

The Role of Emerging Chemotherapeutic Delivery Mechanisms in Metastatic Breast Cancer

AS THERAPEUTIC OPTIONS for metastatic breast cancer (mBC) continue to expand, many recent developments have been based on an improved understanding of the molecular mechanisms leading to tumor progression. Some of these molecular alterations can now be targeted by currently approved agents.¹⁻⁶ Examples include PARP inhibitors for germline *BRCA1/2*-mutated tumors, PI3K inhibitors for *PIK3CA*-mutated tumors, PD-L1–direct monoclonal antibodies for *PD-L1*–expressing tumors and tumors with microsatellite instability–high/mismatch repair–deficient mutations, and tyrosine kinase inhibitors for tumors with *NTRK* fusion.¹⁻⁷ Advances in genomics, epigenomics, and proteomics have identified the therapeutic potential of new targets.⁸ These include novel targets to chemotherapy resistance and functional pathways of tumor cells.⁸

Additional targeted therapies are being investigated in various populations with breast cancer. PARP inhibitors other than olaparib and talazoparib are under investigation in *BRCA*-mutated breast cancer⁹ as the role of androgen receptors in estrogen receptor–negative and progesterone receptor–negative tumors is also being explored.^{10,11} Immunotherapies continue to undergo investigation in mBC, and the FDA recently approved atezolizumab for patients with metastatic triple-negative breast cancer (TNBC) and PD-L1 expression.^{5,12} Additionally, an antibody–drug conjugate, sacituzumab govitecan–hziy, was recently approved for patients with TNBC who have received at least 2 prior lines of therapy in the metastatic setting.^{13,14}

In addition to the many advances in targeted therapies and immunotherapies, new formulations and delivery mechanisms are emerging for existing agents, particularly for chemotherapeutic agents. The formulation of chemotherapeutic agents may contribute to their clinical efficacy and safety. Efforts are under way to improve delivery mechanisms, efficacy, and toxicity profiles of chemotherapeutic agents. For example, nanoparticle technologies are being used to formulate intravenous (IV) paclitaxel to improve its pharmacokinetic/pharmacodynamic profile and tolerability.¹⁵ There is also an increasing interest in developing oral taxane formulations that can increase patient convenience, decrease infusion-related hypersensitivity reactions, eliminate the use of prophylactic corticosteroids, and lessen complications and costs related to IV access.¹⁶⁻¹⁹ Specifically for paclitaxel, oral administration together with a P-glycoprotein (P-gp) efflux pump

inhibitor may allow oral administration without a solvent, which can eliminate solvent-related toxicities and improve efficacy. Given the essential role of chemotherapy as the foundation of treatment for mBC, such advances could result in not only increased convenience for patients but also potentially lessened toxicity and improved outcomes. This article explores the potential of oral chemotherapeutic agents, with a focus on taxane-based regimens.

Parenteral Taxanes

Taxanes are widely used in mBC, but they are highly hydrophobic and insoluble.¹⁵ To make parenteral administration possible, polyoxyethylated castor oil and ethanol are used as the vehicle for paclitaxel. Similarly, docetaxel contains polysorbate 80 and an ethanol diluent as the vehicle.¹⁵ These solvents directly give rise to severe toxicities, including hypersensitivity reactions and prolonged peripheral neuropathy that may not be reversible, in treated patients.¹⁵ Because of the risk of anaphylaxis, patients receiving docetaxel require premedication with corticosteroids, whereas those receiving paclitaxel require corticosteroids, H₂-receptor antagonists, and diphenhydramine.^{20,21} Despite premedication, fatal anaphylaxis can occur. Besides contributing to toxicities, solvents may also decrease the efficacy of taxanes because of entrapment of the active drug in micelles within the patient's plasma, leading to increased systemic exposure and inadequate dose-dependent antitumor activity.¹⁵

