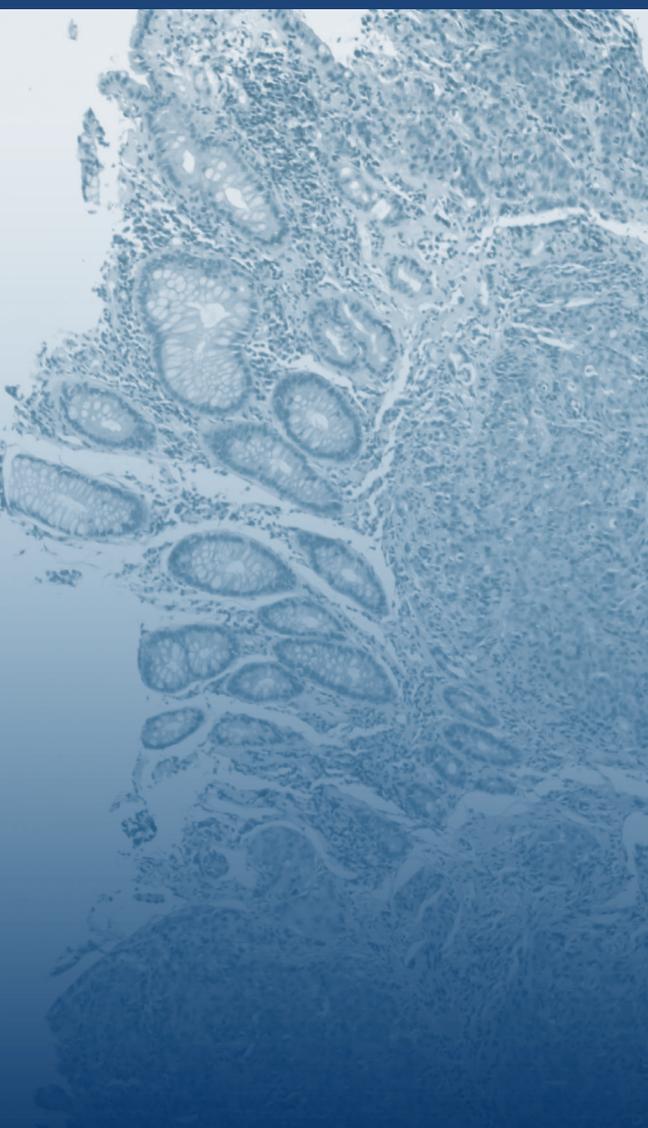


PHARMACY TIMES

ONCOLOGY™

EDITION

DECEMBER 2022 Vol. 4 No. 6



COVER STORY

Immunotherapy Makes Major Strides for First-line Treatment of Unresectable Locally Advanced or Metastatic Esophageal Squamous Cell Carcinoma

KEVIN PANG, PHARM D

HEMATOLOGY

Treatment-Free Remission in Chronic Myeloid Leukemia

CAROLINE MCCASLIN, PHARM D AND JONATHAN COHEN, PHARM D, BCOP

BREAST CANCER

Breast Cancer Research, Current Therapeutic Pipeline Provide Significant Advancements in Diagnosis, Treatment

RACHEL K. ANDERSON, PHARM D, CSP

LUNG CANCER

Neoadjuvant, Adjuvant Therapy for Resectable NSCLC Progresses With Immunotherapy, Targeted Therapy

KEVIN PANG, PHARM D AND NONI THEOCHARIDES, PHARM D CANDIDATE



PHARMACY TIMES ONCOLOGY™ EDITION

DECEMBER 2022 VOLUME 4 NUMBER 6



18 *cover feature*

Immunotherapy Makes Major Strides for First-line Treatment of Unresectable Locally Advanced or Metastatic Esophageal Squamous Cell Carcinoma

KEVIN PANG, PHARM.D

ALSO IN THIS ISSUE

- | | |
|--|---|
| <p>9 PUBLISHER'S NOTE
Significant Opportunities Are Ahead to Improve Health Equity, Provide Patient-Centered Oncology Treatment, Care
MIKE HENNESSEY JR</p> <p>10 ADVISORY BOARD</p> | <p>11 MEDICAL WORLD NEWS™</p> <p>12 FROM THE EDITOR
The Right Professional Connectivity May Get Us Through the Challenges of an Age of Ultracommunication
LISA E. DAVIS, PHARM.D, FCCP, BCPS, BCOP,
EDITOR IN CHIEF</p> |
|--|---|



BREAST CANCER

21 Breast Cancer Research, Current Therapeutic Pipeline Provide Significant Advancements in Diagnosis, Treatment

RACHEL K. ANDERSON, PHARM.D, CSP

HEMATOLOGY

39 Treatment-Free Remission in Chronic Myeloid Leukemia

CAROLINE MCCASLIN, PHARM.D AND JONATHAN COHEN, PHARM.D, BCOP

LUNG CANCER

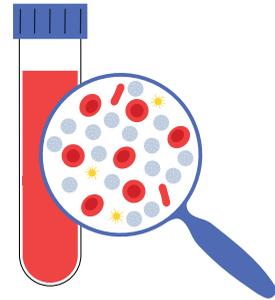
51 Neoadjuvant, Adjuvant Therapy for Resectable NSCLC Progresses With Immunotherapy, Targeted Therapy

KEVIN PANG, PHARM.D AND NONI THEOCHARIDES, PHARM.D CANDIDATE

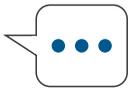
recaps

54 2022 Directions in Oncology Pharmacy®

39



Subscribe to our newsletters for practical tips and valuable resources



Publisher's Note

Connect With
Pharmacy Times
Oncology Edition™

For more information, visit:
www.pharmacytimes.com/publications/directions-in-pharmacy

PHARMACY TIMES **ONCOLOGY™** EDITION

PUBLISHING STAFF

EDITORIAL & PRODUCTION

Editor in Chief Lisa E. Davis, PharmD, FCCP, BCPS, BCOP

Vice President, Content Laura Joszt, MA

Associate Editorial Director Davy James

Managing Editor Alana Hippensteele

Associate Editors Aislinn Antrim, Jill Murphy

Assistant Editors Erin Hunter, Ashley Gallagher

Vice President, Copy Jennifer Potash

Copy Chief Paul Silverman

Copy Supervisor Nicole Canfora Lupo

Senior Copy Editors Cheney Baltz, Marie-Louise Best, Kelly King

Copy Editors Georgina Carson, Kirsty Mackay, Justin Mancini, Ron Panarotti, Mercedes Pérez, Yasmeen Qahwash

Creative Director, Publishing Melissa Feinen

Senior Art Director Marie Maresco

SALES

Vice President, AJMC® & Pharmacy Times®
Gil Hernandez

Executive Assistant Sheena Parimoo

Associate Director, Sales Matthew Miniconzi

Senior National Account Manager Colin Fishbein

National Accounts Associate
Michael Bachalis

OPERATIONS & FINANCE

Circulation Director Jon Severn

Vice President, Finance Leah Babitz, CPA

Controller Katherine Wyckoff

CORPORATE

President & CEO Mike Hennessy Jr

Chief Financial Officer Neil Glasser, CPA/CFE

Chief Operating Officer Michael Ball

Chief Marketing Officer Brett Melillo

Executive Vice President, Global Medical Affairs & Corporate Development Joe Petroziello

Senior Vice President, Content Silas Inman

Senior Vice President, Human Resources & Administration Shari Lundenberg

Senior Vice President, Mergers & Acquisitions, Strategic Innovation Phil Talamo

Executive Creative Director Jeff Brown

Founder
Mike Hennessy Sr
1960-2021



AN **MH** life sciences® BRAND

2 Clarke Drive, Suite 100
Cranbury, NJ 08512
(609) 716-7777

Significant Opportunities Are Ahead to Improve Health Equity, Provide Patient-Centered Oncology Treatment, Care

THE END OF YEAR is a hectic time for oncology professionals. Beyond time off for the holidays and plans for celebrations with family and friends, the month of December contains some of the top conferences in the field. Conferences such as the San Antonio Breast Cancer Symposium (SABCS) and the American Society of Hematology Annual Meeting (ASH) occur during a period of little more than a week, with late-breaking data and news relevant to the field flooding social media channels, email inboxes, and oncology pharmacy media outlets.

As one such media outlet, *Pharmacy Times Oncology Edition™* will be covering SABCS and ASH this year in a special January 2023 issue that will help summarize the content and research of interest to oncology pharmacy professionals. The issue will include interviews with conference session presenters, articles summarizing research from key study authors, and onsite session coverage. The issue aims to provide added insight for those who may have missed a conference altogether or may not have been present for all key SABCS and ASH session presentations, which—considering the extensive agendas of each conference—is likely most everyone.

In this issue, Kevin Pang, PharmD, provides insight into some recent major strides in advancing immunotherapy for first-line treatment of unresectable locally advanced or metastatic esophageal squamous cell carcinoma in the cover story on page 18. Pang explains how the addition of immune checkpoint inhibitors in particular has transformed modern clinical practice.

On page 21, Rachel K. Anderson, PharmD, CSP, describes some of the trends in breast cancer treatment development, with a specific look at the current therapeutic pipeline for the disease.

With significant advancements in oncology treatments and ongoing progress focused toward addressing social determinants of health and greater health equity in cancer care, 2022 has been a noteworthy year for the field. Looking to 2023, there remain significant opportunities on the road ahead to improve patient outcomes and patient-centered oncology treatment and care.

Mike Hennessy Jr
PRESIDENT & CEO

EDITOR IN CHIEF

Lisa E. Davis, PharmD, FCCP, BCPS, BCOP
Clinical Professor, Pharmacy Practice and Science
University of Arizona R. Ken Coit College of Pharmacy
Clinical Pharmacist, Hematology-Oncology Banner - University Medical Center Tucson and University of Arizona Cancer Center

EDITORIAL ADVISORY BOARD

Ray Bailey, BPharm, RPh
Senior Vice President of Pharmacy Services, Florida Cancer Specialists

Douglas Braun, PharmD
Senior Pharmacy Director, American Oncology Network, LLC

William Carroll, PharmD
System Vice President of Pharmacy Services Rochester Regional Health

Joshua Cox, PharmD, BCPS
Director of Pharmacy and Research, Dayton Physicians Network

David DeRemer, PharmD, BCOP, FCCP, FHOPA
Clinical Professor, Department of Pharmacotherapy and Translational Research, University of Florida (UF) College of Pharmacy Assistant Director, Experimental Therapeutics Incubator, UF Health Cancer Center

Andrew J. Donnelly, PharmD, MBA, FASHP
Clinical Professor and Associate Dean, University of Illinois (UI) Chicago College of Pharmacy
Director of Pharmacy Services, UI Health

Heidi D. Finnes, PharmD, BCOP, FHOPA
Senior Manager, Pharmacy Cancer Research, Assistant Professor of Pharmacy, Mayo Clinic Alix School of Medicine
Director of Pharmacy Shared Resources, Mayo Clinic Care Center

Bryan P. Fitzgerald, PharmD, BCOP
Clinical Pharmacist, Oncology, Wilmot Cancer Institute, University of Rochester Specialty Pharmacy

Christopher Hatwig, MS, RPh, FASHP
President, Apexus

Ryan Haumschild, PharmD, MS, MBA
Director of Pharmacy Services, Emory Healthcare

Jerline Hsin, PharmD, BCPS, BCOP
Clinical Pharmacist Specialist, City of Hope

Sophia Zhang Humphreys, PharmD, MHA
Director of System Pharmacy Clinical Services, Providence St Joseph Health

Jacob K. Kettle, PharmD, BCOP
Director, Ellis Fischel Cancer Center Service Line, University of Missouri Health Care

Susannah E. Koontz, PharmD, BCOP, FHOPA
Principal, Koontz Oncology Consulting, LLC

Jeff Lombardo, PharmD, BCOP
Director of Pharmacy Business Development, Catholic Health System

Zahra Mahmoudjafari, PharmD, BCOP, DPLA
Clinical Pharmacy Manager, Blood and Marrow Transplant Program, Division of Hematologic Malignancies and Cellular Therapeutics PGY2 Oncology Residency Program Director The University of Kansas Cancer Center

Matthew Malachowski, PharmD, MHA, BCPS
System Director of Population Health and Ambulatory Care Pharmacy, Ochsner Health System

Christine Pfaff, BPharm, RPh
Regional Director of Operations, American Oncology Network, LLC

Jeffrey Reichard, PharmD, MS, BCOP
System Executive Director of Pharmacy, Specialty, and Home Delivery Pharmacy, UNC Health

Christine Roussel, PharmD, BCOP, BCSCP
Senior Executive Director, Pharmacy, Laboratory, and Medical Research, Doylestown Health

Scott A. Soefje, PharmD, MBA, BCOP, FCCP, FHOPA
Director, Pharmacy Cancer Care, Mayo Clinic

Eric Sredzinski, PharmD, AAHIVP
Senior Vice President, Optum

EDITOR EMERITUS

Dan Steiber, RPh
Principal at Genesis Pharma Consultants

Medical World News™ is a first-of-its-kind, 24-hour online program for health care professionals, by health care professionals. The site provides video editorial content on a variety of cutting-edge topics delivered through a livestream and is available on demand for all health care stakeholders, offering the latest news and information in an easily digestible, one-stop-shop format.



