have not been studied in patients with severe (Child-Pugh C) hepatic impairment.

Patients with Renal Impairment No correlation between sorafenib exposure and renal function was observed following administration of a single oral dose of NEXAVAR 400 mg to subjects with normal renal function and subjects with mild (CLcr 50–80 mL/min), moderate (CLcr 30–<50 mL/min), or severe (CLcr <30 mL/min) renal impairment who are not on dialysis. No dose adjustment is necessary for patients with mild, moderate or severe renal impairment who are not on dialysis. The pharmacokinetics of sorafenib have not been studied in patients who are on dialysis.

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Raising a Red Flag

Patient favoritism crosses boundaries. Why do nurses often breach this professional barrier?

By Elaine S. DeMeyer RN, MSN, AOCN

Playing favorites occurs in many aspects of life. Children often accuse their parents of it; in the workforce, a boss might be perceived as giving a better assignment to a certain worker over another. Favoritism, which is defined as favoring 1 person or group over others with equal claim, also exists in the medical field, with healthcare providers having favorite patients.

Favoritism can be conscious or unconscious behavior. It can breed resentment and negative feelings among patients and colleagues, and it may even be a form of discrimination.

The National Council of State Boards of Nursing identifies favoritism as an early warning sign of a boundary crossing. The concern is that some patients may be treated differently or better than others. Favoritism can be a sign of overinvolvement and straying outside the "zone of helpfulness" of a therapeutic relationship.

Why nurses may like or dislike some patients, as well as how those feelings affect nursing care, has not received great attention in nursing literature. But a qualitative study conducted by researchers from the Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland, examined the physician–patient relationship. Many primary care physicians stated that although they try to treat all patients equally, favorites often receive extra or more timely care. One physician admitted that favorite patients "probably hear back more rapidly than less favorite patients." That mind-set can be picked up by a patient who then tries to become a "favorite" to get better treatment.

Long before I learned about professional boundaries, I fell prey to this thinking, too. For instance, when my family members were in the hospital, I always made sure they had a bowl full of candy to offer staff.

What factors may cause us to favor—or want to avoid—some patients more than others? Below are some that I explored:

- **Personal element.** First, nurses must acknowledge that they are simply going to like and dislike some patients. It's human nature. Patients who have an engaging, captivating personality or hold similar values or beliefs may be easier to like or relate to.
- **Tendency to solve problems.** When nurses see a need, they try to meet it. Often, nurses act without thinking about downstream effects.
- **Special bond.** Nurses can feel close to patients, especially those who are very sick or whom they have known for a long time. That patient often becomes one of the favorites.
- **Transference.** This psychological term describes how past feelings, conflicts, and attitudes can affect present relationships, situations, and circumstances. For example, a patient who sees a nurse more as a nurturing mother or father figure can become less independent or even childlike. This may cause a nurse to treat that patient differently or do more for them.
- **Countertransference.** With this form of transference, the nurse's reaction to a patient may affect care. A patient may remind the nurse of a favorite uncle or critical father, which can positively or negatively affect the care a patient receives.
- **"Difficult" patient.** This label often describes a patient who is considered challenging or high maintenance—someone who is angry, nonadherent, demanding, never satisfied, or highly critical. Difficult patients may cause nurses to feel ineffective or incompetent, frustrated, or even exasperated. Nurses may start to distance themselves or become underinvolved, which is also considered a boundary crossing because it is outside the "zone of helpfulness."
- **"Easy" patient.** A patient who is considered easy (eg, is especially nice, has good veins, requires simple treatment, or expresses gratitude) tends to become a favorite. Nurses may find themselves wanting to be associated with those kinds of patients, spending more time with them or doing favors for them.

Some nurses may at some point err on the side of being overly invested with certain patients, perhaps early on in their career (like Amanda). It is important to remember that this naturally occurs in human bonding. Anne Devine, MA, BSN, a nurse turned writer, wrote about this subject, stating, "Sometimes nurses sense a connection with a patient that we don't fully understand in the moment." Although she tried to make every patient feel special, she said, some became her favorites.

Oncology nurses should realize that they are not alone in their quest for the perfect balance of nurturing/caring and professionalism. They have a responsibility to ensure that all patients with cancer receive the same quality of care. With an emphasis on cancer disparity, it is even more important to be aware of favoritism and its impact. Nurses who do so will be better equipped to stay inside the boundary lines.