Albumin-Bound Paclitaxel

Albumin-bound nanometer-sized paclitaxel (nab-paclitaxel) was developed to lessen the toxicities linked to the polyoxyethylated castor oil vehicle in conventional IV paclitaxel, as well as to increase its therapeutic potential.^{15,22} Nab-paclitaxel is a colloidal suspension and allows infusion of considerably higher doses of the active drug compared with conventional IV paclitaxel.¹⁵ No premedication is needed, and the 30-minute infusion time is shorter than the 3 hours needed for conventional IV paclitaxel. Furthermore, nab-paclitaxel preferentially delivers paclitaxel to tumors by interacting with albumin receptors that facilitate drug transport.¹⁵ In a phase 3 randomized, open-label, international study, patients with mBC were randomized to either conventional paclitaxel (175 mg/m² intravenously over 3 hours with premedication; n = 225) or IV nab-paclitaxel (260 mg/m² intravenously over 30 minutes without premedication; n = 229) every 3

weeks.¹⁵ Grade 3 or 4 treatment-related hypersensitivity reactions did not occur in patients receiving nab-paclitaxel but were experienced by 5 patients receiving conventional paclitaxel despite premedication.¹⁵ Although nab-paclitaxel was administered at a higher dose, treatment-related grade 4 neutropenia was significantly lower among patients receiving nab-paclitaxel than those receiving conventional paclitaxel (9% vs 22%; $P < .001$), suggesting that the polyoxyethylated castor oil vehicle may be partly responsible for the neutropenia associated with conventional paclitaxel.¹⁵ However, the frequency of grade 3 sensory neuropathy was higher in patients receiving nab-paclitaxel vs conventional paclitaxel (10% vs 2%), likely because of nab-paclitaxel's higher dose.¹⁵ Importantly, the objective response rate was significantly higher for nab-paclitaxel than conventional paclitaxel (33% vs 19%; $P = .001$) among all patients and remained significantly higher when stratified into the first-line setting ($P = .029$) and second- and subsequent-line settings ($P = .006$), as well as among patients who had prior anthracycline therapy ($P = .002$).¹⁵ Median time to progression was longer with nab-paclitaxel compared with conventional paclitaxel (23.0 vs 16.9 weeks; HR, 0.75; $P = .006$).¹⁵ Although a difference in overall survival (OS) among patients receiving first-line therapy was not observed, among patients receiving second- and subsequent-line therapy, nab-paclitaxel led to an improved OS (56.4 vs 46.7 weeks; HR, 0.73; $P = .024$).¹⁵ Based on these results, nab-paclitaxel was approved in 2005 for mBC after failure of combination chemotherapy in the metastatic setting and in patients who relapse within 6 months after adjuvant chemotherapy. Previous therapies should have included an anthracycline unless it was clinically contraindicated.²³

NK105

NK105 is a polymeric "core shell-type" micellar nanoparticle formulation of paclitaxel.²⁴ The formulation allows it to be administered intravenously without polyoxyethylated castor oil or ethanol as solvents. NK105 was developed as a macromolecule based on solid tumor characteristics, such as vascular permeability and hypervascularity, that promote extravasation into the tumor.²⁴ In addition, lymphatic clearance of macromolecules is low. These characteristics enable NK105 to have higher plasma exposure and potentially higher tumor exposure.²⁴ In a pharmacokinetic study of IV NK105 (150 mg/m²) and conventional paclitaxel (210 mg/m²) among Japanese patients, plasma area under the curve (AUC) was 15-fold higher in patients receiving NK105.²⁴ In a phase 3 open-label, multinational, noninferiority trial, patients with mBC were randomized to either conventional paclitaxel (80 mg/m² intravenously over 1 hour) or NK105 (65 mg/m² intravenously over 30 minutes) administered weekly for 3 weeks of a 28-day

cycle.²⁵ Patients treated with conventional IV paclitaxel received premedication with a corticosteroid, an antihistamine, and/or an H₂-receptor antagonist. The study did not meet its efficacy end point. The median progression-free survival (PFS) was 8.4 months in the NK105 group and 8.5 months in the conventional paclitaxel group (HR, 1.255; 95% CI, 0.989-1.592), which exceeded the predefined 1.215 noninferiority margin. Median OS was lower in patients receiving NK105 (31.2 months vs 36.2 months; adjusted HR, 1.197; 95% CI, 0.885-1.620). The objective response rate of NK105 was also lower, 31.6% vs 39.0% compared with conventional paclitaxel.²⁵ Patients in the NK105 group had lower incidences of grade 2 (10.3% vs 21.1%) and 3 (1.4% vs 7.5%) peripheral sensory neuropathy compared with those receiving conventional paclitaxel.²⁵ In summary, the phase 3 trial did not demonstrate the noninferiority of NK105 compared with conventional paclitaxel, but investigators did observe a better safety profile in peripheral sensory neuropathy.

