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This CME/CE activity is supported by educational grants from Bristol-Myers Squibb, Genentech BioOncology, and Novartis Pharmaceuticals Corporation.
CONTRACT FOR MUTUAL RESPONSIBILITY IN CME

PROJECTS IN KNOWLEDGE WILL PROVIDE:

1. A trusting learning environment free of commercial bias.
2. An activity that has been peer-reviewed, by an expert in the field who is not a member of the faculty, to ensure that the information presented is independent, objective, scientifically rigorous, fair-balanced, accurate, timely, relevant, and beneficial to patients.
3. An activity that is free of any conflicts of interest, as identified through the faculty disclosure process and resolved through our Trust In Knowledge peer review process.
4. Faculty that embrace and support our efforts.
5. Acknowledgment of off-label uses of pharmaceutical products discussed.
6. Content that will positively impact on your ability to manage your patients.
7. Ample opportunity for questions from the participants to add to the scientific rigor and real-life clinical appropriateness of information provided.
8. Access to a “Content Ombudsman” (via e-mail at ombudsman@projectsinknowledge.com) who will handle questions on enduring materials that are not answered by this activity.
9. A dynamic learning and implementation process that meets our rigorous obligations to multiple accreditation/regulatory bodies, and that shows that Projects In Knowledge will be forever evolving and striving to do the right thing.

CLINICIANS’ RESPONSIBILITIES:

1. Be an active participant in the activity.
2. Ask questions relevant to patient care concerns.
3. Commit yourself to the entire activity time frame, because it is only then that the total learning can be experienced, utilized, and measured.
4. Allow this activity to be only a part of your total learning experience.
5. Aid in developing future activities by being a strong participant. The evaluation form assists us in this process; please give it careful professional consideration when filling it out.
6. Return to your practice and mentor the learning experience with your colleagues. Projects In Knowledge will provide extra material for this effort.

Sincerely,

Robert S. Stern
President
Projects In Knowledge, Inc.
Program Information

Target Audience
This CME activity is designed for oncologists and other clinicians who specialize in and care for patients with breast cancer.

Activity Goal
The goal of this activity is to examine current and emerging strategies for treating and managing patients with breast cancer.

Learning Objectives
• Utilizing an understanding of the molecular basis of breast cancer, evaluate and differentiate the mechanisms of action of microtubule-targeting agents, such as epothilones, taxanes, and vinca alkaloids, on microtubules and cell cycle arrest.
• Formulate future treatment strategies for women with local recurrent and metastatic breast cancer, especially those with resistant/refractory disease, incorporating the use of newer microtubule-targeting agents, such as epothilones, based on an understanding of the efficacy and safety of these agents as well as dosing schedules.
• Evaluate patients considered appropriate for, and who will benefit from, newer microtubule-targeting agents, including epothilones and vinca alkaloids, based on knowledge of the mechanism of action of epothilones and their efficacy and safety data.

CME Information

Statement of Accreditation
Projects In Knowledge is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Credit Designation
Projects In Knowledge designates this educational activity for a maximum of 1.0 AMA PRA Category 1 Credit™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

CE Information: Pharmacists
Projects In Knowledge is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. This activity has been planned and implemented in accordance with the ACPE Criteria for Quality and Interpretive Guidelines. The ACPE Universal Program Number assigned to the program, for 1 contact hour (0.1 CEU) is 052-000-08-039-H01-P.

Disclosure Information
The Disclosure Policy of Projects In Knowledge requires that presenters comply with the Standards for Commercial Support. All faculty are required to disclose any personal interest or relationship they or their spouse/partner have with the supporters of this activity or any commercial interest that is discussed in their presentation. Any discussions of unlabeled/unapproved uses of drugs or devices will also be disclosed in the course materials.

For complete prescribing information on the products discussed during this CME activity, please see your current Physicians’ Desk Reference (PDR).

Faculty Disclosures
Harold J. Burstein, MD, PhD, has indicated that he has no real or apparent conflicts of interest to report. Dr. Burstein will not reference any unlabeled/unapproved uses of drugs or devices in his presentation.