AMANDA, A 38-YEAR-OLD ONCOLOGY NURSE, reflected back on her early years as an oncology research nurse and her favorite patient. Jane, a Baptist missionary, had metastatic melanoma and was participating in a phase I/II clinical trial. Her husband, Ron, had just finished treatment for renal cell carcinoma when she learned of her diagnosis. They had 5 adult children who lived all over the United States but nowhere near the treatment center.

"I instantly bonded with her," Amanda recalled. "I could relate to her values and beliefs; in fact, we discovered we knew some of the same people at my church. I felt terrible that she had not recovered from her husband's cancer only to find out she had cancer. Although their children were supportive, this couple's life was now in the Philippines as missionaries.

"I spent hours just sitting with her during stem cell collection for a research trial," Amanda continued. "I found myself wanting to solve all her problems and continued to help her via email, even after she left the cancer center. I know I gave her preferential treatment and went outside my boundaries as a nurse."

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OncLive Strategic Alliance

Frances Payne Bolton School of Nursing
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Family Caregiver Satisfaction With End-of-Life Care Following Advanced Cancer

Karen O. Moss, PhD, RN, CNL

Postdoctoral fellow, Frances Payne Bolton School of Nursing at Case Western Reserve University
Cleveland, OH

Sara L. Douglas, PhD, RN

Arline H. & Curtis F. Garvin Professor and assistant dean for research, Frances Payne Bolton School of Nursing at Case Western Reserve University
Cleveland, OH

"One of the most salient memories in the minds of family caregivers involves the EOL experience of their loved one, followed by its impact on the grieving process."

Family caregiver satisfaction with end-of-life (EOL) care is key to better understanding patient EOL experiences.[1] In measuring family caregiver satisfaction, it is important to conceptualize what is considered a "good death" or "good dying process."[2] Understanding the bereaved family caregiver's satisfaction can help lead to improved EOL care for patients.[2] In particular, families of patients who die in their preferred location are more likely to be satisfied with EOL care provided.[3]

Most people can identify the elements of their loved one's experience of dying that were "satisfactory." Often, these center around using less-aggressive medical care and earlier hospice referrals.[4]

MEASURING FAMILY CAREGIVER SATISFACTION

A longitudinal National Institutes of Health–funded study (NRO14856) conducted at the Frances Payne Bolton School of Nursing by Sara L. Douglas, PhD, RN, is examining aggressiveness of EOL care in advanced cancer among patients, family caregivers, nurses, and physicians.[5]

Approximately 2 months following the death of a loved one with advanced cancer, a phone interview is conducted with the bereaved family caregiver. The 13-item version of the Family Satisfaction with End-of-Life Care (FAMCARE-P13) scale asks the caregiver to rate responses to questions on symptom management, inclusion of family in treatment decisions, prognosis, healthcare provider (doctor and nurse) availability to the family, coordination of care, and overall satisfaction with care in the week preceding death.[6] Family caregivers rate their level of satisfaction from "very satisfied" to "very dissatisfied."[6]

Additionally, 2 open-ended questions ask family caregivers to discuss (1) aspects of care that may have caused them to think it was time to stop cancer therapy and focus on comfort and (2) if the care and treatment received was consistent with their loved one's wishes. An advantage of assessing family caregiver satisfaction with EOL care both qualitatively and quantitatively is the ability to compare and relate both sets of data to gain a more accurate understanding of the caregiver's perspective,[7] including grief and bereavement outcomes among family caregivers following death. Bereaved family caregivers openly share their thoughts, lending insight that can inform future oncologic EOL research to provide clinical practice guidelines toward improving EOL experiences for patients and families.

IMPLICATIONS FOR ONCOLOGY NURSING

Oncology nurses are well positioned to make significant impacts in EOL satisfaction in advanced cancer. Preparation is key to improving EOL care experiences for these patients and their families. Oncology nurses can encourage patients and families to have conversations about EOL wishes early on, including discussions about patient and family values,[8] which are often shared and can influence EOL decision making.