Nanosomal Docetaxel

Similar to paclitaxel, docetaxel is highly lipophilic and insoluble in water.²⁶ As a result, docetaxel is formulated with polysorbate 80 and ethanol, which leads to solvent-related hypersensitive reactions requiring corticosteroid premedication.²⁶ A nanosomal docetaxel lipid suspension (NDLS) has been developed to avoid solvent-related toxicities.²⁶ In a randomized, open-label, multiple-dose study conducted in Asia, patients with mBC who had failed previous chemotherapy were randomized to conventional docetaxel ($n = 23$) or NDLS ($n = 49$), both administered at 75 mg/m² via a 1-hour IV infusion in each 21-day cycle for up to 6 cycles.²⁶ Patients receiving NDLS were not premedicated. Patients treated with NDLS had an objective response rate of 35.5% (95% CI, 21.9%-48.9%) compared with 26.3% (95% CI, 6.5%-46.1%) in patients receiving conventional docetaxel.²⁶ Grade 3 to 4 treatment-related adverse events (AEs) occurred in 77.6% of patients in the conventional docetaxel arm and 52.2% of those in the NDLS group.²⁶ However, neutropenia was more frequent in the NDLS group compared with the conventional docetaxel arm (77.5% vs 52.2%).²⁶ In summary, NDLS can be administered without steroid premedication, but more efficacy data are needed. A phase 3 trial comparing NDLS at 2 different doses (75 mg/m² and 100 mg/m²) with conventional docetaxel (100 mg/m²) is under way.²⁷

Oral Taxanes

Efforts to develop oral formulations of taxanes have received recent focus. The potential advantages of oral chemotherapeutic agents include a lack of solvent- and infusion-related hypersensitivity reactions, patient convenience, and the potential application in continuous oral

low-dose therapy.²⁸ Oral bioavailability is essential for any orally administered drugs. One hurdle in developing oral chemotherapeutic agents is the need to overcome the drug efflux pump, P-gp, expressed abundantly in the gastrointestinal mucosa.²⁸ P-gp expressed in intestinal epithelial cells limits the bioavailability of orally administered medications that are P-gp substrates.²⁹ Without modification or combination with a P-gp inhibitor, oral paclitaxel has limited bioavailability.³⁰ However, in genetically engineered mice that lack the gene encoding P-gp, oral bioavailability of paclitaxel increases more than 3-fold,³⁰ demonstrating that paclitaxel is actively extruded into the gut lumen by intestinal P-gp. In addition to hindering chemotherapy oral bioavailability, P-gp also mediates chemotherapy resistance. Cancer cells that overexpress P-gp give rise to multidrug resistance.²⁹

Combination with a P-gp inhibitor is one method to overcome problems with the bioavailability of oral chemotherapy. For this reason, several oral chemotherapy agents undergoing development are combined with a P-gp inhibitor, which prevents drug efflux into the intestinal lumen.

Oral Paclitaxel and Encequidar

An oral formulation of paclitaxel has recently been developed that combines paclitaxel with HM30181A (encequidar), a P-gp inhibitor.²⁸ In a phase 1, dose-escalating, open-label study conducted in patients with advanced solid tumors in Korea, oral solutions of paclitaxel without any solvent (doses ranging from 60 mg/m² to 480 mg/m²) were administered after an overnight fast.²⁸ One hour prior to paclitaxel administration, patients received encequidar.²⁸ When coadministered with encequidar, paclitaxel was rapidly absorbed, with peak plasma concentrations achieved within 30 minutes to 1 hour of administration.²⁸ The half-life ranged from 19.9 to 32.1 hours across the dose levels.²⁸ Effective plasma concentration range (0.01–0.1 µM) was maintained for 24 hours at doses of 120 mg/m² and greater.²⁸ Neutropenia (any grade) was observed in 25% of patients, and only 1 patient developed grade 3 neutropenia at a dose of 240 mg/m².²⁸ There were no grade 3 or higher nonhematologic toxicities.²⁸ In summary, this phase 1 study demonstrated that oral paclitaxel at a dose of 120 mg/m² coadministered with encequidar achieved effective cytotoxic plasma concentration without substantial toxicity.²⁸

