

Dear Healthcare Provider:

Enclosed is the current issue of *Clinical Impressions*[™]. In this issue, we will review "Multicenter phase II study of capecitabine in paclitaxel-refractory metastatic breast cancer," authored by Joanne L. Blum, MD, and published in the *Journal of Clinical Oncology* in 1999. Commentary on the journal article is provided for *Clinical Impressions*[™] by Melanie E. Royce, MD, PhD. Dr Royce is the director of the Hereditary Cancer Assessment Program and the Multidisciplinary Breast Cancer Program at the University of New Mexico Cancer Center. She has written numerous articles on breast cancer and has presented at meetings that draw some of the most highly regarded experts in cancer.

For metastatic breast cancer (mBC) patients who are resistant to paclitaxel and anthracyclines, options for effective treatments that are also tolerable for patients become more limited. XELODA[®] (capecitabine) monotherapy has proven efficacy in the treatment of patients with mBC. In a study by Blum et al, 60% of anthracycline and taxane-resistant patients received clinical benefit (defined as complete response [CR] + partial response [PR] + stable disease [SD]) from XELODA treatment, with 40% of patients achieving stable disease and 20% experiencing a CR or PR.¹ XELODA also has an established safety profile and allows patients the convenience of an oral medication with adverse events that are, in most cases, manageable and reversible, although doses may need to be withheld or reduced.

Please see indications and important safety information below.

In the enclosed *Clinical Impressions*[™] Dr Royce shares her clinical insights and in the Clinical Question & Answer section she discusses the trial results as well as monotherapy for treatment of patients with mBC.

We hope you find this issue of *Clinical Impressions*[™] valuable to your practice and the metastatic breast cancer patients you treat.

Sincerely,

Editor-in-Chief
Clinical Impressions[™]

This promotional program was developed in conjunction with and sponsored by Genentech and is consistent with FDA regulations and guidelines.

Dr Melanie E. Royce received a fee from Genentech for her participation in this project.

Indications

XELODA monotherapy is indicated for the treatment of patients with metastatic breast cancer resistant to both paclitaxel and an anthracycline-containing chemotherapy regimen or resistant to paclitaxel and for whom further anthracycline therapy is not indicated, eg, patients who have received cumulative doses of 400 mg/m² of doxorubicin or doxorubicin equivalents. Resistance is defined as progressive disease while on treatment, with or without an initial response, or relapse within 6 months of completing treatment with an anthracycline-containing adjuvant regimen.

XELODA in combination with docetaxel is indicated for the treatment of patients with metastatic breast cancer after failure of prior anthracycline-containing chemotherapy.

Please see enclosed full XELODA Prescribing Information including Boxed Warning for additional Important Safety Information.

Boxed WARNING and Additional Important Safety Information

Boxed Warning

Warfarin Interaction – Coagulopathy

- Patients receiving concomitant capecitabine and oral coumarin-derivative anticoagulant therapy should have their anticoagulant response (INR or prothrombin time) monitored frequently in order to adjust the anticoagulant dose accordingly.
- A clinically important XELODA-Warfarin drug interaction was demonstrated in a clinical pharmacology trial.
- Altered coagulation parameters and/or bleeding, including death, have been reported in patients taking XELODA concomitantly with coumarin-derivative anticoagulants such as warfarin and phenprocoumon.
- Clinically significant increases in prothrombin time (PT) and INR have been observed in patients who were stabilized on anticoagulants at the time XELODA was introduced. These events occurred within several days and up to several months after initiating XELODA therapy, and infrequently within 1 month after stopping XELODA. These events occurred in patients with and without liver metastases.
- Age greater than 60 and a diagnosis of cancer independently predispose patients to an increased risk of coagulopathy.

Contraindications

- XELODA is contraindicated in patients with known hypersensitivity to capecitabine or to any of its components or to 5-fluorouracil. XELODA is also contraindicated in patients with known dihydropyrimidine dehydrogenase (DPD) deficiency, or severe renal impairment.

Adverse Events

- In a single arm study of XELODA monotherapy in metastatic breast cancer, serious adverse events (grade 3/4) occurring in $\geq 5\%$ of patients receiving XELODA (%) were lymphopenia (59), diarrhea (15), hand-foot syndrome (11), hyperbilirubinemia (11), fatigue (8), stomatitis (7), and dehydration (5). The most common adverse events for all grades occurring in $\geq 30\%$ of patients receiving XELODA were lymphopenia (94), anemia (72), diarrhea (57), hand-foot syndrome (57), nausea (53), fatigue (41), dermatitis (37), and vomiting (37).
- In a phase 3 study of XELODA combination therapy (XELODA plus docetaxel) in metastatic breast cancer, serious adverse events (grade 3/4) occurring at a $\geq 2\%$ higher incidence in patients receiving XELODA plus docetaxel vs docetaxel alone (%;%) were lymphocytopenia (89;84), hand-foot syndrome (24;1), stomatitis (<18;5), diarrhea (<15;<6), anemia (10;<6), hyperbilirubinemia (9;4), nausea (7;2), vomiting (5;2), constipation (2;0), and nail disorder (2;0). The most common adverse events for all grades occurring at a $\geq 5\%$ higher incidence in patients receiving XELODA plus docetaxel vs docetaxel alone were diarrhea (67;48), stomatitis (67;43), hand-foot syndrome (63;8), nausea (45;36), thrombocytopenia (41;23), vomiting (35;24), abdominal pain (30;24), hyperbilirubinemia (20;6), weakness (16;11), dyspepsia (14;8), lacrimation increase (12;7), and appetite decrease (10;5).

Please see enclosed full XELODA Prescribing Information including Boxed Warning for additional Important Safety Information.

References

1. Blum JL, Jones SE, Buzdar AU, et al. Multicenter phase II study of capecitabine in paclitaxel-refractory metastatic breast cancer. *J Clin Oncol.* 1999;17(2):485-493.

This promotional program was developed in conjunction with and sponsored by Genentech and is consistent with FDA regulations and guidelines.

Dr Melanie E. Royce received a fee from Genentech for her participation in this project.

Clinical Impressions™ is a trademark of BioPharm Communications, LLC.

Genentech
BIO  NCOLOGY™

Translating science into life