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Paclitaxel-carboplatin combination chemotherapy in advanced breast cancer: accumulating evidence for synergy, efficacy, and safety.

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Source

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Abstract

Patients with metastatic breast cancer receive multiple lines of cytotoxic chemotherapy, with taxane and anthracycline-based regimens being the most active. Anthracyclines carry the risk of significant cardiotoxicity at high cumulative doses and when combined with trastuzumab, an anti-HER2 antibody. Carboplatin has shown promising single-agent activity in advanced breast cancer, is not a P-glycoprotein substrate, and is conveniently administered on an outpatient basis. Preclinical experiments demonstrated schedule-dependent synergistic cytotoxic effects of the paclitaxel first/carboplatin last (PC) combination. Pharmacokinetic parameters of paclitaxel and carboplatin were studied by Hellenic Cooperative Oncology Group (HECOG) and no significant interaction or correlation with clinical parameters were found. We assessed PC both as salvage as well as first-line treatment of advanced breast cancer patients in phase II studies which disclosed 40-60% response rates and median survival times of 12-20 mo with manageable toxicity. These results were confirmed by other groups and prompted us to the first randomized phase III trial comparing PC to the standard of epirubicin/paclitaxel (EP), a trial that showed equivalent efficacy and tolerable toxicity for PC. Registry retrospective analysis identified factors prognostic for improved outcome: good performance status, low tumor burden, lack of anthracycline exposure and of hormonal maintenance therapy. PC combinations with HER1 or HER2 modulators are being evaluated both by HECOG and by international groups. Paclitaxel coupled with carboplatin provides an alternative therapeutic option for anthracycline-exposed patients and warrants further clinical research in the direction of anthracycline-free management of metastatic breast cancer.