Oncology nurses can answer EOL-related questions and refer patients and families to appropriate resources such as chaplaincy, social work, or counseling services as needs are identified at any point on the disease trajectory—and even after death for the bereaved family. In doing this, nurses can help empower patients and families to initiate such conversations with each other and with healthcare providers, as well as reduce anxiety. Research shows that patients who engage in EOL conversations with their physicians are more likely to receive care that is consistent with their wishes, which can reduce suffering near the EOL.[9]

Encouraging patients and families to become comfortable with speaking about death can reduce psychological distress and bereavement and increase the likelihood that the medical care provided will be consistent with the patient's personal preferences.[10] Realizing one's own mortality and how it can change outlook, perhaps even for the better, may also affect how caregivers plan for the end of their own lives.

In summary, the death of a loved one with cancer creates a void in the lives of family and friends left behind. One of the most salient memories in the minds of family caregivers involves the EOL experience of their loved one, followed by its impact on the grieving process. Future research should use oncology nurses, nurse researchers, and an interdisciplinary team to examine family caregiver satisfaction with EOL care provided, with bereavement outcomes measured over time. This will help identify specific areas that require more focus, with a goal of improving the EOL experiences for patients with advanced cancer and subsequently outcomes with their families.

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Promoting *BRCA* Awareness

I recall asking my mother's oncologist in 1997, when *BRCA* gene testing was still in its infancy, about the possibility of testing her blood for this genetic mutation or freezing and storing her blood for future analysis. My mother was dying from recurrent metastatic breast cancer and, 5 years earlier, had been treated for primary ovarian cancer. As a family nurse practitioner, I was not only interested in this new testing for the sake of science but also personally concerned that my older sister, brother, and I might have inherited an increased risk of cancer associated with this genetic anomaly. My inquiry was dismissed with the nonchalant response that *BRCA* testing was just "too new to worry about right now." In retrospect, a definitive result for my mother back then would have guided future healthcare recommendations for us.

After recently viewing the 2015 documentary *Pink & Blue: Colors of Hereditary Cancer*, I began to question why I had not sought genetic testing for the last 20 years. *Pink & Blue* not only educates the viewer about the *BRCA* gene mutations but also powerfully highlights the personal stories of both women and men with positive mutations, depicting their subsequent journeys, including treatment, restoration, remission, or death. The documentary advocates that "knowledge is power" and speaks passionately about the need for increased awareness of genetic testing and breast cancer prevention.

One goal of *Pink & Blue* is to raise awareness of male breast cancer. Despite the overwhelming "pinkness" of the breast cancer world, men inherit *BRCA* mutations as frequently as women do. Regardless of gender, a parent with an inherited mutation has a 50% chance of passing it on to each of their offspring, whether the baby is a girl or boy.[1] It struck me that if I were *BRCA*-positive, even my son could have a genetic mutation that might be transmitted to his children someday.

Up to 10% of all breast cancers may be linked to genetic mutations, with *BRCA1/2* being the most common.[2] A woman with a *BRCA1/2* genetic anomaly may have up to an 80% lifetime risk of developing breast cancer, as well as ovarian, colon, skin, and pancreatic cancers. Although breast cancer is rare in men, the American Cancer Society estimated that about 2470 new cases of male invasive breast cancer were diagnosed in 2017 and that about 460 men would die from the disease.[3] The average lifetime risk of breast cancer in men is about 1 in 1000 (0.1%) compared with 1 in 8 (about 12%) for women. A man with an abnormal *BRCA*2 gene has a lifetime breast cancer risk of about 8%, 80 times greater than that of the average man without a genetic mutation, and is 7 times more likely to develop prostate cancer than men without an abnormal gene.[4] Although survival rates are similar for men and women with the same stage of breast cancer, men are often diagnosed at a later stage. This is often because men did not report early symptoms and/or the cancer spread to adjacent structures due to less breast tissue.[5] Healthcare providers routinely document medical histories and cancer risk of their patients, but many do not always refer high-risk patients, including men, for genetic counseling or testing.