William J. Gradishar, MD, has received grant/research support from Abraxis BioScience, AstraZeneca PLC, GlaxoSmithKline, and Novartis Pharmaceuticals Corporation; and is a consultant for, on the speakers bureau of, and on the advisory board of Abraxis BioScience, AstraZeneca PLC, GlaxoSmithKline, Genentech Inc, Genomic Health, Inc and Novartis Pharmaceuticals Corporation. Dr. Gradishar will be discussing novel therapies for the treatment of advanced or metastatic breast cancer, some or all of which may be unlabeled or unapproved for use in the treatment of patients with advanced or metastatic breast cancer.

Hope S. Rugo, MD, has received grant/research support from Bristol-Myers Squibb, Genentech, Inc, GlaxoSmithKline, Novartis Pharmaceuticals Corporation, Pfizer Inc and Roche Pharmaceuticals; is on the speakers bureau for AstraZeneca PLC and Genomic Health, Inc; and is on the advisory board of Merck & Co, Inc. Dr. Rugo will be discussing novel treatments for treatment of advanced or metastatic breast cancer, some or all of which may be unlabeled or unapproved for use in the treatment of patients with advanced or metastatic breast cancer.

William J. Gradishar, MD, has received grant/research support from Abraxis BioScience, AstraZeneca PLC, GlaxoSmithKline, and Novartis Pharmaceuticals Corporation; and is a consultant for, on the speakers bureau of, and on the advisory board of Abraxis BioScience, AstraZeneca PLC, GlaxoSmithKline, Genentech Inc, Genomic Health, Inc and Novartis Pharmaceuticals Corporation. Dr. Gradishar will be discussing novel therapies for the treatment of advanced or metastatic breast cancer, some or all of which may be unlabeled or unapproved for use in the treatment of patients with advanced or metastatic breast cancer.

Peer Reviewer has no significant relationships to disclose.

Projects In Knowledge’s staff members have no significant relationships to disclose.

Conflicts of interest are thoroughly vetted by the Executive Committee of Projects In Knowledge. All conflicts are resolved prior to the beginning of the activity by the Trust In Knowledge peer review process.

The opinions expressed in this activity are those of the faculty and do not necessarily reflect those of Projects In Knowledge. This CME activity is provided by Projects In Knowledge solely as an educational service. Specific patient care decisions are the responsibility of the physician caring for the patient.

This independent CME activity is supported by an educational grant from Bristol-Myers Squibb, Genentech BioOncology, and Novartis Pharmaceuticals Corporation.
**Targeting the Microtubule: A Novel Approach to Treating Metastatic Breast Cancer**

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**Drugs or Investigational Agents Mentioned in This Presentation**

Projects In Knowledge requires that faculty disclose any reference(s) to unlabeled or unapproved uses of drugs or devices as part of their presentations. The audience is advised that this CME activity will contain such discussion.

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<td>Capecitabine</td>
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<td>Eribulin mesylate (E7389)</td>
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<sup>a</sup> Approved for the treatment of advanced or metastatic breast cancer by FDA.
Dear Colleague:

Clinicians are faced with significant challenges in the care of patients with metastatic breast cancer. The disease must be controlled, but therapeutic toxicity may compromise the patient’s quality of life. In addition, many women recur after previous treatment with adjuvant anthracyclines and taxanes, and finding an effective agent in the setting of anthracycline and taxane resistance is difficult.

Novel treatment strategies and informed drug development may facilitate ways of overcoming resistance. An active area of drug development is therapies that target the microtubule. Epothilones work by stabilizing tubule polymerization, while the vinca alkaloids and eribulin mesylate work by destabilizing polymerization. In each case, cell mitosis is disrupted and apoptosis occurs.

In Targeting the Microtubule: A Novel Approach to Treating Metastatic Breast Cancer, we will begin with an overview of the challenges associated with treating resistant or refractory metastatic breast cancer. The discussion will expand to include efficacy and safety data of currently available epothilones and emerging microtubule-targeting agents. Case studies will conclude the webcast, highlighting the fact that our application of these data is always in the setting of real patients presenting themselves to us for care.

Thank you for joining us!

Sincerely,

Harold J. Burstein, MD, PhD

Chair
CHAIR
Harold J. Burstein, MD, PhD
Assistant Professor of Medicine
Dana-Farber Cancer Institute
Harvard Medical School
Boston, Massachusetts

FACULTY
William J. Gradishar, MD
Professor of Medicine
Hematology/Oncology
Northwestern University
Chicago, Illinois

Harold J. Burstein, MD, PhD, is an assistant professor of medicine at Harvard Medical School and a medical oncologist at Dana-Farber Cancer Institute and Brigham & Women’s Hospital. He is a clinician and clinical investigator specializing in breast cancer. Dr. Burstein attended Harvard College and earned his medical degree at Harvard Medical School where he also earned a PhD in immunology. In addition, he holds a master’s degree in history of science from Harvard. He trained in internal medicine at Massachusetts General Hospital, and was a fellow in medical oncology at Dana-Farber before joining the staff.