AFTER HOURS™

Meditation and Reading

Abdelaziz Mohamed, MD, discusses his meditation practice, the benefits of meditation, and the books he is reading and planning to read.

TO WATCH: <http://bit.ly/3FZISpQ>

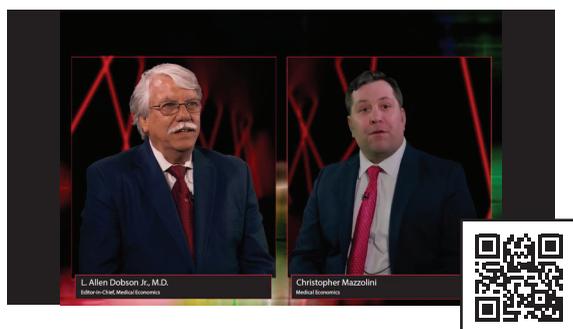


WELLBEING CHECKUP™

Ways to De-stress

Audrey Friedman, RN, CLNC, oncology nurse at UCHealth University of Colorado Hospital, shares how she found her techniques to de-stress after a shift at the hospital. She also provides advice to other health care workers for finding their own methods to center themselves.

TO WATCH: <http://bit.ly/3WNVXlev>



MEDICAL ECONOMICS® PULSE™

2022 Physician Report

Medical Economics® host Christopher Mazzolini sits down with L. Allen Dobson Jr, MD, to discuss the results of the 93rd annual Physician Report, an exclusive survey covering physician salaries, malpractice costs, and other key trends.

TO WATCH: <http://bit.ly/3WV2Bx4>



Editor's Note

Connect With
Pharmacy Times
Oncology Edition™

For the latest oncology news, visit
www.pharmacytimes.com/publications/directions-in-pharmacy.



The Right Professional Connectivity May Get Us Through the Challenges of an Age of Ultracommunication

LISA E. DAVIS, PHARMD, FCCP, BCPS, BCOP, *PHARMACY TIMES ONCOLOGY EDITION*™ EDITOR IN CHIEF



Lisa E. Davis, PharmD,
FCCP, BCPS, BCOP

OVER THIS PAST year, there have been an increasing number of discussions at professional conferences and in hematology/oncology pharmacy publications highlighting the challenges that professionals in the field are facing in their workplace environments. The challenges discussed include increasing workload demands, resource shortages, and a lack of professional opportunities; however, these are but a few of the factors contributing to the increasing rates of burnout among

hematology/oncology pharmacists.

With the close of the year nearly upon us, we often find ourselves reflecting on our professional situations as we plan for a new year. Although some may be contemplating career changes, others are deciding to remain where they are. With these differing decisions among professionals in the same field, the question remains: What are the experiences or situations that are causing some to stay and others to leave?

Workplace stress, fatigue, and burnout are



ABOUT THE EDITOR LISA E. DAVIS, PHARM.D, FCCP, BCPS, BCOP, is the new editor in chief of *Pharmacy Times Oncology Edition*[™]. Davis holds positions as a clinical pharmacist in early-phase clinical trial and breast cancer programs at the University of Arizona (Arizona) Cancer Center and a clinical professor of pharmacy practice and science at the Arizona R. Ken Coit College of Pharmacy. Davis also sits on the Hematology/Oncology Pharmacy Association Board of Directors and is a member of the Cancer Prevention and Control Program and scientific review committee at the Arizona Cancer Center.



**Pharmacy
Times**

SCAN THE QR
CODE or visit
pharmacytimes.com
to learn more.

not new for clinicians in oncology settings. However, the rate of oncology pharmacists leaving practice for alternative careers has accelerated. Since the early 1980s, numerous publications have covered the occurrence of chronic stress, emotional exhaustion, and burnout among professionals in the field. Although personality characteristics may contribute to some factors leading to burnout, we have long known that professionals who have a sense of personal control over what is occurring in their personal lives and professional environments experience a greater ability to protect against some of the common symptoms of burnout.

For this reason, strategies that focus only on developing personal resilience as a means of managing workplace stress and avoiding burnout are unlikely to be sufficient because the relative contribution of personal and workplace factors can differ among individuals, depending on their personal situations and needs. Additionally, it seems unlikely that hematology/oncology pharmacists who have remained in their current position for 5 to 10 years or longer have been able to do so purely due to higher personal resilience characteristics, lower workload demands, or particularly unique workplace environments.

However, it is also worth considering how the nature of hematology/oncology clinical practice has changed over the past few decades. The administrative components of clinical care for individual clinicians were previously less onerous, and although the workload metrics have been (and continue to be) difficult to define and quantify, the pressure to justify a current hematology/oncology pharmacist's position—even in

the setting of a staffing shortage—can be difficult to comprehend. The need for constant connectivity and communication in this new professional environment post pandemic has required the use of multiple interfaces (eg, electronic health record portals, messaging, email, etc) and devices, with each one often requiring time to effectively use and manage. And, of course, cancer therapeutics have become increasingly complex as well.

What has not changed, however, is the importance and value that hematology/oncology pharmacists provide in oncology care and practice. We continue to demonstrate value through innovative practices and measures and professional relationships, as well as within unique settings. Hematology/oncology pharmacists are passionate about their work, are collaborative with their work colleagues, and embrace opportunities to support new practitioners and recent resident graduates taking on roles within their institutions.

The connectivity that hematology/oncology pharmacists feel among one another, as well as with other health care professionals, can be fueled by attending and participating in professional meetings and organizations, participating in workplace and external collaborations, and advocating for patients with cancer and their caregivers. In this way, a focus on developing positive connectivity among colleagues that go beyond the day-to-day may help support hematology/oncology pharmacists' efforts to advocate for roles that optimize their personal and institutional value and highlight their contributions toward enhancing patient care and clinical outcomes. ■



Immunotherapy Makes Major Strides for First-line Treatment of Unresectable Locally Advanced or Metastatic Esophageal Squamous Cell Carcinoma

Specific immune checkpoint inhibitors added to frontline chemotherapy have transformed modern clinical practice.

KEVIN PANG, PHARM.D



ESOPHAGEAL CANCERS ARE histologically classified as either esophageal adenocarcinoma or esophageal squamous cell carcinoma (ESCC), with the latter associated with a poorer prognosis.¹ Traditionally, first-line systemic therapy for advanced esophageal cancer consists of 2 cytotoxic agents (often a fluoropyrimidine and a platinum agent), with the potential for 3 cytotoxic agents for medically fit patients with excellent performance status and easy access to frequent toxicity evaluations.²⁻⁴ Advanced esophageal adenocarcinoma that is HER2 overexpression positive may be supplemented with trastuzumab (Herceptin; Genentech, Inc), a HER2-targeting agent.⁵ The addition of specific immune checkpoint inhibitors to first-line chemotherapy in unresectable locally advanced or metastatic ESCC has resulted in improvements in survival outcomes and has transformed modern clinical practice.

Pembrolizumab Immunotherapy

Pembrolizumab (Keytruda; Merck & Co, Inc) is a PD-1–blocking monoclonal antibody that was initially

FDA approved on July 30, 2019, as subsequent monotherapy for patients with recurrent, locally advanced, or metastatic ESCC with tumors expressing PD-L1 (combined positive score [CPS] ≥ 10), as determined by an FDA-approved test, with disease progression after 1 or more prior lines of systemic therapy.⁶ Pembrolizumab monotherapy is a category 1, preferred second-line treatment for patients with unresectable locally advanced, recurrent, or metastatic ESCC (when local therapy is not indicated) and a PD-L1 CPS of 10 or greater in the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN guidelines) for Esophageal and Esophagogastric Junction Cancers.⁴

In the first-line setting, pembrolizumab in combination with fluoropyrimidine-based and platinum-based chemotherapy received FDA approval on March 22, 2021, for the treatment of locally advanced or metastatic esophageal or gastroesophageal carcinoma that is not amenable to surgical resection or definitive chemoradiation.⁷ This approval was based on the double-blind, randomized, phase 3 KEYNOTE-590

trial (NCT03189719), in which 749 patients with previously untreated, unresectable locally advanced or metastatic esophageal cancer or gastroesophageal junction cancer were randomly assigned 1:1 to receive either pembrolizumab plus chemotherapy (5-fluorouracil and cisplatin) or chemotherapy alone for up to 35 cycles. Approximately 73% of all patients included in the trial specifically had ESCC (n = 548), 51% of all patients had a PD-L1 CPS of 10 or greater (n = 383), and 38% had both ESCC and PD-L1 CPS 10 or greater (n = 286).⁸

In KEYNOTE-590, the coprimary end point of overall survival (OS) in all major prespecified subgroups and the overall study population was met. In patients with both ESCC and a PD-L1 CPS of 10 or greater, the pembrolizumab-plus-chemotherapy treatment arm had an improved median OS of 13.9 months compared with 8.8 months in the chemotherapy-alone treatment arm (HR, 0.57; 95% CI, 0.43-0.75; $P < .0001$). In all patients with ESCC, pembrolizumab plus chemotherapy improved median OS compared with chemotherapy alone (12.6 months vs 9.8 months; HR, 0.72; 95% CI, 0.60-0.88; $P = .0006$). In all patients with a PD-L1 CPS of 10 or greater, pembrolizumab plus chemotherapy similarly improved median OS (13.5 months vs 9.4 months; HR, 0.62; 95% CI, 0.49-0.78; $P < .0001$). In the overall study population, pembrolizumab plus chemotherapy demonstrated clinical superiority (12.4 months vs 9.8 months; HR, 0.73; 95% CI, 0.62-0.86; $P < .0001$).⁸ Additionally, the coprimary end point of progression-free survival (PFS) in all major prespecified subgroups and the overall study population was met. In all patients with ESCC, there was an improvement in median PFS with pembrolizumab plus chemotherapy vs chemotherapy alone (6.3 months vs 5.8 months; HR, 0.65; 95% CI, 0.54-0.78; $P < .0001$). In all patients with a PD-L1 CPS of 10 or greater, there was similarly a substantial PFS benefit with pembrolizumab plus chemotherapy vs chemotherapy alone (7.5 months vs 5.5 months; HR, 0.51; 95% CI, 0.41-0.65; $P < .0001$). In the overall study population, pembrolizumab plus chemotherapy demonstrated clinical superiority (6.3 months vs 5.8 months; HR, 0.65; 95% CI, 0.55-0.76; $P < .0001$). However, a PFS analysis for the subgroup of patients

with both ESCC and a PD-L1 CPS of 10 or greater was not reported.⁸

Based on the results of the KEYNOTE-590 trial, pembrolizumab in combination with a fluoropyrimidine (5-fluorouracil or capecitabine) and a platinum-based agent (cisplatin or oxaliplatin) is a preferred first-line therapy for HER2 overexpression-negative patients with unresectable locally advanced, recurrent, or metastatic ESCC (when local therapy is not indicated) in the NCCN guidelines. Cisplatin-containing pembrolizumab regimens have a category 1 recommendation for a PD-L1 CPS of 10 or greater, and oxaliplatin-containing pembrolizumab regimens have a category 2A recommendation for a PD-L1 CPS of 10 or greater. Both platinum-based pembrolizumab regimens have a category 2B recommendation for a PD-L1 CPS of 10 or less.⁴

Nivolumab Immunotherapy

Nivolumab (Opdivo; Bristol Myers Squibb) is a PD-1-blocking monoclonal antibody that was initially approved on June 10, 2020, as subsequent monotherapy for patients with unresectable locally advanced, recurrent, or metastatic ESCC after prior fluoropyrimidine-based and platinum-based chemotherapy.⁹ Nivolumab monotherapy is a category 1, preferred subsequent therapy for patients with unresectable locally advanced, recurrent, or metastatic ESCC (when local therapy is not indicated) in the NCCN guidelines.⁴

More recently, nivolumab has shown efficacy as first-line therapy both in combination with chemotherapy and in combination with CTLA-4-targeting monoclonal antibody ipilimumab (Yervoy; Bristol Myers Squibb). On May 27, 2022, nivolumab in combination with fluoropyrimidine-based and platinum-based chemotherapy and nivolumab in combination with ipilimumab received FDA approval as first-line therapies for patients with advanced or metastatic ESCC.¹⁰ These approvals were based on the open-label, randomized, phase 3 CheckMate 648 trial (NCT03143153), in which 970 patients with previously untreated or recurrent (but who had not received previous systemic therapy for advanced disease), unresectable locally advanced, or metastatic ESCC were randomly assigned 1:1:1 to receive nivolumab

plus chemotherapy (5-fluorouracil and cisplatin), nivolumab plus ipilimumab (referred to as dual immunotherapy), or chemotherapy alone for up to 2 years. Among the trial participants, 49% had PD-L1 expression of 1% or greater ($n = 473$), approximately 7% had locoregional recurrent disease ($n = 71$), and 21% had distant recurrent disease ($n = 205$).¹¹

