Antivascular activity of lapatinib and bevacizumab in primary microcluster cultures of breast cancer and other human neoplasms

L. Weisenthal, D.J. Lee, and N. Patel

Weisenthal Cancer Group, Huntington Beach, CA  http://weisenthal.org  http://weisenthalcancer.com

INTRODUCTION

While the other clinically-available "nib" drugs have been shown to have antivascular activity, antivascular of lapatinib has not been previously reported.

We studied the direct antitumor and antivascular effects of lapatinib, sorafenib, and bevacizumab in fresh biopsy specimens of breast cancer and other human neoplasms.

METHODS

Cell culture detection of microvascular cell death in clinical specimens of human neoplasms and peripheral blood

L. R. Weisenthal, K. T. and K. R. Weisenthal

Weisenthal Cancer Group, Huntington Beach, CA

Breast Cancer: Example of specimen-specific synergy between bevacizumab and herein kinase inhibitors (148 drug).

Breast Cancer: Detection of direct antitumor activity

Method for testing Anti-angiogenesis Drug in Vitro

Breast Cancer: Effective antitumor drugs tend to produce fragmentation of tumor microclusters.

Breast Cancer: Detection of direct antitumor activity

Equipment needed: Cytospins, "multi-spot" cuvettes and filter papers

Conclusions

1. Lapatinib 16.5 μM and 8.25 μM (data not shown) has both direct antitumor effects and antivascular effects on short-term (96 hours) cultures of fresh human tumor microclusters.

2. At concentrations producing equivalent direct toxicity to tumor cells, lapatinib has antivascular activity which is markedly superior to that of sorafenib but inferior to that of bevacizumab.

3. Lapatinib clearly enhances the antivascular activity of bevacizumab, even in many Her2 negative tumors, while sorafenib does not.

4. Intermittent high dose bolus schedules of lapatinib to coincide with periods of maximal VEGF depletion by bevacizumab should be considered to maximize the destruction of the tumor-associated microvascularity and possibly to reduce both expense and toxicity.