Dr. Burstein’s clinical practice is devoted entirely to breast cancer patients. His clinical research interests include novel treatments for early- and advanced-stage breast cancer, and studies of quality of life and health behavior among women with breast cancer. Dr. Burstein has written widely on breast cancer in both traditional medical journals and on the web. Representative publications of Dr. Burstein’s can be found in the New England Journal of Medicine, the Journal of Clinical Oncology, and other leading medical journals. With Gary Lyman, he is co-editor of the book Translational Therapy for Breast Cancer, published in 2007. He has served or is serving on international committees focusing on cancer treatments, such as the NCCN Breast Cancer Panel, the St. Gallen Breast Cancer Panel, the CALGB Breast Cancer Committee, the ASCO Health Services Research and Clinical Research Committees, the National Quality Forum Breast Cancer Technical Panel, and several ASCO expert panels related to breast cancer. He teaches students, house staff, and fellows at Harvard Medical School, Dana-Farber, Brigham & Women's Hospital, and affiliated training hospitals.

William J. Gradishar, MD, is a professor of medicine in the Division of Hematology and Medical Oncology/Department of Medicine at Northwestern University Medical School and a member of the Robert H. Lurie Comprehensive Cancer Center. Institutionally, he is director of breast medical oncology and co-director of the Lynn Sage Breast Program. He is also program director of Northwestern University’s Hematology/Oncology Fellowship Training Program.

Dr. Gradishar completed his medical school training at the University of Illinois Abraham School of Medicine. He completed a residency and chief residency in internal medicine at Michael Reese Hospital and Medical Center in Chicago. A fellowship in medical oncology was completed at the University of Chicago in 1990. He is a Diplomate of the American Board of Internal Medicine in both internal medicine and medical oncology.

Dr. Gradishar is a member of several professional organizations, including the American College of Physicians (Fellow), American Association for Cancer Research, American Federation for Clinical Research, Association of Subspecialty Professors, and the American Society of Breast Disease. He is a member of the Publication Committee and the Oncology Training Program Committee of the American Society of Clinical Oncology (ASCO). He also serves as vice chair of the ASCO Communication Committee.

Dr. Gradishar is a member of the Breast Cancer Core Committee of the Eastern Cooperative Oncology Group. He is a member of several expert panels, including the National Comprehensive Cancer Network (NCCN) Breast Cancer Practice Guideline Committee and the NCCN Breast Cancer Prevention Committee. He has served on the ASCO
Chemoprotectant Expert Panel. He has been a member of several study sections including: Susan G. Komen Breast Cancer Foundation, the Committee on Cell Structure and Metastases of the American Cancer Society, Cell Biology Committee of the American Cancer Society, Department of Defense Breast Cancer Research Program (1. Epidemiology; 2. Clinical and Experimental Therapeutics), and NIH National Action Plan on Breast Cancer. He currently has funding through the Department of Defense to evaluate the efficacy of networked breast cancer conferences as a means of increasing access to clinical trials.

Dr. Gradishar is a reviewer for numerous journals, including the *Journal of the National Cancer Institute*, *Journal of Clinical Oncology*, and *Clinical Cancer Research*. He has published in the area of breast cancer therapeutics with a focus on new endocrine therapy and chemotherapy. His research interest focuses on the development of novel therapeutics for the treatment of breast cancer.

**FACULTY**

**Hope S. Rugo, MD**

Clinical Professor of Medicine
University of California San Francisco Helen Diller Family Comprehensive Cancer Center
San Francisco, California

Hope S. Rugo, MD, is a clinical professor of medicine and director of the Breast Oncology Clinical Trials Program in the Division of Hematology and Oncology at the University of California San Francisco (UCSF) Helen Diller Family Comprehensive Cancer Center. Currently, she works in the UCSF Breast Cancer Center specializing in breast cancer and breast cancer clinical research. Her research interests include novel therapies for advanced breast cancer and supportive care. She is an investigator of the Bay Area SPORE at UCSF Breast Cancer Center, and the principal investigator of a number of clinical trials.

