Totect® (dexrazoxane) – New indication

- On November 2, 2020, the FDA approved Clinigen's Totect (dexrazoxane), for reducing the incidence and severity of cardiomyopathy associated with doxorubicin administration in women with metastatic breast cancer who have received a cumulative doxorubicin dose of 300 mg/m^2 and who will continue to receive doxorubicin therapy to maintain tumor control.
    - Totect should not be used with the initiation of doxorubicin therapy.
- Totect is also approved for the treatment of extravasation resulting from intravenous anthracycline chemotherapy.
- The approval of Totect for the new indication was based on three prospectively randomized placebo-controlled studies. In these studies, patients were treated with a doxorubicin-containing regimen and either dexrazoxane or placebo starting with the first course of chemotherapy. There was no restriction on the cumulative dose of doxorubicin. Cardiac function was assessed by measurement of the left ventricular ejection fraction (LVEF).
    - Patients receiving dexrazoxane had significantly smaller mean decreases from baseline in LVEF and lower incidences of congestive heart failure than the control group; however, in the largest study, patients with advanced breast cancer receiving FAC (fluorouracil, doxorubicin, and cyclophosphamide) with dexrazoxane had a lower response rate (48% vs. 63%) and a shorter time to progression than patients who received FAC vs. placebo.
    - In the clinical trials, patients who were initially randomized to receive placebo were allowed to receive dexrazoxane after a cumulative dose of doxorubicin above 300 mg/m^2. Retrospective historical analyses showed that the risk of experiencing a cardiac event at a cumulative dose of doxorubicin above 300 mg/m^2 was greater in the patients who did not receive dexrazoxane beginning with their seventh course of FAC than in the patients who did receive dexrazoxane (hazard ratio 13.08; 95% CI: 3.72, 46.03; $p < 0.001$).
- The most common adverse reaction (≥ 10% and increased vs. placebo) with Totect use for cardiomyopathy was injection site pain.
- For cardiomyopathy, the recommended dosage ratio of Totect to doxorubicin is 10:1 (eg, 500 mg/m^2 Totect to 50 mg/m^2 doxorubicin). Doxorubicin should be administered within 30 minutes after the completion of Totect infusion. Totect should be administered via intravenous infusion over 15 minutes prior to doxorubicin administration until discontinuation of doxorubicin.
    - Refer to the Totect drug label for dosing for extravasation.

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