An international, open-label, randomized, crossover bioequivalence study was performed in patients with advanced cancer.³¹ Patients were randomized to oral paclitaxel 205 mg/m² plus encequidar 15 mg once daily for 3 consecutive days followed by IV paclitaxel 80 mg/m² at least 1 week later, or the reverse order. The study's results showed that the oral formulation had a bioavailability

of 11.8% and was bioequivalent to IV paclitaxel.³¹ The majority of patients (81%) preferred the oral formulation. Reported reasons included the ability to take the medication at home and increased convenience. Only 19% preferred IV treatment.³¹ Two grade 3 or 4 treatment-related AEs were observed, but this finding should be interpreted with the caveat that patients received only 1 week of treatment.³¹ Similar results were observed in a 4-week study among patients with advanced solid tumors using the same dose of oral and IV paclitaxel and repeated dosing over 4 weeks. Repeated administration did not change the pharmacokinetic profile of oral paclitaxel plus encequidar.³²

Oral paclitaxel plus encequidar has also been studied in patients with mBC. In a single-arm, open-label multicenter study of 28 patients with mBC, oral paclitaxel 205 mg/m² plus encequidar 15 mg was administered for 3 consecutive days and then weekly for up to 16 weeks.³³ The majority of patients (26 of 28) had failed previous anticancer therapy.³³ Systemic exposures as demonstrated by AUC in weeks 1 and 4 were similar.³³ After a median follow-up of 16 weeks, 11 patients (42.3%) had achieved a partial response and 12 patients (46.2%) had achieved stable disease. Grade 3 or higher treatment-related neutropenia occurred in 3 patients.³³

In the largest study to date, Umanzor et al randomized patients with mBC to oral paclitaxel plus encequidar (n = 240) or conventional IV paclitaxel (n = 120).¹⁶ Oral paclitaxel was dosed at 205 mg/m² and was administered as 30-mg capsules, and encequidar (15-mg tablet) was administered for 3 consecutive days per week for each 3-week cycle. IV paclitaxel 175 mg/m² was administered as a 3-hour infusion every 3 weeks.¹⁶ In the intention-to-treat population, the proportion of patients achieving stable disease and progressive disease was 23.8% and 16.2%, respectively, in the group receiving oral paclitaxel and 39.2% and 21.6%, respectively, in those receiving IV paclitaxel. The confirmed response rate was 40.4% in the oral paclitaxel group compared with 25.6% in the IV group (*P* = .005).¹⁶ Median PFS was 9.3 months in the oral regimen group and 8.3 months in the IV arm (HR, 0.760; 95% CI, 0.551–1.049).¹⁶ Importantly, median OS was 27.9 months in patients receiving oral paclitaxel plus encequidar vs 16.9 months in those receiving conventional IV paclitaxel (HR, 0.684; 95% CI, 0.475–0.985).¹⁶ Additionally, the clinical response was durable, and 33.7% of patients treated with the oral regimen maintained response beyond 200 days.¹⁶ Oral paclitaxel plus encequidar led to a marked reduction in grade 2 or higher treatment-emergent neuropathy (7.6% vs 31.1%) and grade 2 alopecia (28.8% vs 48.1%). Incidences of grade 3 or higher neutropenia were similar between the groups (29.8% and 28.1% in the oral and IV paclitaxel groups, respectively). Gastrointestinal AEs

were more common with the oral regimen. Grade 3 or higher diarrhea (5.3% vs 1.5%) and vomiting/nausea (6.8% vs 0.7%) were more common with oral paclitaxel plus encequidar than conventional IV paclitaxel.¹⁶ In summary, although PFS was similar, this phase 3 trial demonstrated that oral paclitaxel plus encequidar improved OS compared with conventional IV paclitaxel in patients with mBC who have received at least 1 line of prior chemotherapy. Oral paclitaxel also led to a lower incidence of neuropathy and alopecia but a higher rate of low-grade gastrointestinal AEs. The results suggest that paclitaxel plus encequidar provides a meaningful improvement to paclitaxel's clinical profile and an advancement in oral therapeutic options for patients with mBC.

