

Journal of Clinical Oncology, 2008 ASCO Annual Meeting Proceedings (Post-Meeting Edition).
Vol 26, No 15S (May 20 Supplement), 2008: 1070
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Abstract

Larotaxel (L) in combination with trastuzumab in patients with HER2 + metastatic breast cancer (MBC): Interim analysis of an open phase II label study

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Background: Larotaxel (L), a semi-synthetic taxoid, has shown preclinical and clinical activity against taxane-resistant BC, and it presents the ability to cross the blood brain barrier. In HER2 + BC, trastuzumab (H) combined with taxanes is highly active, particularly in early stage BC. However, there is a need to develop new combinations for HER2+ pts who develop metastasis (mets), especially brain mets. **Methods:** MBC pts, < 1 prior chemotherapy (Ct) for metastatic disease, measurable disease, HER2 + (IHC $\geq 3+$ and/or FISH +), baseline LVEF $\geq 50\%$, were eligible to receive 90 mg/m² L, 1-hour infusion and 6 mg/kg (8 mg/kg loading dose) H, every 3 weeks(w). Inclusion of patients with asymptomatic brain mets (mandatory baseline CTscan) was allowed. Main objectives: activity of LH combination (ORR as per RECIST), progression free-survival, CNS outcome or occurrence, overall survival, safety and pharmacokinetic (PK) profiles. Tumor assessments and LVEF were done every 2 cycles(cy). **Results:** As of Dec. 2007, 41/50 pts were treated. The first 26 evaluable pts are presented in this per-protocol interim analysis: median age of 55.5 y (30–78), 19 pts (73%) with ≥ 2 organs involved (including 4 with brain mets), 17pts with prior Ct for metastatic disease (prior taxane: 13 and prior H:15). The median number of cy was 6 (1–12). Most common gr 3–4 adverse events: febrile neutropenia/neutropenic infection (4), diarrhea (2), asthenia (6). Eleven (42.3%) confirmed partial responses (PR) were reported in 1st or in 2nd line with 1 PR and 3 stable disease (SD) lasting ≥ 18 w in pts with brain mets. Preliminary PK results: clearance of L at cy1 and 6 are similar to those

observed in monotherapy. **Conclusions:** L and H at full doses can be combined with a manageable toxicity. Preliminary data suggest good activity in pretreated pts with high tumor burden, including pts with brain mets. PK analysis will be presented on the whole population.

Author Disclosure

Employment or Leadership	Consultant or Advisory Role	Stock Ownership	Honoraria	Research	Expert Testimony	Other Remuneration
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Abstract presentation from the 2008 ASCO Annual Meeting