CÁNCER DE MAMA

Phase I dose-escalation and pharmacokinetic study of ispinesib, a kinesin spindle protein inhibitor, administered on days 1 and 15 of a 28-day schedule in patients with no prior treatment for advanced breast cancer.

Gomez HL, Philco M, Pimentel P, Kiyan M, Monsalvo ML, Conlan MG, Saikali KG, Chen MM, Seroogy JJ, Wolff AA, Escandon RD.

Anticancer Drugs. 2012 Mar;23(3):335-41.

Abstract

The objective of the study was to evaluate the safety, pharmacokinetics, and antitumor activity of ispinesib, a kinesin spindle protein inhibitor. Patients with locally advanced or metastatic breast cancer who had received only prior neoadjuvant or adjuvant chemotherapy were treated with escalating doses of ispinesib administered as a 1-h infusion on days 1 and 15 every 28 days until toxicity or progression of disease. Doses were escalated until dose-limiting toxicity was observed in two out of six patients during cycle 1. A total of 16 patients were treated at three dose levels: 10 mg/m (n=3), 12 mg/m (n=6), and 14 mg/m (n=7). Forty-four percent of the patients had locally advanced disease and 56% had metastatic disease; 50% were estrogen receptor positive, 44% were progesterone receptor positive, 25% human epidermal growth factor 2 were positive, and 31% triple (estrogen receptor, progesterone receptor, human epidermal growth factor 2) negative. Sixty-nine percent of patients were chemo-naive. The maximum tolerated dose was 12 mg/m and dose-limiting toxicity was grade 3 increased aspartate aminotransferase and alanine aminotransferase. The most common toxicities included neutropenia (88%; 38% grade 3 and 44% grade 4), increased alanine aminotransferase (56%), anemia (38%), increased aspartate aminotransferase (31%), and diarrhea (31%). No neuropathy, mucositis, or alopecia was reported. Among the 15 patients evaluable for antitumor activity, there were three partial responses, one confirmed by the response evaluation criteria in solid tumors (7% response rate). Nine patients (60%) had stable disease lasting at least 42 days, with four (27%) lasting for at least 90 days. Disease stabilization (partial responses+stable disease) was observed in 11 (73.3%) patients. In conclusion, ispinesib was well tolerated when administered on days 1 and 15 every 28 days. Limited activity was observed with this schedule in patients with previously untreated advanced breast cancer.

Behaviour of breast cancer molecular subtypes through tumour progression.

Castaneda CA, Andrés E, Barcena C, Gómez HL, Cortés-Funés H, Ciruelos E.

Clin Transl Oncol. 2012 Jun;14(6):481-5.

Abstract

Breast cancer (BC) becomes more aggressive throughout disease progression. Clinical stage is correlated with patient outcome. We hypothesised that BC molecular subtypes are associated with a poor prognosis in advanced clinical stages. We analysed the distribution and behaviour of molecular subtypes at different BC tumour size and variation of molecular subtype in recurrent lesions. We studied 1647 consecutive patients with non-metastatic invasive and microinvasive (Tmi) BC treated from January 1997 to December 2007. Patients were categorised by tumour size and molecular subtype. A chi-square method was used for multiple group comparisons. Kaplan-Meier product limit method was used to calculate overall survival and disease-free survival. Median follow-up was 7.2 years. For patients with invasive BC the median age was 56 years. Four hundred and fifteen patients recurred and 225 died. Larger tumours were more frequently of triplenegative (TN) subtype than small ones or Tmi lesions. Any molecular subtype change from primary tumour to recurrent lesions is more likely to happen from a good prognosis to a subtype of worse prognosis than the opposite. Larger tumours of luminal A, luminal B and TN, but not HER2 subtype, are more likely to carry aggressive markers and to have worse outcomes than small ones. We found accumulation of TN subtype, migration to a poor prognosis subtype and increasing aggressiveness of luminal and TN subtypes throughout tumour progression. Tumours belonging to the HER2 subtype behave aggressively regardless of the primary size.