Genetic counseling and subsequent testing require serious consideration. Some individuals may not wish to have additional medical testing or recommended prophylactic surgery if faced with the knowledge of a positive result. Because genetic mutations affect all biological relatives, there may be emotional tension and fear within the family, factoring into decisions regarding marriage, childbearing, and career choices. Fear, hesitation, and doubt abound in the areas of employment discrimination; potentially higher health, life, and mortgage insurance rates; test reliability; and financial coverage for genetic testing. Individuals who may have positive genetic mutations might also experience feelings of guilt and loss of control. However, the federal Genetic Information Nondiscrimination Act of 2008, along with many state laws, prohibits discrimination based on genetic information in relation to health insurance and employment, although it does not cover life insurance, disability insurance, or long-term care insurance.[6]

In addition to films like *Pink & Blue*, many online resources address cancer risk. A risk calculator on Bright Pink, a national nonprofit organization (BrightPink.org), quickly provides information regarding the user's chances of developing breast or ovarian cancer. The Male Breast Cancer Coalition, a nonprofit organization, reminds the public that "men have breasts, too" and offers a related series (HISbreastcancer.org). Both organizations add blue to the traditional pink ribbon to recognize breast cancer in both genders.

Today, I am bold enough to pursue genetic counseling and testing for not only *BRCA1/2* but also the comprehensive 34-gene panel that may identify my risk of as many as 8 different cancers. My decision was based on neither my own 25 years' experience and medical knowledge as a nurse practitioner nor my healthcare providers' prompting. It was made after I viewed *Pink & Blue* and heard the powerful stories of people whose lives were positively changed by knowledge of their genetics. By taking the nonthreatening approach of consulting a genetic counselor, plus the simple act of sending out a freshly collected 1-cc sample of saliva, I will affect not only my health but also the well-being of my daughters, son, and grandchildren.

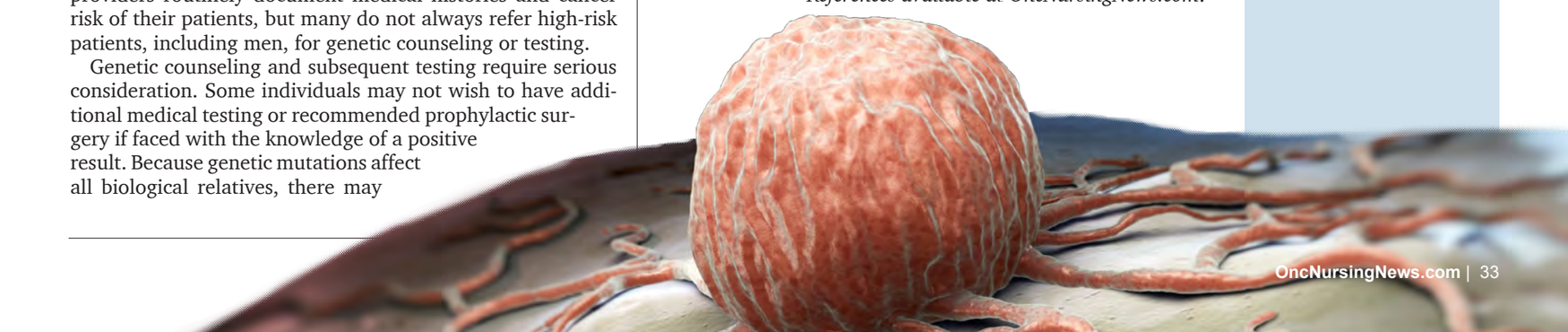
Some high-risk individuals might also be stirred to action by modalities such as film, social media, websites, and blogs. But why is it that we as healthcare providers do not consistently promote awareness of breast cancer risk to both women and men, as well as genetic counseling referral (when indicated) to our patients? When taking the family medical history, we all can address breast cancer risk, symptom recognition, and prevention. A caring, sensitive attitude is crucial to dispel myths and alleviate fears, especially those of a man who may feel emasculated by talk of self-breast exam, areolar masses, and nipple discharge. When indicated, providers must encourage patients with multiple breast cancer risk factors, regardless of gender, to consider genetic counseling and/or *BRCA* testing. For those who opt for testing, the results, whether negative or positive, not only deliver the power of knowledge but also afford healthcare providers the ability to make better management and treatment decisions.

References available at OncNursingNews.com.

Donna R. White, DNP, RN, CRNP, FNP-BC

Donna R. White, DNP, RN, CRNP, FNP-BC, is the director of graduate clinical faculty and clinical affairs at Duquesne University School of Nursing in Pittsburgh, PA.

"Despite the overwhelming 'pinkness' of the breast cancer world, men inherit BRCA mutations as frequently as women do."



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