The coprimary end point of OS in the patient subpopulation of PD-L1 expression of 1% and greater and in the overall study population was met in both the nivolumab-plus-chemotherapy and the dual immunotherapy treatment arms. Patients with PD-L1 expression of 1% or greater in the nivolumab-plus-chemotherapy arm demonstrated an improved median OS vs chemotherapy alone (15.4 months vs 9.1 months; HR, 0.54; 99.5% CI, 0.37-0.80; $P < .001$). There was statistically significant improvement with nivolumab plus chemotherapy in the overall study population (13.2 months vs 10.7 months; HR, 0.74; 99.1% CI, 0.58-0.96; $P = .002$). Patients with PD-L1 expression of 1% or greater in the dual immunotherapy arm demonstrated an improved median OS vs chemotherapy alone (13.7 months vs 9.1 months; HR, 0.64; 98.6% CI, 0.46-0.90; $P = .001$). In the overall study population, dual immunotherapy improved median OS as well (12.7 months vs 10.7 months; HR, 0.78; 98.2% CI, 0.62-0.98; $P = .01$).¹¹

The coprimary end point of PFS in the patient subpopulation with PD-L1 expression of 1% or greater was met only in the nivolumab-plus-chemotherapy arm (6.9 months vs 4.4 months; HR, 0.65; 98.5% CI, 0.46-0.92; $P = .002$). However, there was not a significant difference in median PFS in the overall study population with nivolumab plus chemotherapy (5.8 months vs 5.6 months; HR, 0.81; 98.5% CI, 0.64-1.04; $P = .04$). Dual immunotherapy did not result in a significant difference in median PFS in patients with PD-L1 expression of 1% or greater (4.0 months vs 4.4 months; HR, 1.02; 98.5%, 0.73-1.43; $P = .90$). Because of the lack of statistical

significance in the subpopulation of PD-L1 expression of 1% or greater, PFS analysis was not conducted in the overall study population for the dual immunotherapy arm.¹¹

Based on the results of the CheckMate 648 study, nivolumab in combination with a fluoropyrimidine (5-fluorouracil or capecitabine) and a platinum-based agent (cisplatin or oxaliplatin) is a category 2A, preferred first-line therapy for HER2 overexpression–negative patients with unresectable locally advanced, recurrent, or metastatic ESCC (when local therapy is not indicated) in the NCCN guidelines. Nivolumab in combination with ipilimumab is additionally recommended as a category 2A, preferred first-line therapy in this patient population.⁴

Conclusion

Immunotherapy has been a widely explored treatment option in numerous solid tumor disease states, and recently it has been shown to have clinical benefit in unresectable locally advanced or metastatic ESCC as first-line therapy. Pembrolizumab plus chemotherapy demonstrated clinical superiority vs chemotherapy alone in median OS and median PFS in all major prespecified subgroups and in the overall study population in the KEYNOTE-590 trial.⁸ Both nivolumab-based regimens resulted in statistically significant improvements in median OS in the subgroup of PD-L1 expression of 1% or greater and in the overall study population.^{4,9,11} However, it should be noted that there were mixed results for nivolumab-based regimens in the PFS analyses across multiple subgroups and in the overall study population. These PFS interpretations should be analyzed in the context of differing statistical methods in the nivolumab study (98.5% CI compared with medical standard of 95% CI).¹¹ Additional immunotherapy research through large randomized clinical trials is needed to further improve survival outcomes in unresectable locally advanced or metastatic ESCC. ■

© VISIT PHARMACYTIMES.COM FOR REFERENCES.



Breast Cancer Research, Current Therapeutic Pipeline Provide Significant Advancements in Diagnosis, Treatment

Trends in treatment development involve more targeted, safe, and efficacious therapies.

RACHEL K. ANDERSON, PHARM.D, CSP



ABOUT THE AUTHOR
RACHEL K. ANDERSON, PHARM.D, CSP, is the clinical program manager at AllianceRx Walgreens Pharmacy.

OVER THE PAST several years, researchers have commanded significant innovation to improve the diagnosis, treatment, and prognosis for patients with breast cancer. Notable developments in early-stage breast cancer are improving outcomes by matching the right individualized treatment for patients to obtain the most benefit.^{1,2} Different preventive measures and treatment modalities are being studied, including advancements in screening techniques, modifiable risk factors, enhanced surgical options, and novel therapeutics uniquely targeting the disease.

Breast cancer is the most common type of cancer, accounting for 15% of all new cancer diagnoses.^{1,2} In the United States, more than 290,000 new cases are expected in 2022, with more than 43,000 estimated deaths.^{1,2} When included as a member of oncology patient care teams, specialty pharmacists are not only uniquely positioned to provide patients with advice on managing medications, but also can encourage screening, increase adherence, offer in-depth disease state education, and connect patients and caregivers with valuable resources.

Basics in Understanding Breast Cancer

Breast cancer begins when cells in 1 or both breasts begin to grow out of control, and it spreads by moving into the blood

or lymphatic system and is then carried throughout the body. Although breast cancer occurs most often in women, men can also be diagnosed with the disease.^{3,4}

Signs of breast cancer include changes in the size or shape of the breast, scaling, redness, swelling, dimpling or puckering in the skin, an inverted nipple, fluid other than breast milk from the nipple, or a lump in or near the breast or underarm area. Tests that examine the breasts are used to screen for cancer, including a clinical breast exam, mammogram, ultrasound, MRI, blood chemistry, and biopsy.^{3,4}

Several known risk factors may contribute to the development of breast cancer. Modifiable risk factors include physical activity level, weight, alcohol consumption, exogenous hormones, and certain aspects of a woman's reproductive history, such as age at first pregnancy and breastfeeding. Nonmodifiable risk factors include older age, genetic mutations, age at onset of menstruation and menopause, breast density, personal or family history of breast or ovarian cancer or certain noncancerous breast diseases, previous radiation therapy, and exposure to certain chemicals, such as the drug diethylstilbestrol.^{3,4,5}

Among women with breast cancer, less than 15% have a first-degree relative with the disease.⁶ Breast cancer can be caused by inherited mutations to the *BRCA1* or *BRCA2* tumor suppressor »



genes, but these mutations are uncommon, with an overall rate in the United States of approximately 1 in 400.⁷ There are many different possible mutations of *BRCA1/2*, and some increase the risk for cancer. The lifetime risk of breast cancer for women in the United States who do not have a *BRCA1/2* mutation is 13%.^{7,8} With certain *BRCA1/2* mutations, this risk increases to up to 75%.⁸

Different types of breast cancer are determined by the specific kinds of cells affected and are categorized by certain types of genes or proteins the cancer cells may generate, which are differentiated as hormone receptor–positive (HR+) or HR negative based on whether they have these receptors.^{3,4} HR+ breast cancer cells have either estrogen receptors (ER+), progesterone receptors, or both.^{3,4}

Approximately 15% to 20% of breast tumors have higher levels of HER2 protein, which helps breast cancer cells grow rapidly.⁹ Cancer cells with no to very low levels of ERs, progesterone receptors, and HER2 are called triple-negative breast cancer (TNBC). Knowing the HR status of the cancer allows the health care team to best determine how to approach treatment. Additionally, tumor cells are reviewed to determine both the grade and stage of the cancer; this information is then used to help guide decisions regarding treatment options.

The stage of the cancer defines how large the cancer is and whether it has spread, whereas grading determines how abnormal the cancer cells appear under a microscope.⁴ In general, the lower the grade number, the slower growing and less likely the cancer is to spread.^{3,4}

Current Treatment Options

A variety of therapies and a spectrum of medication classes, including biosimilars, are available to treat the many different types of breast cancer. Further, treatment guidelines continue to evolve, and selection depends on variables including tumor biology and molecular identity, HR+/- status, HER2 expression, tumor size, disease stage, nodal involvement, menopausal status, other comorbidities, and patient preferences.¹⁰

Today, the 6 types of standard treatment used are surgery, radiation, chemotherapy, hormone therapy, targeted therapy, and immunotherapy; patients with early-stage breast cancer typically undergo surgery, followed by adjuvant treatment.^{3,4} However, for

patients with advanced or metastatic breast cancer (mBC), the disease is usually treated with medication because surgical intervention is no longer an option. In certain cases, surgery may be an option used in the palliative care setting.^{3,4}

Several specific molecular targets represent the current armamentarium for tackling the disease. Because of its cytotoxic nature, traditional chemotherapy often comes with off-target adverse effects (AEs), but these regimens still have a role in treatment as monotherapy or in combinations. When started early, HR regimens are often as effective as traditional chemotherapy options and reduce the likelihood of experiencing many AEs.¹¹ HER2 has been successfully targeted with the combination of pertuzumab (Perjeta; Roche Holding AG) plus trastuzumab (Herceptin; Roche Holding AG) as well as margetuximab-cmkb (Margenza; MacroGenics, Inc) for certain patients, and more cytotoxic drug conjugates are making progress in clinical trials.¹²

PARP inhibitors combat breast cancer that expresses germline *BRCA1/2* mutations.¹³ The PD-1/PD-L1 pathway is another area of focus in the immunotherapy space when brain metastases may be involved.¹⁴ CDK4/6 inhibitors have been established as the standard of care in HR+/HER2-negative (HER2-) mBC but with no clear preference regarding which should be used first line.^{15,16} Blocking the PI3K signaling pathway combats *PIK3CA*-mutated tumors of HR+ mBC.¹⁷ Tyrosine kinase inhibitors play a role in fighting HER2+ mBC and may protect against brain metastases.¹⁸ The first monoclonal antibody targeting Trop-2, sacituzumab govitecan-hziy (Trodely; Gilead Sciences, Inc), was approved in 2021 for the treatment of metastatic TNBC, and more agents are being studied in this novel class (TABLE 1^{10,15,19}).²⁰

What to Watch for in Breast Cancer Therapeutics

The anticipated expansion of novel therapies in the near-term pipeline may continue to change the current standards of care in breast cancer and offer additional promising treatment options for patients. Several noteworthy updates have occurred in the field of breast cancer this year, particularly in developments for early-stage disease.

The 2022 American Society for Clinical Oncology (ASCO) Annual Meeting featured several important



TABLE 1. APPROVED THERAPEUTICS IN BREAST CANCER^{10,15,19}

Drug name	Lead company	Target(s)
Abemaciclib (Verzenio)	Eli Lilly and Company	CDK4/6
Ado-trastuzumab emtansine (Kadcyla)	Roche Holding AG	HER2 Microtubules (tubulin)
Alpelisib (Piqray)	Novartis AG	p110α/PIK3CA PI3K/AKT pathway
Anastrozole (Arimidex) ^a	ANI Pharmaceuticals, Inc	Aromatase
Atezolizumab (Tecentriq)	Roche Holding AG	PD-1/PD-L1 and PD-L2
Capecitabine (Xeloda) ^a	Roche Holding AG	Thymidylate synthase
Cyclophosphamide (Cytoxan) ^a	Baxter International Inc	DNA
Docetaxel (Taxotere) ^a	Sanofi	Microtubules (tubulin)
Docetaxel injection ^a	Various	Microtubules (tubulin)
Doxorubicin hydrochloride ^a	Various	DNA DNA synthesis Topoisomerase II
Epirubicin hydrochloride injection (Ellence) ^a	Pfizer Inc	DNA DNA synthesis Topoisomerase II (DNA gyrase)
Eribulin mesylate (Halaven)	Eisai Co, Ltd	Microtubules (tubulin)
Everolimus (Afinitor Disperz)	Novartis AG	mTOR/mTORC
Everolimus (Afinitor) ^a	Novartis AG	mTOR/mTORC
Exemestane (Aromasin) ^a	Pfizer Inc	Aromatase
Fam-trastuzumab deruxtecan-nxki (Enhertu)	Daiichi Sankyo Co, Ltd	HER2 Topoisomerase I
Fluorouracil injection ^a	Various	Thymidylate synthase
Fulvestrant (Faslodex) ^a	AstraZeneca	Estrogen receptor β Estrogen receptor α
Gemcitabine hydrochloride (Gemzar) ^a	Eli Lilly and Company	DNA synthesis
Gemcitabine hydrochloride in 0.9% sodium chloride injection (Infugem)	Sun Pharmaceutical Industries Ltd	DNA synthesis
Goserelin acetate (Zoladex)	TerSera Therapeutics LLC	Gonadotropin-releasing hormone receptor
Ixabepilone (Ixempra)	R-Pharm US	Microtubules (tubulin)
Lapatinib ditosylate (Tykerb) ^a	Novartis AG	EGFR HER2
Letrozole (Femara) ^a	Novartis AG	Aromatase
Margetuximab-cmkb (Margenza)	MacroGenics, Inc	HER2
Megestrol acetate (Megace) ^a	Bristol Myers Squibb	Progesterone receptor
Methotrexate sodium ^a	Various	DNA DNA synthesis
Neratinib (Nerlynx)	Puma Biotechnology, Inc	EGFR ErbB4/HER4 HER2

^aProducts have approved generic competition.

^bProducts have approved biosimilar competition.

