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Titel des Beitrags: PREPARE trial: a randomized phase III trial comparing preoperative, dose-dense, dose-intensified chemotherapy with epirubicin, paclitaxel and CMF versus a standard-dosed epirubicin/cyclophosphamide followed by paclitaxel +/- darbepoetin alfa in primary

Abstract: BACKGROUND: Preoperative chemotherapy is a recommended treatment of both primary operable and locally advanced breast cancer. Strategies to improve efficacy include the use of anthracyclines, taxanes, and intensified dose with bone marrow support. PATIENTS AND METHODS: Patients received neoadjuvant epirubicin 90 mg/m² plus cyclophosphamide 600 mg/m² followed by paclitaxel 175 mg/m² (EC→T), each 3-weekly for four cycles (n = 370), or epirubicin 150 mg/m² followed by paclitaxel 225 mg/m² with pegfilgrastim followed by CMF (cyclophosphamide 500 mg/m², methotrexate 40 mg/m², fluorouracil 600 mg/m²) on days 1 and 8 (E(dd)→T(dd)→CMF), each 2-weekly and for three cycles (n = 363). Patients were randomly allocated to either simultaneous darbepoetin alfa (DA) (n = 356) or none (n = 377). RESULTS: Pathological complete response (pCR) rate (breast) was higher with
E(dd)->T(dd)->CMF, 18.7% versus 13.2% with EC->T; P = 0.043, ypT0/Tis; ypN0 was reported in 20.9% versus 14.3% respectively; P = 0.019. Patients with grade 3 tumors and negative hormone receptor status had a significantly higher pCR rate. Mean hemoglobin values maintained higher with DA (13.6 versus 12.6 g/dl). E(dd)->T(dd)->CMF regimen showed more grade 3-4 mucositis, sensory neuropathy, and neurological complaints. Thromboembolic events were more frequent on DA (3% versus 6%; P = 0.055). CONCLUSION: Dose-dense and -intensified neoadjuvant chemotherapy with E(dd)->T(dd)->CMF was potentially superior to EC->T in terms of pCR. Primary use of DA did not affect pCR.