She earned her undergraduate degree summa cum laude from Tufts University. Dr. Rugo received her MD from the University of Pennsylvania School of Medicine and completed both a residency in internal medicine and fellowship in hematology and oncology at UCSF. She also completed a 2-year postdoctoral fellowship in immunology at Stanford University.

Currently, Dr. Rugo is serving on several University of California committees, including the Clinical Resource Center Committee, the Continuing Medical Education Committee, the Protocol Review Committee, and the Quality Assurance, Department of Medicine Committee. She is also a member of the CALGB breast core and the symptom control subcommittee. Previously, she sat on the Blue Shield Oncology Advisory Committee, among others. Recently, Dr. Rugo has been collaborating with colleagues to create a local clinical research network in her community.

Dr. Rugo has published many peer-reviewed papers and has given presentations on a variety of cancer-related topics.
Challenges in Treating Resistant/Refractory Metastatic Breast Cancer

Harold J. Burstein, MD, PhD

Key Points

- Despite the availability of “targeted” agents, chemotherapy—particularly anthracyclines and taxanes—remains a key treatment for advanced breast cancer.
- Significant challenges of treating women with advanced breast cancer include resistance to anthracyclines and taxanes and recurrence after, or progression in spite of, treatment.
- Novel treatment strategies and informed drug development may facilitate ways of overcoming resistance.

Treatment of advanced breast cancer remains an important clinical challenge. Each year in the United States, 40,000 women are diagnosed with advanced breast cancer. A variety of treatments are available for these women, yet none are considered curative at this time. Increasingly, “targeted” treatments are directed against known biomarkers of clinical activity. Examples of these targeted treatments include anti-estrogen therapies for estrogen-receptor–positive tumors and anti-HER2 therapies for HER2-expressing breast cancers. Although these are powerful treatments, chemotherapy remains a key treatment for advanced breast cancer.

Principles of chemotherapy treatment have been well established in prospective clinical trials. First-line therapy is more likely to be effective, and effective for longer, compared with second-line therapy. Likewise, second-line therapy is more likely to be effective, and effective for longer, compared with third-line. Patients whose tumors respond to chemotherapy tend to have longer periods of tumor control, and ultimately survival, compared with patients whose tumors do not respond, although these relationships are not directly related.

Chemotherapy often relieves or prevents cancer-related symptoms, such as tumor pain or shortness of breath. Chemotherapy, however, also brings side effects, including fatigue, hair loss, low blood counts, nausea, vomiting, diarrhea, neuropathy, and other adverse effects. Historically, anthracyclines and taxanes have been considered the “most active” agents in treatment of advanced breast cancer. A variety of other drugs have been shown to have clinical activity in refractory breast cancer, including capecitabine, gemcitabine, vinorelbine, platinum chemotherapy and other alkylating agents, and a host of other chemotherapies. The specific sequencing of these drugs has not been shown to have major impact on long-term outcomes, although each carries different side effects.

One of the challenges in modern care for women with advanced breast cancer is that many women recur after previous treatment with anthracyclines and taxanes given in the adjuvant setting. There are relatively few clinical trials data on management of women treated with such drugs in the adjuvant setting. For such patients, the challenge has been to develop novel regimens that have activity despite prior treatment and/or resistance to anthracycline and taxane-based chemotherapy. For other patients, whose tumors progress despite first- or second-line chemotherapy with taxanes, there is also the clear need for novel treatments.

A variety of approaches are being explored to optimize treatment with taxanes and for taxane-resistant breast cancer. New taxane strategies include novel derivatives, such as nab paclitaxel, which may have activity in patients previously treated with taxanes, and new treatment
schedules, such as weekly paclitaxel, which appears superior to every-3-week paclitaxel. New anti-angiogenesis drugs, particularly bevacizumab, have been shown to increase the response rate and time to progression when given with paclitaxel chemotherapy. This effect was noted in first-line treatment of metastatic disease and was specifically seen also in women with adjuvant taxane treatment.