(continued on next page)



TABLE 1. APPROVED THERAPEUTICS IN BREAST CANCER^{10,15,19} (continued)

Olaparib (Lynparza)	AstraZeneca	PARP
Paclitaxel (Taxol) ^a	Bristol Myers Squibb	Microtubules (tubulin)
Paclitaxel albumin-stabilized nanoparticle formulation (Abraxane) ^a	Bristol Myers Squibb Company	Microtubules (tubulin)
Palbociclib (Ibrance)	Pfizer Inc	CDK4/6
Pamidronate disodium (Aredia) ^a	Novartis AG	Osteoclast
Pembrolizumab (Keytruda)	Merck	PD-1/PD-L1 and PD-L2
Pertuzumab (Perjeta)	Roche Holding AG	HER2
Pertuzumab/trastuzumab/hyaluronidase-zzxf (Phesgo)	Roche Holding AG	HER2
Raloxifene hydrochloride (Evista) ^a	Eli Lilly and Company	Estrogen receptor α EDNRB
Ribociclib (Kisqali)	Novartis AG	CDK4/6
Ribociclib/letrozole (Kisqali Femara Co-Pack)	Novartis AG	Aromatase CDK4/6
Sacituzumab govitecan-hziy (Trodelvy)	Gilead Sciences, Inc	Trop-2
Talazoparib (Talzenna)	Pfizer Inc	PARP
Tamoxifen citrate ^a	Various	Estrogen receptor β Estrogen receptor α
Thiotepa (Tepadina) ^a	Amneal Pharmaceuticals, Inc	DNA
Toremifene (Fareston) ^a	Kyowa Kirin, Inc	Estrogen receptor β
Trastuzumab (Herceptin) ^b	Roche Holding AG	HER2
Trastuzumab and hyaluronidase-oysk (Herceptin Hylecta)	Roche Holding AG	HER2
Trastuzumab-anns (Kanjinti) ^b	Amgen Inc	HER2
Trastuzumab-dkst (Ogivri) ^b	Viartis Inc	HER2
Trastuzumab-dttb (Ontruzant) ^b	Organon & Co	HER
Trastuzumab-pkrb (Herzuma) ^b	Teva Pharmaceutical Industries Ltd	HER2
Trastuzumab-qyyp (Trazimera) ^b	Pfizer Inc	HER2
Tucatinib (Tukysa)	Seagen Inc	HER2
Vinblastine sulfate ^a	Various	Microtubules (tubulin)

^aProducts have approved generic competition.

^bProducts have approved biosimilar competition.

presentations, including²¹:

- tailoring adjuvant therapy;
- immunotherapy to improve response in patients with early-stage TNBC;
- tumor molecular profiling for predicting treatment response in patients with early-stage HER2+ disease;
- new tests to help identify patients with ER+ breast

cancer who would be most likely to benefit from chemotherapy;

- the use of an osteoporosis drug to decrease bone fractures and improve outcomes in patients receiving aromatase inhibitor therapy; and
- and commentary on older patients with early-stage breast cancer who may forgo chemotherapy.



TABLE 2. HIGHLIGHTS OF NEAR-TERM PIPELINE THERAPEUTICS FOR BREAST CANCER^{10,19,a}

Drug name	Lead company	Target(s)	Current phase
Camizestrant	AstraZeneca	Estrogen receptor (Selective estrogen receptor degrader)	3
Trilaciclib (Cosela)	G1 Therapeutics, Inc	CDK4/6	3
Datopotamab deruxtecan	Daiichi Sankyo Co, Ltd	TROP-2	3
Elacestrant	Menarini Group	Estrogen receptor β Estrogen receptor α (Selective estrogen receptor degrader)	NDA (2/17/2023)
Enobosarm	Veru Inc	Androgen receptors	3
Giredestrant	Roche Holding AG	Estrogen receptor (Selective estrogen receptor degrader)	3
GLSI-100	Greenwich LifeSciences	HER2	3
Imlunestrant	Eli Lilly and Company	Estrogen receptor (Selective estrogen receptor degrader)	3
Nivolumab (Opdivo)	Bristol Myers Squibb	Immune system PD-1/PD-L1 and PD-L2	3
Oral paclitaxel and encequidar (Oraxol)	Athenex, Inc	Microtubules (tubulin) P-glycoprotein	3 (Cancer Research Laboratory 3/1/21)
Veliparib	AbbVie Inc	PARP	3
SYD985 (Vic-trastuzumab duo-carmazine)	Byondis BV	HER2 DNA DNA synthesis Antibody-drug conjugate	BLA (5/12/23)
Niraparib (Zejula)	GSK	PARP	3

BLA, biologics license application; NDA, new drug application.

^aList is not all-inclusive.

A key treatment is fam-trastuzumab deruxtecan-nxki (Enhertu; Daiichi Sankyo Co, Ltd), which was recently approved based on the DESTINY-Breast03 clinical trial (NCT03529110) results for the treatment of adult patients with unresectable or HER2+ mBC who have received a prior anti-HER2-based regimen either in the metastatic setting or in the neoadjuvant or adjuvant setting and have developed disease recurrence during or within 6 months of completing therapy.¹⁰ Of note, fam-trastuzumab deruxtecan-nxki received a priority review and breakthrough therapy designation from the FDA and was also recently approved for the treatment of adult patients with unresectable or metastatic HER2-low breast cancer who have received a prior chemotherapy in the mBC setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy.¹⁹

HER2 low is a newly defined subset of HER2-

breast cancer in which there are some HER2 proteins on the cell surface but not enough to be classified as HER2+.^{6,19} The phase 3 DESTINY-Breast04 trial (NCT03734029) results showed fam-trastuzumab deruxtecan-nxki reduced the risk of disease progression or death and improved median overall survival (OS) by more than 6 months versus chemotherapy.²⁰ Fam-trastuzumab deruxtecan-nxki is the first HER2-directed therapy to demonstrate survival benefit in patients with HER2-low mBC compared with standard of care, and with the expanded approval, it has the potential to redefine treatment for approximately half of all patients with breast cancer.¹⁹

Another important takeaway from the ASCO meeting, based on the OlympiA clinical trial (NCT02032823), olaparib (Lynparza; AstraZeneca) was approved in 2022 for the adjuvant treatment of adult patients with deleterious or suspected



deleterious germline *BRCA*-mutated HER2– high-risk early breast cancer who have been treated with neoadjuvant or adjuvant chemotherapy.¹⁰

CDK4/6 inhibitor agents as a class have demonstrated an increase in progression-free survival (PFS) in clinical trials, but more recent postmarketing trials have highlighted several differences in efficacy, including OS statistics.^{15,19} If proven effective, combining CDK4/6 agents with endocrine therapies against HR+ mBCs may facilitate avoiding traditional chemotherapy.¹⁶ Analysts predict that an uptake in ribociclib (Kisqali; Novartis AG) utilization may occur as the result of its clinically significant OS data and could pave the way for it to potentially become the preferred agent in this class and open the door for potential contracting.^{15,19} Further, the phase 3 HARMONIA trial (NCT05207709) is slated to assist in understanding optimal treatment approaches for patients with HER2-enriched disease, a subtype that is associated with very poor prognosis and endocrine resistance.^{15,19} Another phase 3 trial, NATALEE (NCT03701334), is scheduled to evaluate ribociclib as adjuvant treatment for HR+/HER2– stages 2 and 3 breast cancers (TABLE 2^{10,19}).^{15,19}

Of note, an oral formulation of paclitaxel (Oraxol; Athenex, Inc) in combination with encephalid, a gastrointestinal tract-specific P-glycoprotein pump inhibitor that allows the drug to be orally absorbed, is being studied in a phase 3 trial.^{10,15,19} The product was compared with intravenous paclitaxel in patients with mBC, including those with HR+/HER+ disease, TNBC, and receptor status unknown.^{10,15,19} The oral form demonstrated a higher overall response rate and was associated with lower rates of neuropathy but higher rates of neutropenia.^{10,15,19} Drawbacks to the product include administration, which requires fasting for 9 hours per day for 3 consecutive days per week, and higher gastrointestinal toxicities.^{10,15,19}

Vic-trastuzumab duocarmazine is an investigational, next-generation anti-HER2 antibody-drug conjugate pursuing placement as treatment for third-line mBC and second line after ado-trastuzumab emtansine (Kadcyla; Roche Holding AG).^{10,15,20} The biologics license application was accepted for the treatment of patients with HER2+ unresectable, locally advanced mBC or mBC.^{10,15,19}

Several oral selective estrogen receptor degrader (SERD) drugs are in development for patients with

previously treated ER+/HER2– mBC.^{10,15,19} Their use is being investigated as second- and third-line options in postmenopausal women who have progressed with prior endocrine and targeted therapies, and studies suggest they may be most beneficial in *ESR1*-mutated tumors.^{10,15,19} Analysts estimate the market for SERDs could be worth at least \$2 billion to \$3 billion a year.¹⁵ Currently, elacestrant (Menarini Group and Radius Health, Inc) appears to have the most promising data from its phase 3 EMERALD trial (NCT03778931), meeting the primary end point of PFS.¹⁵ Giredestrant (Genentech, Inc) failed the primary end point of PFS in its aceLERA Breast Cancer trial (NCT04576455), but coopERA Breast Cancer (NCT04436744) is the first randomized study to show superior antiproliferative activity of an oral SERD vs an aromatase inhibitor in ER+/HER2– early breast cancer.^{15,19} Studies are ongoing to further assess the product's clinical benefit, and Roche plans to file for approval in second-line/third-line mBC in 2022.¹⁹

Supporting Patients With Breast Cancer by Engaging the Specialty Pharmacist

At AllianceRx Walgreens Pharmacy, everything our specialty pharmacists do centers on the well-being of our patients. Being given a potentially life-altering diagnosis like breast cancer can be overwhelming, but starting a specialty medication shouldn't be. Medication therapy management for patients involves education with drug-specific and disease-state counseling, emphasizing the importance of adherence to the prescribed regimen, guiding patients in preventing and managing AEs, and monitoring for any potential drug interactions.

Specialty pharmacists may also help point patients in the right direction for additional resources and are available to address any concerns or questions patients and caregivers may have regarding therapy. Because specialty drugs are often associated with higher costs, specialty pharmacies can help patients explore all options to find the most affordable care. This may include searching for various foundations and supporting patients in applying for co-pay assistance or other pharmacy-related financial assistance programs when available. Working together with other health care providers, specialty pharmacists can serve as therapeutic navigators helping to ensure patients achieve the most optimal outcomes, both clinically and financially.



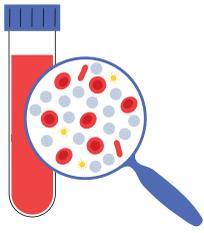
Conclusion

Significant support for breast cancer awareness, research, and funding has paved the way for advancements in the diagnosis and treatment of the disease. Survival rates have increased, and the number of deaths associated with breast cancer is steadily declining, largely because of factors such as early detection, personalized approaches to treatment, and a better understanding of the disease overall.^{10,15,19} The growing trends in breast cancer treatment involve more targeted, safer, and efficacious therapies that better align with patient goals and outcomes. The advancements in research offer astounding opportunities focused on overall survival, historically treatment-resistant disease, and reducing disease progression.^{10,15,19} Analysts expect more effective oral options for HER2+ breast cancer, with de-escalation of chemotherapy or surgery as superior choices.^{10,15,19}

Specialty pharmacists, such as those at AllianceRx Walgreens Pharmacy, understand treatment decisions are very personal, and patients should discuss all options with their providers in a shared decision-making process to agree on a treatment plan. As standards of practice continue to evolve, specialty pharmacists can help develop individualized management plans for patients with breast cancer and support them throughout their treatment journey. Additionally, a key focus for pharmacists moving forward in the battle against breast cancer is continuing to encourage patients to schedule breast cancer screenings because early detection plays a major role in successfully overcoming this disease. ■

