High incidence of central nervous system involvement in patients with metastatic or locally advanced breast cancer treated with epirubicin and docetaxel


BACKGROUND: Clinically overt central nervous system (CNS) involvement occurs in 10%-15% of patients with advanced breast cancer. PATIENTS AND METHODS: The International Breast Cancer Study Group (IBCSG) conducted a dose-finding phase I trial of epirubicin (E) and docetaxel (D) as first-line therapy in advanced breast cancer patients. The study was expanded into a phase II at the recommended doses of E 90 mg/m2 and D 75 mg/m2 every three weeks. From July 1996 to May 1998, a total of 92 patients (median age 50 years) entered the two studies. RESULTS: Twenty-eight out of ninety-two patients treated with the combination of E and D (30%) developed CNS metastases (95% confidence limits, 26%-35%), which were cerebral in twenty-five patients, leptomeningeal in two, and both in one. Of these 28 patients, 19 (68%) had an objective response. Median time for the development of CNS metastases from the start of chemotherapy was 15 months (range 5-42), if excluding the 6 patients presenting CNS progression within 3 months from start of treatment. It is notable that 11 patients (39%) had progression in the CNS only. Median survival from appearance of brain metastases in the whole group was only three months (range 1-22). C-erbB-2 overexpression was found in 14 out of 16 patients (87%) in whom the assay was performed (3+ in 10, 2+ in 1 and 1+ in 3 cases). CONCLUSIONS: As anthracycline- and taxane-containing regimens are increasingly used both in the metastatic and in the adjuvant setting, a careful monitoring of any neurological symptom is advisable. Our preliminary observation on the possible increase of incidence of CNS involvement in patients with advanced breast cancer receiving this effective drug combination requires further evaluation.