Tesetaxel

Tesetaxel (DJ-927) was developed as a soluble taxane analogue that can overcome P-gp–mediated resistance. In contrast with paclitaxel and docetaxel, tesetaxel has anti-tumor activity against P-gp–expressing cells with multidrug resistance *in vitro* and *in vivo*, most likely because of its improved intracellular concentrations.³⁴

In a phase 2 multicenter study, 38 patients with HER2-negative (HER2-) mBC were administered oral tesetaxel as first-line chemotherapy.³⁵ The starting dose was 27 mg/m² on day 1 of a 21-day cycle, and if tolerated, the dose was escalated to 35 mg/m² in subsequent cycles. Patients did not receive premedication for hypersensitivity reactions.³⁵ The objective response rate was 45% (95% CI, 29%-62%), and the median duration of response was 8.7 months (95% CI, 4.3-13.6). Median PFS was 5.7 months (95% CI, 4.1-9.8). The most common grade 3 or higher AE was neutropenia, which occurred in 29% of patients. However, grade 3 or higher peripheral neuropathy was not observed. Grade 1 and 2 alopecia occurred in 29% and 21% of patients, respectively.³⁵ A phase 2 nonrandomized trial is under way to evaluate clinical response of tesetaxel administered at a dose of either 27 mg/m² orally once every 3 weeks or 15 mg/m² once every 7 days for 3 consecutive weeks in a 28-day cycle (NCT01221870).³⁶ Additionally, a phase 3 international, randomized, multicenter trial (CONTESSA; NCT03326674) is under way in patients with hormone receptor–positive/HER2- locally advanced or mBC.³⁷ The study will compare PFS between tesetaxel (27 mg/m² orally on day 1 of a 21-day cycle) in combination with reduced-dose capecitabine (825 mg/m² orally twice daily from day 1 to day 15 of each 21-day cycle) vs capecitabine alone at its approved dose (1250 mg/m² orally twice daily on day 1 to day 15 of each 21-day cycle).³⁷

Liporaxel

Liporaxel (DHP107) is an oral paclitaxel formulation consisting of a semisolid wax, which melts at

approximately 30 °C, rendering it an oily liquid at body temperature.³⁸ As such, it can be administered as an oral solution. The formulation contains monoolein, tricaprylin, polysorbate 80, and 1% paclitaxel (weight per volume).³⁸ In a rodent study, repeated doses of DHP107 led to increased P-gp expression, as well as cytochrome P450 (CYP) 3A4 metabolizing enzyme expression, which may lessen bioavailability.³⁸ Systemic exposure after the second dose was smaller than that after the first dose, which correlated with the induction of P-gp and CYP expression in the livers and small intestines.³⁸ Based on these findings, the investigators concluded that oral DHP107 should be administered at specific dosing intervals to avoid the timing of highest expression of P-gp and CYP that may decrease DHP107's systemic exposure.³⁸

In a phase 3 multicenter, open-label, randomized clinical trial (DREAM; NCT01839773), oral DHP107 was compared with IV paclitaxel in patients with advanced gastric cancer after front-line treatment failure.³⁹ DHP107 was administered without premedication 1 hour after breakfast and 1 hour after dinner to give an interval of 10 hours between doses.³⁹ In this population with advanced gastric cancer, DHP107's efficacy on PFS was noninferior to that of IV paclitaxel, and AEs were comparable.³⁹

Currently, in China and Korea, the OPTIMAL phase 3 study is under way to evaluate the efficacy of DHP107 in recurrent breast cancer or mBC in the front-line setting.⁴⁰ In non-Asian patients, the phase 2 open-label, multicenter, randomized OPERA trial (NCT03326102) will evaluate DHP107 in patients with recurrent or metastatic hormone receptor–positive/HER2- breast cancer or TNBC.⁴⁰ Included patients may have received up to 3 prior lines of therapy for advanced disease.⁴⁰ Patients will be randomized 2:1 to DHP107 (200 mg/m² orally twice a day) or IV paclitaxel (80 mg/m² on days 1, 8, and 15 of a 28-day cycle).⁴⁰ Blood samples from a subset of 12 patients will be obtained for pharmacokinetic analyses.⁴⁰ The primary end point is objective response rate. Enrollment of 72 evaluable subjects is expected to complete in 2020.⁴⁰

ModraDoc006/r

In addition to oral paclitaxel, the development of an oral formulation of docetaxel has also begun. ModraDoc is a solid dispersion formulation combining freeze- or spray-dried docetaxel with a surfactant and hydrophilic carrier.⁴¹ Both ModraDoc001 capsule (10-mg freeze-dried docetaxel) and ModraDoc006 tablet (10-mg spray-dried docetaxel) have been studied.⁴¹ These oral formulations of docetaxel are coadministered with ritonavir, a CYP3A4 and P-gp inhibitor, based on preclinical data that coadministration of CYP3A4 or P-gp inhibitors increases docetaxel's bioavailability.⁴¹ In pharmacokinetic studies evaluating doses of Modradoc001 and Modradoc006 ranging from