REFERENCES

1. Common cancer types. National Cancer Institute. Updated May 10, 2022. Accessed July 27, 2022. www.cancer.gov/types/common-cancers#:~:text=The%20most%20common%20type%20of,are%20combined%20for%20the%20list
2. Cancer stat facts: female breast cancer. National Cancer Institute: Surveillance, Epidemiology, and End Results Program. 2022. Accessed July 27, 2022. seer.cancer.gov/statfacts/html/breast.html
3. Breast Cancer Prevention (PDQ)—Patient Version. National Cancer Institute. Updated December 10, 2021. Accessed July 27, 2022. www.cancer.gov/types/breast/patient/breast-prevention-pdq
4. Breast cancer. The American Cancer Society. Accessed July 27, 2022. www.cancer.org/cancer/breast-cancer.html
5. What are the risk factors for breast cancer? CDC. Updated Sept 26, 2022. Accessed July 27, 2022. www.cdc.gov/cancer/breast/basic_info/risk_factors.htm
6. Lynch JA, Venne V, Berse B. Genetic tests to identify risk for breast cancer. *Semin Oncol Nurs*. 2015;31(2):100-107. doi:10.1016/j.soncn.2015.02.007
7. *BRCA1* and *BRCA2* inherited gene mutations in women. Susan G. Komen. Updated March 21, 2022. Accessed September 16, 2022. <https://www.komen.org/breast-cancer/risk-factor/topics/brca-genes>
8. BRCA overview. Basser Center for BRCA. Accessed September 16, 2022. <https://www.basser.org/brca>
9. Breast cancer hormone receptor status. American Cancer Society. Updated November 8, 2021. Accessed July 27, 2022. www.cancer.org/cancer/breast-cancer/understanding-a-breast-cancer-diagnosis/breast-cancer-hormone-receptor-status.html
10. Oncology: breast cancer. IPD Analytics. Accessed July 27, 2022. secure.ipdanalytics.com/User/Pharma/RxStrategy/Page/bfbb1763-919a-4303-b614-8cdce426b48f#section-group-332627
11. Martí C, Sánchez-Méndez JI. The present and future of neoadjuvant endocrine therapy for breast cancer treatment. *Cancers (Basel)*. 2021;13(11):2538. doi:10.3390/cancers13112538
12. FDA approves margetuximab for metastatic HER2-positive breast cancer. FDA. Updated December 17, 2020. Accessed July 27, 2022. www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-margetuximab-metastatic-her2-positive-breast-cancer
13. Tung NM, Robson ME, Ventz S, et al. TBCRC 048: phase II study of olaparib for metastatic breast cancer and mutations in homologous recombination-related genes. *J Clin Oncol*. 2020;38(36):4274-4282. doi:10.1200/jco.20.02151
14. Kim JS, Kim IA. Evolving treatment strategies of brain metastases from breast cancer: current status and future direction. *Ther Adv Med Oncol*. 2020;12:1758835920936117. doi:10.1177/1758835920936117
15. IPD Analytics. Strategy reports: the evolving landscape of CDK 4/6 inhibitors in metastatic breast cancer. July 25, 2022. Accessed July 27, 2022. secure.ipdanalytics.com/IPDAnalytics_RxInsights_Evolving_Landscape_of_CDK_4_and_6_Inhibitors_in_Metastatic_Breast_Cancer_07_2022.pdf
16. Tolaney SM, Wardley AM, Zambelli S, et al. Abemaciclib plus trastuzumab with or without fulvestrant versus trastuzumab plus standard-of-care chemotherapy in women with hormone receptor-positive, HER2-positive advanced breast cancer (monarchHER): a randomised, open-label, phase 2 trial. *Lancet Oncol*. 2020;21(6):763-775. doi:10.1016/s1470-2045(20)30112-1
17. Piqray. Prescribing Information. Novartis Pharmaceuticals Corp; May 2022. Accessed July 27, 2022. www.novartis.com/us-en/sites/novartis_us/files/piqray.pdf
18. Garcia-Alvarez A, Papakonstantinou A, Oliveira M. Brain metastases in HER2-positive breast cancer: current and novel treatment strategies. *Cancers (Basel)*. 2021;13(12):2927. doi:10.3390/cancers13122927
19. Biomedtracker. Informa Pharma Intelligence. Accessed September 6, 2022. biomed-tracker.com
20. FDA grants regular approval to sacituzumab govitecan for triple-negative breast cancer. FDA. Updated April 8, 2021. Accessed July 27, 2022. www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-regular-approval-sacituzumab-govitecan-triple-negative-breast-cancer
21. ASCO 2022: early-stage breast cancer updates. Breast Cancer Research Foundation. July 15, 2022. Accessed July 27, 2022. www.bcrf.org/blog/asco-2022-early-stage-breast-cancer-research-updates-bcrf/



Treatment-Free Remission in Chronic Myeloid Leukemia

Targeted therapies have greatly improved patient outcomes over the past 20 years.

CAROLINE MCCASLIN, PHARM.D AND JONATHAN COHEN, PHARM.D, BCOP



ABOUT THE AUTHORS

CAROLINE MCCASLIN, PHARM.D, is a postgraduate year 2 oncology pharmacy resident at University of Washington Medicine and Fred Hutchinson Cancer Center in Seattle, Washington.

JONATHAN COHEN, PHARM.D, BCOP, is a clinical pharmacy specialist at University of Washington Medicine and the Fred Hutchinson Cancer Center in Seattle, Washington.

CHRONIC MYELOID LEUKEMIA (CML) is a myeloproliferative neoplasm that makes up 15% of new adult leukemia diagnoses; the average age at diagnosis is 64 years.¹ CML is defined by the presence of the Philadelphia (Ph) chromosome, characterized by chromosomal translocation t(9;22), which is a product of the fusion of the *BCR* gene and the *ABL1* gene.² This fusion leads to a constitutively active tyrosine kinase, resulting in the aberrant division of myeloid cells. Following the introduction of targeted therapies, outcomes for patients with CML have improved over the past 20 years.

History of CML

There are 3 phases of CML: chronic, accelerated, and blast. At the time of diagnosis, most patients will present in chronic. Chronic CML can transform into accelerated or blast at any time. Risk stratification of disease transformation to accelerated or blast and related outcomes have been assessed using prognostic tools such as Sokal or Hasford scores and more recently the European Treatment and Outcome Study long-term survival score.³

Prior to the discovery of the Ph chromosome and introduction of BCR-ABL1 tyrosine kinase inhibitors (TKIs), the prognosis for patients with CML was poor, with a 10-year survival rate of 20%.² Pre-TKI therapy

options included busulfan (Busulfex; Otsuka America Pharmaceutical, Inc), hydroxyurea (Hydrea; Bristol Myers Squibb), interferon beta-1a (Rebif; Merck KGaA), and, for a small subset of patients, hematopoietic stem cell transplant.⁴

Today, TKIs are the mainstay of therapy and transplant remains a potentially curative therapy option for select patients. In 2001, imatinib (Gleevec; Novartis Pharmaceuticals Corporation) became the first FDA-approved TKI for CML, targeting BCR-ABL1. Since the approval of this first-generation TKI, and the subsequent approval of second- and third-generation agents, the 10-year survival rate of patients with CML has improved by 80% to 90%.²

TKI Considerations

In the era of TKI therapy, treatment response is largely divided into 3 categories: hematologic, cytogenetic, and molecular. Furthermore, patients with increased depth and rapidity of response are more likely to have durable responses and improved long-term outcomes. With TKI therapy, patients with CML are expected to have a “normal” life span that, depending on their age at the time of diagnosis, can mean long-term management of adverse effects (AEs) and potential financial burden.

For example, serious TKI-associated AEs include pleural effusions and »



TABLE 1. IMPORTANT RESPONSE AND RELAPSE CRITERIA IN CML^{3,a}

Response/relapse	Definition
Complete hematologic response	<ul style="list-style-type: none"> Complete normalization of peripheral blood counts with leukocyte count $<10 \times 10^9/L$ Platelet count $<450 \times 10^9/L$ No immature cells, such as myelocytes, promyelocytes, or blasts in peripheral blood No signs and symptoms of disease with resolution of palpable splenomegaly
Cytogenetic response	<ul style="list-style-type: none"> CCyR: no Ph-positive metaphases MCyR: 0% to 35% Ph-positive metaphases
Molecular response	<ul style="list-style-type: none"> MMR BCR-ABL1 IS $\leq 0.1\%$ or ≥ 3-log reduction in BCR-ABL1 transcripts from the standardized baseline if qPCR IS is not available DMR: MR 4.0-fold reduction: BCR-ABL1 IS $\leq 0.01\%$ or MR 4.5-fold reduction: BCR-ABL1 IS $\leq 0.0032\%$
Relapse	<ul style="list-style-type: none"> Any sign of loss of hematologic response Any sign of loss of CCyR or its molecular response correlate defined as an increase in BCR-ABL1 transcript to $>1\%$ 1-log increase in BCR-ABL1 transcript levels with loss of MMR

CCyR, complete cytogenetic response; CML, chronic myeloid leukemia; DMR, deep molecular response; IS, international scale; MCyR, major cytogenetic response; MMR, major molecular response; qPCR, quantitative polymerase chain reaction test.
*Adapted from National Comprehensive Cancer Network Guidelines.

myelosuppression with dasatinib (Sprycel; Bristol Myers Squibb); cardiovascular events (specifically corrected QT interval prolongation and metabolic effects) with nilotinib (Tasigna; Novartis Pharmaceuticals Corporation); diarrhea with bosutinib (Bosulif; Pfizer Inc), and several severe AEs necessitating a boxed warning with ponatinib (Iclusig; Takeda Pharmaceuticals America, Inc).² The cost of generic imatinib ranges from \$4400 to \$82,000 annually, and costs of second-generation TKIs (dasatinib, nilotinib, and bosutinib) all exceed \$150,000 annually.^{2,5}

Trials Assessing TKI Discontinuation

Because of TKI-induced toxicity, cost considerations, and the observed durable, deep responses to TKI therapy, studies have evaluated the outcomes of patients who have achieved these deep responses and subsequently discontinued their TKI therapy.

Increasing data to support TKI discontinuation and maintained remission, or treatment-free remission, have started discussions of a relative “cure” for patients with CML. Most studies that have evaluated the feasibility of TKI discontinuation have been

TABLE 2. CRITERIA FOR TKI DISCONTINUATION^{3,a}

Aged ≥ 18 years
Chronic-phase CML with no prior history of accelerated- or blast-phase CML
On approved TKI therapy for at least 3 years
Prior evidence of quantifiable BCR-ABL1 transcript
Stable MR (MR 4.0-fold reduction; BCR-ABL1 IS $\leq 0.01\%$) for ≥ 2 years, as documented on at least 4 tests performed at least 3 months apart

CML, chronic myeloid leukemia; IS, international scale; MR, molecular response; TKI, tyrosine kinase inhibitor.

*Adapted from National Comprehensive Cancer Network guidelines.

smaller and focused on specific TKIs with variable discontinuation criteria. The National Comprehensive Cancer Network (NCCN) has published standardized response criteria for CML (TABLE 1).³

In the NCCN criteria, deep molecular response is defined as 4.0-fold or 4.5-fold reduction in BCR-ABL1 transcripts (BCR-ABL1 international scale [IS] $\leq 0.01\%$, BCR-ABL1 IS $\leq 0.0032\%$, respectively). Complete molecular response (CMR) is noted as being achieved when BCR-ABL1 transcripts are undetectable by quantitative polymerase chain reaction test (qPCR). In cases of relapse, most patients are able to achieve disease control again upon resumption of TKI therapy.

An early study evaluating treatment discontinuation was the STIM trial (NCT00478985), in which 100 patients were enrolled who had taken imatinib for a minimum of 3 years and had at least 2 years of continued CMR. Relapse was defined as the loss of CMR, which was defined as BCR-ABL1 transcript positive qPCR (ratio of BCR-ABL to ABL of 10^{-5} or more). With a median overall follow-up of 17 months, 42 (61%) of 69 patients with at least 12 months of follow-up relapsed within 3 to 6 months of discontinuation. After restarting imatinib, 16 patients (38%) once again achieved CMR within a median of 3 months.⁶

In the largest discontinuation trial to date, the EURO-SKI trial (NCT01596114) enrolled 758 patients with the objective to determine criteria to discontinue TKI therapy (imatinib, nilotinib, or dasatinib) and the duration of major molecular response (MMR) after discontinuation. The trial investigators found that for patients with CML who discontinued their TKI after 3 years and had achieved a deep molecular response for at least 1 year, molecular relapse-free survival was 61% and 50% at 6 months and 24 months, respectively.



Of the 755 evaluable patients, 371 (49%) relapsed (MMR > 0.1% BCR-ABL1 IS) after discontinuation of their TKI.⁷

Upon TKI reinitiation, 321 (86%) of 371 patients were able to achieve disease control after relapse. Of note, 2 patients lost MMR despite restarting TKI therapy. Several other studies have evaluated TKI discontinuation and found similar results, which are summarized in the NCCN guidelines.³

NCCN has published guidelines for TKI discontinuation, which stem from supporting data from trials (TABLE 2³). Of note, the novel TKI asciminib (Scemblix; Novartis Pharmaceuticals Corporation) was approved by the FDA in 2021 for patients with CML who were previously treated with 2 or more TKIs. Currently, there are insufficient data to consider patients on asciminib for TKI discontinuation and treatment-free remission.²

Patient Perspective

Patient perspective should be considered when weighing TKI discontinuation. Sharf et al surveyed more than 1000 patients with CML regarding their perspectives on discontinuation. After a discussion with their provider, 55% (n = 555) of patients were still concerned about the attempt being unsuccessful and the potential for relapsed disease. Of the 494 patients who reported having stopped treatment, 32% (n = 159) of them reported a CML relapse, requiring TKI reinitiation. Upon relapse, 59% (n = 81) of these patients strongly agreed/agreed that they were feeling scared/anxious, and 91% (n = 138) strongly agreed/agreed they were feeling disappointed.⁸

As evidenced by this survey, sharing decision-making with the patient and providing emotional support are important factors during TKI discontinuation. Within 1 to 2 months of stopping therapy, 25% to 30% of patients may also experience TKI withdrawal syndrome, which is characterized by diffuse musculoskeletal pain and can be managed with nonsteroidal anti-inflammatory agents or steroids.⁹ Upon TKI resumption, this pain typically resolves; however, it is not recommended to resume TKI therapy unless the patient has a CML relapse. Patients should be counseled on TKI withdrawal syndrome and its management prior to TKI discontinuation.

