The objective of this prospectively randomized phase II trial (Trial registration: EUCTR2004-004007-37-DE) was to compare the clinical response of primary breast cancer patients to neoadjuvant therapy with letrozole alone (LET) or letrozole and zoledronic acid (LET + ZOL). Patients were randomly assigned to receive either LET 2.5 mg/day (n = 79) or the combination of LET 2.5 mg/day and a total of seven infusions of ZOL 4 mg every 4 weeks (n = 89) for 6 months. Primary endpoint was clinical response rate as assessed by mammogram readings. The study was terminated prematurely due to insufficient recruitment. We report here on an exploratory analysis of this data. Central assessment of tumor sizes during the treatment period was available for 131 patients (66 LET, 65 LET + ZOL). Clinical responses (complete or partial) were seen in 54.5% (95% CI: 41.8-66.9) of the patients in the LET arm and 69.2% (95% CI: 56.6-80.1) of those in the LET + ZOL arm (P = 0.106). A multivariate model showed an OR of...
1.72 (95% CI: 0.83-3.59) for the experimental arm. No increase in the clinical response rate was observed with the addition of ZOL to a neoadjuvant treatment regimen with LET. However, a trend towards a better response in the LET + ZOL arm could be observed. This trend is consistent with previous studies that have investigated the addition of ZOL to chemotherapy, and it may support the evidence for a direct antitumor action of zoledronic acid.