30 mg to 80 mg among patients with solid tumors, the recommended phase 2 dose for both ModraDoc001 capsule and ModraDoc006 tablet was 60 mg once weekly together with 100-mg ritonavir.⁴¹ The most common AEs of any grade were diarrhea (70%), nausea (67%), fatigue (67%), vomiting (42%), alopecia (33%), and mucositis (24%). Neutropenia occurred in 9% of patients.⁴¹ A multi-center, single-arm, phase 2a trial evaluating the safety and efficacy of ModraDoc006 coadministered with ritonavir (ModraDoc006/r) in patients with recurrent or metastatic HER2- breast cancer is ongoing (NCT03890744).⁴² The primary end point will be objective response rate. Secondary outcomes include tolerability, toxicities, and PFS.⁴²

Oral Nontaxanes

Eribulin

Eribulin is a synthetic analogue of halichondrin B and exerts its cytotoxic activity by inhibiting microtubule polymerization, resulting in cancer cell apoptosis.⁴³ Eribulin is FDA approved for patients with mBC who have been previously treated with at least 2 chemotherapeutic regimens, including an anthracycline and a taxane.⁴⁴ Currently, eribulin is administered by IV infusion.⁴⁴ Similar to taxanes, P-gp on the intestinal mucosa limits the oral bioavailability of eribulin.⁴⁵ A novel oral formulation, eribulin ORA, has recently been developed by Athenex Inc.⁴⁶ The formulation combines oral eribulin with encephalidin, a P-gp inhibitor.⁴⁶ In a rodent model, encephalidin significantly increased the systemic exposure of oral eribulin by more than 5-fold and improved oral bioavailability from 16.1% to 35.0%.⁴⁶ All tested eribulin ORA doses (0.5, 1.0, and 1.5 mg/kg 3 times weekly for 4 weeks) induced tumor regression in mice bearing breast tumor xenografts.⁴⁶ Except for weight loss of less than 10% in the highest-dose group, eribulin ORA was well tolerated in the rodent model.⁴⁶

Future Directions in Treatment With Oral Chemotherapy

With several oral chemotherapy agents in development, the oncology community expects that challenges associated with chemotherapy IV infusion can be mitigated once these oral agents become available. Disadvantages of IV chemotherapy include patient and caregiver burden associated with travel to and from infusion clinics, wait time at the infusion appointments, interference with daily life (eg, work and relationships), lack of autonomy, as well as infusion-related discomfort,⁴⁷ health care costs,^{48,49} and AEs (eg, vein sclerosis, thrombosis, extravasation, and infections associated with chronic IV access).⁵⁰

For taxanes, the vehicle for conventional IV formulations contributes directly to hypersensitivity reactions,

neutropenia, and peripheral neuropathy. One of the oral taxane formulations, oral paclitaxel plus encephalidin, has demonstrated a lower risk of grade 2 and 3 treatment-emergent neuropathy (7.6% vs 31.1%) and grade 2 alopecia (28.8% vs 48.1%) compared with conventional IV paclitaxel.¹⁶ Oral taxane administration also does not require corticosteroid premedication necessary for conventional IV taxanes. With an oral taxane formulation, the benefit of avoiding systemic corticosteroids, which can complicate glycemic control, is especially relevant for patients with diabetes.

Beyond treatment burden and treatment-related complications, oral formulations of chemotherapy may improve efficacy. In the largest phase 3 trial with an oral taxane reported to date, the confirmed response rate in the oral paclitaxel plus encephalidin group was 40.4% compared with 25.6% in the conventional IV paclitaxel group ($P = .005$).¹⁶ Importantly, the median OS was 27.9 months in patients receiving oral paclitaxel plus encephalidin versus 16.9 months in those receiving conventional IV paclitaxel (HR, 0.684; 95% CI, 0.475-0.985).¹⁶ Additionally, the clinical response was durable, and 33.7% of patients treated with oral paclitaxel plus encephalidin maintained response beyond 200 days.¹⁶

Data on oral chemotherapy have been promising so far, suggesting that oral paclitaxel plus encephalidin has the potential to improve treatment outcomes while alleviating treatment burden for patients with mBC. Results of other clinical trials with oral chemotherapy agents are eagerly awaited. Additional clinical trial data of other oral taxanes, as well as oral eribulin, are on the horizon and may advance the care of patients with mBC. ♦

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