Pharmacist Role

TKI discontinuation is reasonable in a subset of patients with CML who have achieved deep molecular response for at least 2 years and have been on TKI therapy for at least 3 years. Routine surveillance is needed to ensure MMR is sustained and to monitor for blast crisis, although its incidence is rare: Of the 371 patients who relapsed off TKI therapy in the EURO-SKI trial, none progressed to blast CML.⁷

Pharmacists can play an important role in patient counseling with respect to discontinuation and management of TKI withdrawal syndrome. The decision to discontinue TKI therapy should be a shared decision with the patient after careful consideration and discussion. ■

REFERENCES

1. Key statistics for chronic myeloid leukemia. American Cancer Society. Updated January 12, 2022. Accessed September 10, 2022. <https://www.cancer.org/cancer/chronic-myeloid-leukemia/about/statistics.html>
2. Jabbour E, Kantarjian H. Chronic myeloid leukemia: 2020 update on diagnosis, therapy and monitoring. *Am J Hematol*. 2020;95(6):691-709. doi:10.1002/ajh.25792
3. NCCN. Clinical Practice Guidelines in Oncology. Chronic Myeloid Leukemia, version 1.2023. Accessed September 10, 2022. https://www.nccn.org/professionals/physician_gls/pdf/cml.pdf
4. Goldman JM. Chronic myeloid leukemia: a historical perspective. *Semin Hematol*. 2010;47(4):302-311. doi:10.1053/j.seminhematol.2010.07.001
5. Shih YT, Cortes JE, Kantarjian HM. Treatment value of second-generation BCR-ABL1 tyrosine kinase inhibitors compared with imatinib to achieve treatment-free remission in patients with chronic myeloid leukaemia: a modelling study. *Lancet Haematol*. 2019;6(8):e398-e408. Published correction appears in *Lancet Haematol*. 2020;7(1):e11.
6. Mahon FX, Réa D, Guilhot J, et al; Intergroupe Français des Leucémies Myéloïdes Chroniques. Discontinuation of imatinib in patients with chronic myeloid leukaemia who have maintained complete molecular remission for at least 2 years: the prospective, multicentre Stop Imatinib (STIM) trial. *Lancet Oncol*. 2010;11(11):1029-1035. doi:10.1016/S1470-2045(10)70233-3
7. Saussele S, Richter J, Guilhot J, et al; EURO-SKI investigators. Discontinuation of tyrosine kinase inhibitor therapy in chronic myeloid leukaemia (EURO-SKI): a prespecified interim analysis of a prospective, multicentre, non-randomised, trial. *Lancet Oncol*. 2018;19(6):747-757. doi:10.1016/S1470-2045(18)30192-X
8. Sharf G, Marin C, Bradley JA, et al. Treatment-free remission in chronic myeloid leukemia: the patient perspective and areas of unmet needs. *Leukemia*. 2020;34(8):2102-2112. doi:10.1038/s41375-020-0867-0
9. Sweet K. Starting tyrosine kinase inhibitor cessation in chronic-phase chronic myeloid leukemia patient. *The Hematologist*. 2018;15(4). doi:10.1182/hem.V15.4.8717



Neoadjuvant, Adjuvant Therapy for Resectable NSCLC Progresses With Immunotherapy, Targeted Therapy

Significant advancements have changed the treatment landscape and clinical practice procedures.

KEVIN PANG, PHARM D AND NONI THEOCHARIDES, PHARM D CANDIDATE



ABOUT THE AUTHORS

KEVIN PANG, PHARM D, is an associate scientist at the National Comprehensive Cancer Network.

NONI THEOCHARIDES

is a PharmD candidate at Rutgers University Ernest Mario School of Pharmacy.

NON-SMALL CELL LUNG cancer (NSCLC) is a disease state that has undergone substantial advancements in the immunotherapy and targeted therapy spaces, with immune checkpoint inhibitors and tyrosine kinase inhibitors (TKIs) becoming feasible treatment options for advanced or metastatic disease. However, surgery continues to be the preferred treatment approach in resectable NSCLC and has historically been coupled with neoadjuvant or adjuvant chemotherapy.

Neoadjuvant Therapy

To support the use of neoadjuvant chemotherapy in operable disease, the NSCLC Meta-analysis Collaborative Group conducted a comprehensive assessment of 15 randomized, controlled trials that included 2385 patients and compared preoperative chemotherapy vs surgery alone. Ten trials studied neoadjuvant chemotherapy alone, and 5 trials studied neoadjuvant chemotherapy followed by adjuvant chemotherapy (usually in responders). Eight trials included postoperative radiotherapy in addition to the randomized intervention in both treatment arms. The HR for overall survival (OS) across all 15 trials was 0.87 (95% CI, 0.78-0.96; $P=.007$), corresponding to a 5-year absolute benefit of 5% from neoadjuvant chemotherapy.¹

Neoadjuvant immunotherapy is a recent development in the treatment of early-stage resectable NSCLC. One such therapy is nivolumab (Opdivo; Bristol

Myers Squibb), which is a PD-1–blocking human monoclonal antibody that restores the function of existing antitumor T cells and has been proven efficacious in numerous solid tumors, including advanced or metastatic NSCLC. On March 4, 2022, nivolumab in combination with platinum-doublet chemotherapy received FDA approval and is recommended by the National Comprehensive Cancer Network (NCCN) as neoadjuvant therapy for patients with resectable stage IB (tumors ≥ 4 cm or node positive) to stage IIIA NSCLC (category 2A).^{2,3} The approved dosing regimen is nivolumab 360 mg administered on the same day as platinum-doublet chemotherapy every 3 weeks for 3 cycles.

This approval is based on the randomized, open-label, phase 3 CheckMate 816 trial (NCT02998528), which randomly assigned 358 patients with resectable stage IB (≥ 4 cm tumor size) to stage IIIA NSCLC in a 1:1 ratio to receive either neoadjuvant nivolumab plus platinum-doublet chemotherapy or platinum-doublet chemotherapy alone. During the trial, each patient underwent 3 cycles of their respective treatment followed by resection. The primary efficacy end points of CheckMate 816 included event-free survival (EFS) and pathological complete response of 0% viable tumor in resected lung and lymph nodes.⁴

The neoadjuvant nivolumab-plus-chemotherapy treatment arm had a median EFS of 31.6 months (95% CI, 30.2–not



estimable [NE]), whereas the chemotherapy-alone treatment arm had a median EFS of 20.8 months (95% CI, 14.0-26.7). The HR for disease recurrence, disease progression, or death was 0.63 (97.38% CI, 0.43-0.91; $P=.005$). Additionally, 24.0% of patients in the nivolumab-plus-chemotherapy arm had a pathological complete response (95% CI, 18.0-31.0) compared with 2.2% of patients in the chemotherapy-alone arm (95% CI, 0.6-5.6); the odds ratio of this finding was 13.94 (99% CI, 3.49-55.75; $P<.001$). Further, 33.5% of patients in the nivolumab-plus-chemotherapy group and 36.9% of patients in the chemotherapy-alone group experienced a grade 3 or 4 treatment-related adverse event.⁴

Adjuvant Therapy

To support the use of adjuvant chemotherapy in completely resected NSCLC, the Lung Adjuvant Cisplatin Evaluation Collaborative Group analyzed the 5 largest randomized, controlled trials (4584 patients) of cisplatin-based postoperative chemotherapy vs surgery alone. Patients who received postoperative radiotherapy in addition to their randomized intervention were also included. Over a 5-year horizon, the HR for OS was 0.89 (95% CI, 0.82-0.96; $P=.005$), corresponding to a 5-year absolute benefit of 5.4% from adjuvant chemotherapy.⁵

Currently, adjuvant therapy in resectable NSCLC consists of platinum-based chemotherapy followed by a targeted agent or immunotherapy, if eligible. Patients may be treated with certain agents if the surgical tissue or biopsy meets specific biomarker thresholds or if they have confirmed genetic mutations. Thus, because of the potential for targeted therapy or immunotherapy use in resected NSCLC with negative margins, biomarker testing for *EGFR* mutation (stage IB-III A) and PD-L1 status (stage II-III A) on surgical tissue or biopsy is recommended.³

Atezolizumab (Tecentriq; Genentech, Inc) is a PD-L1 inhibitor that is FDA approved and recommended by NCCN guidelines for patients with completely resected stage IIB to III A NSCLC or high-risk stage IIA NSCLC with PD-L1 of 1% or greater who received previous adjuvant chemotherapy (category 2A).^{3,6} This approval is based on the randomized,

open-label, phase 3 IMpower010 trial (NCT02486718), in which 1005 patients with completely resected stage IB to III A NSCLC were randomly assigned 1:1 to receive either atezolizumab 1200 mg every 21 days for 1 year or best supportive care alone after 1 to 4 cycles of adjuvant platinum-based chemotherapy. The primary end points of IMpower010 were disease-free survival (DFS) in stage II to III A NSCLC with PD-L1 expression of 1% or greater, DFS in all stage II to III A NSCLC regardless of PD-L1 expression, and DFS in the intention-to-treat (ITT) population.⁷

In the subpopulation with stage II to III A NSCLC with PD-L1 of 1% or greater ($n=476$), atezolizumab improved median DFS compared with best supportive care alone (HR, 0.66; 95% CI, 0.50-0.88; $P=.0039$). In the entire stage II to III A population ($n=882$), regardless of PD-L1 expression, atezolizumab similarly improved median DFS compared with best supportive care alone (HR, 0.79; 95% CI, 0.64-0.96; $P=.020$). In the ITT population encompassing stage IB to III A NSCLC ($n=1005$), the HR for median DFS was 0.81 (95% CI, 0.67-0.99; $P=.040$). Although the upper boundary for the 95% CI was not technically crossed, the authors did not consider this HR statistically significant. OS analyses were not formally conducted because the primary end point of DFS in the ITT population was not met and median OS data were immature.⁷

Osimertinib (Tagrisso; AstraZeneca) is an *EGFR* TKI that is FDA approved and recommended by NCCN guidelines for patients with completely resected stage IB to III A *EGFR*-mutated (exon 19 deletion or exon 21 L858R) NSCLC who have received previous adjuvant chemotherapy or are ineligible to receive platinum-based chemotherapy (category 2A).^{3,8} This approval is based on the randomized, double-blind, phase 3 ADAURA trial (NCT02511106), in which 682 patients with completely resected *EGFR* mutation-positive NSCLC were randomly assigned 1:1 to receive either osimertinib 80 mg orally daily or placebo for 3 years. Each stage of NSCLC (stage IB, II, and III A) was evenly represented in the overall study population. The prevalence of *EGFR* exon 19 deletion or *EGFR* exon 21 L858R mutations was 55% and 45%, respectively, with approximately 60% of patients in both treatment »



arms receiving platinum-based adjuvant chemotherapy prior to randomization.⁹

The primary efficacy end point of DFS in the stage II to IIIA NSCLC subpopulation (n=470) was met. Further, 90% of patients in the osimertinib treatment arm were alive and disease free at 24 months compared with 44% in the placebo treatment arm (HR, 0.17; 99.06% CI, 0.11-0.26; $P < .001$). The median DFS was not reached in the osimertinib arm (95% CI, 38.8-NE), and the median DFS in the placebo arm was 19.6 months (95% CI, 16.6-24.5). In the overall population encompassing stage IB to IIIA disease (n=682), there was a similarly statistically significant survival benefit in DFS at 24 months with osimertinib vs placebo (HR, 0.20; 99.12% CI, 0.14-0.30; $P < .001$).⁹

Among patients who received platinum-based adjuvant chemotherapy prior to randomization, osimertinib significantly improved DFS at 24 months vs placebo (HR, 0.16; 95% CI, 0.10-0.26). Similarly, patients who did not receive previous adjuvant chemotherapy had improved DFS at 24 months with osimertinib vs placebo (HR, 0.23; 95% CI, 0.13-0.40). Regardless of prior treatment with platinum-based adjuvant chemotherapy, osimertinib following surgery demonstrated clinical superiority vs placebo in completely resected stage IB to IIIA *EGFR* mutation-positive NSCLC.⁹

Conclusion

Significant advancements in neoadjuvant therapy and adjuvant therapy were made recently, which ultimately have changed clinical practice procedures. Neoadjuvant therapy consists of platinum-doublet chemotherapy but now may be supplemented with an immunotherapy. Further, patients who received neoadjuvant nivolumab plus chemotherapy were found to experience an improved median EFS and an improved pathological complete response of 0% viable tumor upon resection compared with neoadjuvant chemotherapy alone.⁴

Additionally, the available adjuvant treatment options have expanded to include either an immunotherapy or an *EGFR* TKI for eligible patients. Atezolizumab has demonstrated significant improvements vs best supportive care alone in median DFS for patients with completely resected stage II to IIIA NSCLC

who received previous adjuvant chemotherapy.⁷ Also, osimertinib has demonstrated clinical superiority vs placebo in DFS at 24 months for patients with completely resected stage IB to IIIA *EGFR*-mutated NSCLC, regardless of prior treatment with platinum-based adjuvant chemotherapy.⁹ Further improvements in the treatment landscape of resectable NSCLC are underway with additional well-designed clinical trials in the neoadjuvant or adjuvant treatment setting. ■

REFERENCES

1. NSCLC Meta-analysis Collaborative Group. Preoperative chemotherapy for non-small-cell lung cancer: a systematic review and meta-analysis of individual participant data. *Lancet*. 2014;383(9928):1561-1571. doi:10.1016/S0140-6736(13)62159-5
2. FDA approves neoadjuvant nivolumab and platinum-doublet chemotherapy for early-stage non-small cell lung cancer. FDA. Updated March 4, 2022. Accessed October 20, 2022. <https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-neoadjuvant-nivolumab-and-platinum-doublet-chemotherapy-early-stage-non-small-cell-lung>
3. NCCN. Clinical Practice Guidelines in Oncology. Non-small cell lung cancer, version 5.2022. Accessed October 20, 2022. https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf
4. Forde PM, Spicer J, Lu S, et al; CheckMate 816 Investigators. Neoadjuvant nivolumab plus chemotherapy in resectable lung cancer. *N Engl J Med*. 2022;386(21):1973-1985. doi:10.1056/NEJMoa2202170
5. Pignon JP, Tribodet H, Scagliotti GV, et al; LACE Collaborative Group. Lung adjuvant cisplatin evaluation: a pooled analysis by the LACE Collaborative Group. *J Clin Oncol*. 2008;26(21):3552-3559. doi:10.1200/JCO.2007.13.9030
6. FDA approves atezolizumab as adjuvant treatment for non-small cell lung cancer. FDA. Updated October 15, 2021. Accessed October 20, 2022. <https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-atezolizumab-adjuvant-treatment-non-small-cell-lung-cancer>
7. Felip E, Altorki N, Zhou C, et al; IMpower010 Investigators. Adjuvant atezolizumab after adjuvant chemotherapy in resected stage IB-IIIa non-small-cell lung cancer (IMpower010): a randomised, multicentre, open-label, phase 3 trial. *Lancet*. 2021;398(10308):1344-1357. doi:10.1016/S0140-6736(21)02098-5
8. FDA approves osimertinib as adjuvant therapy for non-small cell lung cancer with *EGFR* mutations. FDA. Updated December 18, 2020. Accessed October 20, 2022. <https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-osimertinib-adjuvant-therapy-non-small-cell-lung-cancer-egfr-mutations>
9. Wu YL, Tsuboi M, He J, et al; ADAURA Investigators. Osimertinib in resected *EGFR*-mutated non-small-cell lung cancer. *N Engl J Med*. 2020;383(18):1711-1723. doi:10.1056/NEJMoa2027071

PTCE WOULD LIKE TO ACKNOWLEDGE MERCK & CO., INC FOR THEIR GENEROUS SUPPORT OF PHARMACIST EDUCATION.