Taxanes work by targeting the microtubule, a component of the cell cytoskeleton that is essential for normal and tumor cell function and division. The clinically relevant mechanisms of taxane resistance are not well characterized. In the laboratory, there has been considerable interest in studying taxane resistance, and mechanisms have been identified that include changes in microtubule structure and physiology. Additionally, changes in chemotherapy drug metabolism, such as multi-drug resistance, may be relevant. Due to these apparent targets, there is much interest in the development of agents that target different aspects of the microtubule or may be resistant to multi-drug resistance-type changes in cancer cells. The epothilone class of drugs appears to meet these needs and is being heavily explored in advanced breast cancer and other solid tumors.

Suggested Readings


Seidman AD, Berry D, Cirrincione C, et al. CALGB 9840: phase III study of weekly (W) paclitaxel (P) via 1-hour(h) infusion versus standard (S) 3h infusion every third week in the treatment of metastatic breast cancer (MBC), with trastuzumab (T) for HER2 positive MBC and randomized for T in HER2 normal MBC. J Clin Oncol. 2004;22:Abstract 512.
Role of Currently Available Epothilones in Resistant/Refractory Metastatic Breast Cancer

Hope S. Rugo, MD

Key Points

• Epothilones appear to avoid developing cross-resistance with taxanes, perhaps due to their unique binding site on β-tubulin.

• In clinical trials, epothilones have shown activity in resistant/refractory metastatic breast cancer.

• Ixabepilone (aza-epothilone B) was approved by the Food and Drug Administration (FDA) in October 2007 as a single agent for triple-resistant disease, and in combination with capecitabine for anthracycline- and taxane-resistant disease.

• Clinical development of ixabepilone and other epothilones is ongoing.

Innate or acquired drug resistance is one of the greatest limitations to the efficacy of taxane therapy. Preclinical data suggest that multi-drug resistance, the key mechanism for resistance to tubulin-binding agents, is probably mediated by permeability to glycoprotein or multi-drug resistance-associated protein. Other mechanisms of resistance include altered tubulin binding sites and tubulin mutations with changes in isotype expression.

The epothilones were discovered along the Zambezi River in Africa as secondary metabolites of Sorangium cellulosum. The class includes a number of individual epothilones: A through F. Epothilones are structurally unrelated to taxanes but are similar in function. Although epothilones and taxanes compete for tubulin binding, they bind at different sites, and epothilones appear to avoid developing cross-resistance with taxanes.

Ixabepilone was approved by the FDA in October 2007 for the treatment of locally advanced or metastatic breast cancer in combination with capecitabine for the treatment of taxane- and anthracycline-resistant disease, or as monotherapy for the treatment of disease resistant to taxanes, anthracyclines, and capecitabine (triple-resistant disease). Its approval was based on findings from a phase II trial by Perez et al in taxane- and anthracycline-resistant disease and a phase III trial by Thomas et al in triple-resistant disease.

Perez et al treated 113 women with ixabepilone at the FDA-approved dose of 40 mg/m² on day 1 of a 3-week treatment cycle for a median of four treatment cycles. The overall response rate was found to be 18% by study investigators and 11.5% by an independent radiology review group. The median response duration was 5.7 months and toxicity was modest. Other phase II trials of ixabepilone in other settings confirm the favorable toxicity profile reported by Perez. Among the trials, neutropenia was the most common toxicity. Peripheral neuropathy was seen in approximately 20% of participants overall, and myalgia was mild to moderate. Diarrhea, a concern at higher doses, was seen in a minority of patients, as was febrile neutropenia.

In another group of women with very limited treatment options, Thomas et al randomized 752 patients with triple-resistant metastatic disease to either ixabepilone plus capecitabine or ixabepilone alone. All enrolled patients were heavily pretreated with a poor prognosis, and stratification was based on known risk prognostic factors. Over a median of five treatment cycles, progression-free survival was significantly improved in patients receiving combination therapy compared with those who received capecitabine alone: 5.8 months versus 4.2
months ($P = .0003$). In predetermined subgroup analysis by tumor immunohistochemical markers, all groups benefited from the combination regimen compared with monotherapy. In all patients, the overall response rate more than doubled: 14% in capecitabine alone compared with 35% with ixabepilone plus capecitabine. In patients with very resistant triple-negative disease (ER/PR/HER2 negative), the rate tripled from 9% with monotherapy to 27% with combination therapy. The most common grade 3/4 adverse events in the combination arm were neutropenia and reversible peripheral sensory neuropathy. Febrile neutropenia occurred in only 5% of patients in the combination arm. Peripheral neuropathy was the only adverse event that occurred in the combination arm (22%) and not in the capecitabine arm (0%).

