Dual Blockade with AFatinib and Trastuzumab as NEoadjuvant Treatment for Patients with Locally Advanced or Operable Breast Cancer Receiving Taxane-Anthracycline Containing Chemotherapy-DAFNE (GBG-70).

Abstract:
Dual anti-HER2 blockade with trastuzumab/pertuzumab or trastuzumab/lapatinib in combination with anthracycline/taxane-based chemotherapy can reach pathologic complete response (pCR) rates of up to 60% in HER2-positive breast cancer. The DAFNE (Dual blockade with AFatinib and trastuzumab as NEoadjuvant treatment) phase II study (NCT015591477) investigated a dual blockade with the irreversible pan-HER inhibitor afatinib and trastuzumab in this setting. Participants with untreated, centrally HER2-positive breast cancer were treated for 6 weeks with afatinib (20 mg/d) and trastuzumab [(8) 6 mg/kg/3 weeks] alone; followed by 12-week treatment with paclitaxel (80 mg/m(2)/1 week), trastuzumab, and afatinib; followed by 12 weeks with epirubicin (90 mg/m(2)/3 weeks), cyclophosphamide (600 mg/m(2)/3 weeks), and trastuzumab before surgery. Primary objective was pCR rate, defined as ypT0/is ypN0. We expected a pCR rate of 70%; 65 patients were needed to exclude a rate of<=55%. pCR rate was 49.2%
[90% confidence interval (CI), 38.5-60.1] in 65 treated patients. Patients with hormone receptor-negative (N = 19) or hormone receptor-positive (N = 46) tumors showed pCR rates of 63.2% and 43.5%, respectively (P = 0.153). Patients with (N = 9) or without (N = 56) lymphocyte predominant breast cancer (LPBC) showed pCR rates of 100% and 41.1%, respectively (P< 0.001). PCR rate was not different in patients with or without PIK3CA tumor mutations (P = 0.363). Clinical responses were seen in 96.3% of 54 evaluable patients, and breast conserving surgery was possible in 59.4% of 62 assessable patients. Most frequent nonhematologic grade 3-4 toxicities were diarrhea (7.7%), increased creatinine (4.6%), and infection (4.6%). One patient developed symptomatic congestive heart failure. Neoadjuvant treatment with afatinib, trastuzumab, and chemotherapy showed acceptable tolerability, and a pCR rate comparable with that of other anti-HER2 doublets but below challenging expectations.