Immune Revolution in Cutaneous Melanoma

SURVIVAL RATES IN all stages of cutaneous melanoma have markedly improved due to the approval of multiple new agents and regimens over the past decade. Laura M. Alwan, PharmD, BCOP, dove into the data prompting the shift in the treatment landscape in a live **2022 Directions in Oncology Pharmacy®** conference session titled “The Role of ICIs in Cutaneous Melanoma: Evaluating Therapeutic Trends.”

Alwan guided pharmacists through the treatment paradigm for cutaneous melanoma based on the National Comprehensive Cancer Network (NCCN) guidelines. She explained the NCCN guidelines recommend consideration of adjuvant therapy with pembrolizumab for stage IIB/IIC disease and nivolumab or pembrolizumab for patients with stage III disease and stage IV disease that has been resected. Alwan emphasized that adjuvant therapies improve relapse-free survival, but an overall survival benefit compared with observation has not been proven in the adjuvant setting. She recommended consideration of age, performance status, history of autoimmune disease, and patients’ risk tolerance for adverse effects prior to initiation of adjuvant therapy for cutaneous melanoma.

In patients with metastatic melanoma, Alwan illustrated that immune checkpoint inhibitors (ICIs) are preferred in the first-line setting with choice of regimen based on patient fitness and preferences for therapy, sites of metastasis, and response to prior therapy. Preferred regimens in the NCCN guidelines for metastatic melanoma include nivolumab, pembrolizumab, nivolumab plus ipilimumab, and nivolumab plus relatlimab-rmbw. Alwan explained that patients with a *BRAF* V600 activating mutation benefit from combination targeted therapy such as atezolizumab combined with vemurafenib and cobimetinib. If not previously prescribed, options in second-line, metastatic melanoma include nivolumab, pembrolizumab, nivolumab plus ipilimumab, and

“Early recognition of irAEs is key to early intervention with corticosteroids.”

—Laura M. Alwan, PharmD, BCOP

pembrolizumab plus low-dose ipilimumab (1 mg/kg). Alwan underscored that the optimal duration of therapy for metastatic disease is unknown.

Following a review of recommended monitoring for immune-related adverse events (irAEs) associated with ICIs, Alwan reviewed irAE management strategies. She differentiated rash, diarrhea/colitis, hepatitis, and arthritis as reversible irAEs and hyperglycemia, hypothyroidism, and hypophysitis as irreversible irAEs. Patients developing endocrine irAEs will require lifelong hormone replacement, explained Alwan; however, patients do not generally need to discontinue ICI therapy for these irAEs.

In contrast, reversible irAEs are typically managed with immunosuppressive therapy, including high-dose corticosteroids with addition of infliximab or vedolizumab for unresponsive diarrhea/colitis, mycophenolate for unresponsive hepatitis, and disease-modifying antirheumatic drugs for arthritis unresponsive to steroids. She explained that for most grade 2 irAEs, treatment is held until the toxicity improves to grade 1 and then ICIs can be resumed; exceptions to this include myocarditis and nervous system irAEs where ICIs are permanently discontinued. She wrapped up by emphasizing that some patients may resume treatment with ICIs after irAE improvement, taking into account the grade of toxicity, resolution of symptoms, and disease response to treatment. ■

TO VIEW THE ON-DEMAND CE SESSION, PLEASE VISIT WWW.PHARMACYTIMES.ORG/diop-2022-on-demand

PTCE WOULD LIKE TO ACKNOWLEDGE SEAGEN INC; DAIICHI SANKYO, INC; AND ASTRAZENECA FOR THEIR GENEROUS SUPPORT OF PHARMACIST EDUCATION.

Redefining What It Means to Be HER2 Positive

APPROXIMATELY ONE-FOURTH OF breast cancers overexpress human epidermal growth factor receptor 2 (HER2), an actionable target for drug therapies. Allison Butts, PharmD, BCOP, shared data driving optimal therapy selection in a live **2022 Directions in Oncology Pharmacy®** conference session titled “Clinical Updates in the Treatment of HER2-Positive Breast Cancer.”

Butts began with an update on determination of HER2 status. HER2 status is measured by immunohistochemistry (IHC), fluorescence in situ hybridization (FISH), and/or HER2 gene copy number. She explained that rather than a dichotomy of positive or negative, patients may also be categorized as HER2-low when IHC is 1+ or IHC is 2+ and FISH is negative.

Butts reviewed multiple mechanisms by which therapies target HER2: monoclonal antibodies (trastuzumab, pertuzumab, margetuximab-cmkb); dual monoclonal antibodies (trastuzumab plus pertuzumab); tyrosine kinase inhibitors (lapatinib, neratinib, tucatinib); and antibody-drug conjugates (trastuzumab emtansine, trastuzumab deruxtecan). She noted that biosimilars are available for trastuzumab and that trastuzumab and pertuzumab have been formulated with hyaluronidase to deliver a larger volume subcutaneously over a condensed time.

For early-stage, HER2+ breast cancer, Butts differentiated that adjuvant therapy is typically provided to patients with stage I disease. Regimens in this setting are administered following surgery and may include paclitaxel and trastuzumab; docetaxel, carboplatin, and trastuzumab; or docetaxel, carboplatin, trastuzumab, and pertuzumab. Butts explained that patients with stage II or III disease generally receive neoadjuvant docetaxel, carboplatin, trastuzumab, and pertuzumab before surgery. Patients with complete response receive adjuvant trastuzumab with or without pertuzumab and patients with residual disease receive ado-trastuzumab emtansine. Patients may also receive “extended adjuvant” therapy with neratinib for an additional year.

“Pharmacists should be aware of the clinical data surrounding these therapies as well as how to detect and manage their significant toxicities.”

—Allison Butts, PharmD, BCOP

Butts illustrated the treatment algorithm for metastatic HER2+ breast cancer includes first-line trastuzumab and pertuzumab combined with a taxane. In second line, she pointed out trastuzumab deruxtecan received FDA approval for patients with HER2-low metastatic breast cancer. She highlighted that optimal treatment sequencing following second-line therapy has not been studied; however, in practice, treatment pathways diverge in third line based on the presence or absence of significant central nervous system (CNS) disease. Patients with significant CNS disease receive tucatinib, trastuzumab, and capecitabine followed by trastuzumab emtansine or trastuzumab combined with chemotherapy in fourth line. Butts explained that in patients with no or minor CNS disease, they typically sequence tucatinib, trastuzumab, and capecitabine as fourth-line therapy. She noted fifth-line and subsequent therapies include trastuzumab or margetuximab plus chemotherapy, or lapatinib or neratinib plus capecitabine.

Butts emphasized that patient acceptance and tolerability is a significant consideration in treatment decisions. She noted the incidence of diarrhea, pulmonary toxicity, and cardiotoxicity varies among agents and provided strategies for managing these toxicities. Butts highlighted that patients have options for route of administration (intravenous, subcutaneous, and oral), each with differing treatment costs and patient access. ■

TO VIEW THE ON-DEMAND CE SESSION, PLEASE VISIT WWW.PHARMACYTIMES.ORG/diop-2022-on-demand

PTCE WOULD LIKE TO ACKNOWLEDGE GENENTECH, A MEMBER OF THE ROCHE GROUP,
FOR THEIR GENEROUS SUPPORT OF PHARMACIST EDUCATION.

Actionable Mutations and Targeted Therapies in Acute Myeloid Leukemia

THE TREATMENT LANDSCAPE of acute myeloid leukemia (AML) is rapidly evolving due to the introduction of targeted therapies following FDA approval of 7 novel therapies in the past 5 years. Jessie Signorelli, PharmD, BCOP, described the shift in management of AML toward personalized medicine in a live **2022 Directions in Oncology Pharmacy®** conference session titled “Acute Myeloid Leukemia: Novel Targeted Therapies and the Role of the Pharmacist.”

Signorelli emphasized that addition of targeted agents to the AML treatment armamentarium has increased treatment options for patients who are ineligible for intensive induction chemotherapy and for patients with FMS-like tyrosine kinase 3 (FLT3) mutations receiving intensive induction therapy. She illustrated the mechanism of action for FLT3 inhibitors (midostaurin, gilteritinib, quizartinib); isocitrate dehydrogenase (IDH) inhibitors (enasidenib and ivosidenib); B-cell lymphoma 2 (BCL-2) inhibitors (venetoclax); and hedgehog inhibitors (glasdegib) in AML. Most initial treatment decisions for AML are based on age, history of prior myelodysplasia or cytotoxic therapy, actionable mutations if present, and performance status, explained Signorelli. She noted that with the exception of oral azacitidine, all of the recent approvals for AML have been for induction therapy. Oral azacitidine is effective maintenance therapy in intermediate- or poor-risk patients who are not candidates for allogeneic stem cell transplantation and midostaurin is incorporated into induction, consolidation, and maintenance therapy for patients with FLT3 mutations. She differentiated venetoclax as a targeted agent that does not require an actionable mutation to be used in AML; it is used in combination with azacitidine, decitabine, or low-dose cytarabine in induction therapy for patients with unfavorable risk profiles regardless of eligibility for intensive induction therapies. Glasdegib plus low-dose cytarabine is another option for patients with AML who are

“Pharmacists play a vital role in recommending agents based on individual patient characteristics as well as adverse effect monitoring and management in AML.”

—Jessie Signorelli, PharmD, BCOP

not eligible for intensive remission induction therapy without actionable mutations, explained Signorelli.

In the latter half of the presentation, Signorelli homed in on adverse effects with targeted therapies. She cautioned pharmacists to monitor for differentiation syndrome with gilteritinib and IDH inhibitors and QT prolongation with midostaurin, gilteritinib, ivosidenib, and glasdegib. She noted myelosuppression is typically observed because these agents are used in combination with other myelosuppressive therapy; however, an additive effect is seen with midostaurin, venetoclax, glasdegib, and azacitidine. Apart from venetoclax, she warned that gastrointestinal toxicities are observed with all the agents and antiemetic prophylaxis is needed with midostaurin, enasidenib, and oral azacitidine. Lastly, she explained that a low incidence of tumor lysis syndrome was observed in venetoclax clinical trials due to the preventive measures employed. She recommended following the ramp-up dosing in AML and providing hydration, allopurinol, and rasburicase, if indicated, for patients receiving venetoclax.

Signorelli summarized the session by emphasizing that targeted therapies encourage personalized therapy in AML based on mutation status, anticipated adverse effects, and the compatibility of comorbidities and patients' lifestyle with their therapy. ■

TO VIEW THE ON-DEMAND CE SESSION, PLEASE VISIT WWW.PHARMACYTIMES.ORG/diop-2022-on-demand

PTCE WOULD LIKE TO ACKNOWLEDGE SEAGEN INC FOR THEIR GENEROUS SUPPORT OF PHARMACIST EDUCATION.

Antibody-Drug Conjugates Explode into the Oncology Treatment Landscape

THE LANDSCAPE OF antibody-drug conjugates (ADCs) has exploded over the past 5 years, explained Jolynn K. Sessions, PharmD, BCOP, CPP, FHOPA, in a live **2022 Directions in Oncology Pharmacy®** conference session titled “Antibody-Drug Conjugates (ADCs): The Implications of Emerging Trends on Oncology Pharmacy Practice.” Several ADCs are approved by the FDA for first-line therapy in multiple malignancies and Sessions illustrated where they have demonstrated improved outcomes over previous standard-of-care treatments.