Additional clinical trials of ixabepilone are ongoing or planned, including a phase III trial of first-line metastatic breast cancer to open later in 2008, in which patients will be randomized to one of three treatment arms: paclitaxel, nab paclitaxel, or ixabepilone, each combined with bevacizumab.

**Suggested Readings**


Emerging Microtubule-Targeting Agents: Strategies for Their Use in Resistant/Refractory Metastatic Breast Cancer

William J. Gradishar, MD

Key Points

- New microtubule-targeted agents have shown benefit in the treatment of advanced breast cancer.
- Ongoing and planned trials will help to elucidate markers of resistance and sensitivity.
- Expanded treatment options allow more opportunity for individualized choice of therapy.

Microtubules are structures within the cell’s cytoskeleton that are essential for multiple functions. Due to their key role in cell division, microtubules are an important target in antitumor therapies. Taxanes, such as paclitaxel and docetaxel, achieve cytotoxic effect by stabilizing the mitotic complex, thereby reducing the functionality of microtubules. In contrast, vinca alkaloids, such as vinorelbine and vincristine, achieve their cytotoxic effect and reduce microtubule functionality by destabilizing the complex.

Naturally occurring epothilones and their analogs also stabilize the microtubule, but by targeting a different binding site than that targeted by taxanes. Thus, this new drug class offers taxane-like cytotoxicity and may be effective in the presence of taxane resistance and multi-drug resistance-type changes in cancer cells. One epothilone, ixabepilone, is currently approved for the treatment of breast cancer and others are in various phases of clinical development.

Patupilone, naturally occurring epothilone B, is currently in phase II development in patients with breast cancer. Two phase I trials in patients with advanced tumors, including breast cancer, showed stabilization of disease in up to one third of study participants, with some patients achieving partial or significant response. Diarrhea was the dose-limiting toxicity.

BMS-310705 is a water-soluble, semisynthetic analog of epothilone B. It has shown excellent preclinical activity in both taxane-sensitive and -resistant tumors, including those with multi-drug–resistance overexpression and beta-tubulin mutation. Clinical responses were observed in phase I trials in patients with advanced cancer; diarrhea was a dose-limiting toxicity, along with neutropenia, hypotension, and vomiting. Phase I/II development in multiple tumor types continues.

ZK-EPO (sagopilone) is a fully synthetic analog of epothilone B. Phase II trials have shown clinically relevant responses in patients with recurrent gliomas, platinum-sensitive ovarian cancer, and androgen-independent prostate cancer, with dose-limiting toxicities of peripheral neuropathy and ataxia. A phase II trial of ZK-EPO in patients with advanced breast cancer is now recruiting.

KOS-862, an epothilone D analog produced by recombinant DNA technology, has shown cytotoxic activity in several breast cancer models and is now in phase II trials in women with breast cancer. One phase II study of KOS-862 in anthracycline- and taxane-resistant breast cancer reported a 14% partial response rate with 19% of patients experiencing grade 3 neurotoxicity, including ataxia and neuropathy. KOS-1584, a second-generation epothilone D analog, is currently in phase I development.

Emerging vinca alkaloids include vinflunine and eribulin mesylate (E7389). These agents disrupt
microtubule function by destabilizing, or inhibiting, tubulin polymerization. In a phase II trial of vinflunine in anthracycline- and taxane-resistant advanced breast cancer, 36% of patients achieved partial response. In combination with trastuzumab, vinflunine produced even higher partial response rates, up to 74% in phase I and 58% in phase II, with manageable toxicity. A phase II trial in HER2+ disease is ongoing, as is phase I/II development in combination with other cytotoxic agents. E7389 exhibits a unique tubulin-based mechanism with noncompetitive binding at the vinca site and has demonstrated a 15% partial response rate in phase II development in anthracycline- and taxane-resistant disease. Grade 3/4 neutropenia and grade 3 peripheral neuropathy was reported in 61% and 4% of patients, respectively. Trials in breast cancer are ongoing. These emerging epothilone and vinca alkaloid agents show promise for patients with advanced breast cancer in terms of efficacy and manageable toxicity. Further testing in the setting of breast cancer will elucidate their future role in the management of advanced disease.

**Suggested Readings**


