PLoS One. 2013 Jul 23;8(7):e69256. doi: 10.1371/journal.pone.0069256. Print 2013.

Ixabepilone administered weekly or every three weeks in HER2-negative metastatic breast cancer patients; a randomized non-comparative phase II trial.

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Source

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Abstract

To explore the activity and safety of two schedules of ixabepilone, as first line chemotherapy, in patients with metastatic breast cancer previously treated with adjuvant chemotherapy, a randomized non-comparative phase II study was conducted. From November 2008 until December 2010, 64 patients were treated with either ixabepilone 40 mg/m(2) every 3 weeks (Group A, 32 patients) or ixabepilone 20 mg/m(2) on days 1, 8 and 15 every 4 weeks (Group B, 32 patients). Overall response rate (the primary end point) was 47% in Group A and 50% in Group B. The most frequent severe adverse events were neutropenia (32% vs. 23%), metabolic disturbances (29% vs. 27%) and sensory neuropathy (12% vs. 27%). Two patients in Group A and 3 in Group B developed febrile neutropenia. After a median follow-up of 22.7 months, median progression-free survival (PFS) was 9 months in Group A and 12 months in Group B. Median survival was 26 months in Group A, whereas it was not reached in Group B. Multiple genetic and molecular markers were examined in tumor and peripheral blood DNA, but none of them was associated with ORR or drug toxicity. Favorable prognostic markers included: the T-variants of ABCB1 SNPs c.2677G/A/T, c.1236C/T and c.3435C/T, as well as high MAPT mRNA and Tau protein expression, which were all associated with the ER/PgR-positive phenotype; absence of TopoIIa; and, an interaction between low TUBB3 mRNA expression and Group B. Upon multivariate analysis, tumor ER-positivity was a favorable (p=0.0092) and TopoIIa an unfavorable (p=0.002) prognostic factor for PFS; PgR-positivity was favorable (p=0.028) for survival. In conclusion, ixabepilone had a manageable safety profile in both the 3-weekly and weekly schedules. A number of markers identified in the present trial appear to deserve further evaluation for their prognostic and/or predictive value in larger multi-arm studies.

TRIAL REGISTRATION:

ClinicalTrials.gov NCT 00790894.