Sessions began with the basics, noting that all ADCs comprise a monoclonal antibody, linker, and cytotoxin. She grouped ADCs by the “bomb,” or cytotoxic payload, and highlighted that their mechanism of cytotoxicity and adverse effect profile is related to the cytotoxin component. Emtansine, vedotin, and mafodotin release microtubule toxins, explained Sessions. In contrast, tesirine and ozogamicin discharge alkylating agents and deruxtecan and govitecan liberate topoisomerase inhibitors leading to DNA damage.

Whereas ADCs use monoclonal antibodies to deliver a cytotoxin to a specific cell type, Sessions noted that only gemtuzumab ozogamicin (CD33), brentuximab vedotin (CD30), and trastuzumab emtansine and trastuzumab deruxtecan (HER2) require testing for a specific target. She described the efficacy and safety for ADCs approved in solid tumors including enfortumab vedotin for metastatic urothelial cancer (mUC); sacituzumab govitecan for metastatic, triple-negative breast cancer and mUC; and tisotumab vedotin for recurrent or metastatic cervical cancer.

In hematologic malignancies, Sessions described the role of brentuximab vedotin in Hodgkin lymphoma, anaplastic large cell lymphoma, and CD30+ peripheral T-cell lymphoma or mycoses fungoides; polatuzumab vedotin and loncastuximab tesirine in

“Unique toxicities warrant new skills and collaborations of the oncology pharmacist to be able to provide adequate care for patients on ADCs and optimize their drug therapy.”

—Jolynn K. Sessions, PharmD, BCOP, CPP, FHOPA

diffuse large B-cell lymphoma; and belantamab mafodotin in relapsed/refractory multiple myeloma.

Sessions emphasized black box warnings for ADCs including severe and fatal cutaneous adverse reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis with enfortumab vedotin; severe or life-threatening neutropenia and severe diarrhea with sacituzumab govitecan; progressive multifocal leukoencephalopathy with brentuximab vedotin; and ocular toxicity with tisotumab vedotin and belantamab mafodotin. She noted ADCs are administered by intravenous infusion, have the potential to cause hypersensitivity reactions, pose a risk for embryo-fetal toxicity, and follow dosing adjustments for the cytotoxin. A key difference among the ADCs highlighted by Sessions is the need for acetaminophen and histamine 1/2 receptor antagonists to prevent hypersensitivity reactions for gemtuzumab ozogamicin, inotuzumab ozogamicin, moxetumomab pasudotox, polatuzumab vedotin, and sacituzumab govitecan. Loncastuximab tesirine requires steroid premedication to prevent fluid retention. The other ADCs do not require routine premedications. Sessions wrapped up the program by highlighting emerging ADCs in clinical trials for solid tumors and hematologic malignancies. ■

TO VIEW THE ON-DEMAND CE SESSION, PLEASE VISIT WWW.PHARMACYTIMES.ORG/diop-2022-on-demand

PTCE WOULD LIKE TO ACKNOWLEDGE REGENERON PHARMACEUTICALS, INC FOR THEIR GENEROUS SUPPORT OF PHARMACIST EDUCATION.

Immune Checkpoint Inhibitors Lead to Improved Outcomes for Advanced Non-Melanoma Skin Cancers

BASAL CELL CARCINOMA (BCC) and cutaneous squamous cell carcinoma (CSCC) are the 2 most common skin cancers and while they rarely metastasize, they are associated with substantial morbidity. Theresa S. Brown, PharmD, BCOP, CPP, updated pharmacists on the evolving role of systemic therapy in a **2022 Directions in Oncology Pharmacy®** conference session titled “Advances in the Use of Immune Checkpoint Inhibitors to Treat Non-Melanoma Skin Cancers: Updates for Oncology Pharmacists.”

Brown educated audience members on risk factors, pathophysiology, clinical presentation, and the role of surgery and radiation in BCC and CSCC. She illustrated that systemic therapy plays a role in patients with BCC and CSCC with localized, high-risk disease as well as in patients with recurrent or advanced disease.

She explained that in BCC, hedgehog inhibitors (ie, sonidegib, vismodegib) are used in patients with high-risk localized disease for nonsurgical candidates; however, most patients progress on, or are intolerant to, hedgehog inhibitors. Brown noted cemiplimab is the preferred second-line option for advanced BCC after hedgehog inhibitors. She indicated both hedgehog inhibitors and cemiplimab may be used in patients with primary/recurrent nodal metastases and for distal metastases in patients who are not surgical candidates.

In CSCC, Brown differentiated that systemic therapy is employed when curative radiation is not feasible and in patients with distance metastases. She explained that platinum-based regimens or EGFR inhibitors may be combined with radiation for systemic therapy of CSCC. In patients with CSCC managed with systemic therapy alone, the National Comprehensive Cancer Network guidelines preferred regimens include cemiplimab and pembrolizumab because both agents lead to durable responses. She also highlighted emerging data supporting a role for cemiplimab in the neoadjuvant setting for resectable CSCC.

“Patient education is extremely important because early recognition and intervention remain key in effective management of dermatologic irAEs.”

—Theresa S. Brown, PharmD, BCOP, CPP

In the second half of the presentation, Brown described the pathophysiology and spectrum of immune-related adverse events (irAEs). She explained dermatologic irAEs are the most common irAE and occur earliest after treatment initiation. Brown depicted the dermatologic irAEs associated with immune checkpoint inhibitors (ICIs), including maculopapular rash, pruritus, bullous dermatitis, vitiligo, Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN). She highlighted the role of multidisciplinary care in management of dermatologic irAEs and provided recommendations for when to engage a dermatologist based on type and severity of dermatologic irAEs.

Brown explained that SJS/TEN require permanent discontinuation of ICI and patients require intensive inpatient management with high-dose corticosteroids, immunosuppressants, and potentially intravenous immunoglobulin. Similarly, patients with mild bullous dermatitis may also necessitate holding ICIs and aggressive systemic therapy. At the other end of the spectrum, she explained that patients with grade 1 or 2 pruritus or maculopapular rash do not need to interrupt ICI therapy. Brown differentiated pruritus and maculopapular rash from other irAEs in that some grade 1 or 2 irAEs can be managed with oral antihistamines, topical corticosteroids, and other symptomatic care. ■

TO VIEW THE ON-DEMAND CE SESSION, PLEASE VISIT WWW.PHARMACYTIMES.ORG/diop-2022-on-demand

PTCE WOULD LIKE TO ACKNOWLEDGE MERCK & CO., INC AND EISAI, INC FOR THEIR GENEROUS SUPPORT OF PHARMACIST EDUCATION.

Biomarker-Directed Therapies Earn a Spot in Endometrial Cancer

IN A LIVE session, titled “Advancing Treatment for Endometrial Cancer: Updates for Pharmacists,” at the **2022 Directions in Oncology Pharmacy®** conference, Rachel Justus, PharmD, BCPS, BCOP, provided a concise update on the changing management of endometrial cancer.

Justus began by explaining that the management of endometrial cancer is guided by disease stage, line of therapy, pathology, and biomarkers. She shared that first-line treatment involves surgery with or without radiation and chemotherapy. With the exception of human epidermal growth factor receptor 2 (HER2)-directed therapies, biomarker-directed therapies are implemented in second-line and subsequent therapy for endometrial cancer.

Justus illustrated that polymerase epsilon (POLE) mutations confer a good prognosis, microsatellite instability-high (MSI-H) and tumor mutational burden-low are associated with an intermediate prognosis, and tumor mutational burden-high (TMB-H) is associated with a poor prognosis. Other biomarkers include programmed cell death ligand 1 (PD-L1) and neurotrophic tyrosine receptor kinase (*NTRK*) gene fusion. She explained the National Comprehensive Cancer Network (NCCN) guidelines recommend universal testing for mismatch repair deficiency (dMMR); however, the decision to evaluate other biomarkers is based on the availability of resources and the multidisciplinary team caring for the patient. Justus shared some of the challenges with biomarker-directed therapy in endometrial cancer including the availability and ordering of testing, reimbursement of testing, interpretation of test results in relation to prognosis and treatment options, categorization of tumors with one or more mutations, as well as sequencing of testing.

She highlighted treatment recommendations for biomarker-directed systemic therapy in patients with recurrent endometrial cancer based on the NCCN guidelines, including the following:

- Lenvatinib plus pembrolizumab (non-MSI-H/non-dMMR)

“For advanced, recurrent or metastatic endometrial cancer, biomarker testing directs treatment options to ICIs and targeted therapies.”

—Rachel Justus, PharmD, BCPS, BCOP

- Pembrolizumab (TMB-H or MSI-H/dMMR)
- Nivolumab (MSI-H/dMMR)
- Dostarlimab-gxly (MSI-H/dMMR)

In the latter half of the presentation, Justus shifted the focus to adverse events (AEs), noting that patient education and monitoring are key to keeping patients on therapy. She illustrated that immune checkpoint inhibitors (ICIs) may lead to immune-related AEs (irAEs) in any organ or tissue and encouraged pharmacists to consider all AEs as treatment related until proven otherwise. The development of irAEs does not always require discontinuation of the ICI, emphasized Justus. For example, with endocrinopathies, patients typically receive replacement of the affected hormone and continue therapy. For grade 2 or higher irAEs, she explained that the ICI is temporarily held, and low doses of corticosteroids are initiated. High-dose steroids, with or without additional immunosuppressive therapy, are implemented for both grade 3 and 4 irAEs. Justus noted that the ICI is generally discontinued for grade 4 AEs and grade 3 irAEs that do not improve with 4 to 6 weeks of immunosuppressive therapy. She highlighted that AEs of lenvatinib overlap with those of ICIs, including diarrhea, arthralgias/myalgia, skin rash, hypothyroidism, fatigue, and anorexia. She encouraged pharmacists to consider the presentation timeline and pharmacokinetics of each therapy to guide management of overlapping toxicities. ■

TO VIEW THE ON-DEMAND CE SESSION, PLEASE VISIT WWW.PHARMACYTIMES.ORG/diop-2022-on-demand

PTCE WOULD LIKE TO ACKNOWLEDGE GLAXOSMITHKLINE FOR THEIR GENEROUS SUPPORT OF PHARMACIST EDUCATION.

Roadmap for PARP Inhibitors in Ovarian Cancer

JASON BERGSBAKEN, PHARMD, MBA, BCOP, highlighted that PARP inhibitors (PARPi) represent a significant advancement in the management of advanced ovarian cancer, particularly for those with *BRCA1/2* mutations or homologous recombination (HR) deficiency. He shared recent data in a live **2022 Directions in Oncology Pharmacy®** conference session titled “Updates on the Utility of PARP Inhibitors in the Treatment of Ovarian Cancer: Opportunities for Pharmacists to Improve Patient Care.”

Bergsbaken began by illustrating where PARPi fit in the treatment roadmap for advanced ovarian cancer. He explained that PARPi are recommended in National Comprehensive Cancer Network guidelines as first-line maintenance therapy for patients with a complete or partial response to surgical debulking and platinum-based chemotherapy. Increased clinical efficacy is seen in patients with *BRCA* mutations and other HR deficiencies, explained Bergsbaken; however, PARPi differ with respect to requirement for the presence of the mutation in the FDA labeling. Niraparib is recommended for patients with or without *BRCA* mutations and when *BRCA* mutation status is unknown; olaparib is recommended for patients with *BRCA* mutations; and olaparib can be combined with bevacizumab in patients who received bevacizumab in combination with the initial platinum doublet therapy who have known *BRCA* mutations or in patients without a *BRCA* mutation/unknown *BRCA* status who are HR proficient or status unknown.

The next point in therapy where PARPi are incorporated, explained Bergsbaken, is in patients with recurrent disease following complete or partial response to platinum-based chemotherapy. As recurrent maintenance therapy, patients may be candidates for niraparib, olaparib, or rucaparib (if not previously prescribed), irrespective of knowledge of mutation status. Recently the FDA indications for PARPi in recurrent/metastatic

“Pharmacists optimize outcomes for patients receiving PARPi through patient education, assistance with identification and management of adverse effects, adherence strategies, and mitigation of financial toxicity.”

—Jason Bergsbaken, PharmD, MBA, BCOP

disease were voluntarily withdrawn due to lack of overall survival benefit seen in trials with olaparib and rucaparib.

Bergsbaken explained that PARPi have class-wide adverse effects, but also demonstrate unique toxicities, laboratory monitoring, and drug interactions. He highlighted that myelosuppression, fatigue, and nausea and vomiting are class effects of PARPi. Some patients may require prophylactic antiemetics 30 minutes before dosing a PARPi, underscored Bergsbaken, because the agents are moderately to highly emetogenic. He noted niraparib is associated with a higher incidence of myelosuppression, insomnia, and hypertension, whereas rucaparib is associated with an increased risk for elevated hepatic transaminases and serum creatinine. Olaparib is associated with pneumonitis. Bergsbaken underscored the role for pharmacists in monitoring and management of adverse effects because approximately 60% of patients require dose reduction of PARPi, and 15% of patients discontinue therapy. He encouraged pharmacists to identify patient factors that may increase risk for nonadherence and provide strategies to improve adherence. In the final portion of the presentation, he linked financial toxicity to nonadherence and provided resources for helping patients manage their out-of-pocket costs. ■

TO VIEW THE ON-DEMAND CE SESSION, PLEASE VISIT WWW.PHARMACYTIMES.ORG/diop-2022-on-demand