

Phase I evaluation of lapatinib (L) and epirubicin (E) in patients (pts) with anthracycline (anth)-naive metastatic breast cancer (MBC)

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Abstract: Background:

HER-2 alteration confers enhanced anth. sensitivity in MBC, although HER2 is not a target for anth.

Topoisomerase 2A (Topo) is a target for anth. Topo amplification has been reported to occur only with

HER2 amplification, in approximately 1/3 of HER2 amplified BC, providing a rationale for anth +trastuzumab(H) therapy in MBC with co-amplified HER2/Topo. T+anth is cardiotoxic. L may have similar single agent activity, but less cardiotoxicity than H. L competes with anth for p-glycoprotein and might enhance its activity. The cardiac safety of L + anth needed to be established.

Methods:

We conducted a phase I evaluation of fixed dose lapatinib (1250 mg/day) with escalating doses of epirubicin (Epi-planned dose levels I-IV :75/80/90/100 mg/m²) in pts with HER2+/-, anth-naive metastatic BC. Epirubicin was administered q3 weeks. A minimum of 3 (if no dose-limiting toxicity) and a maximum of 6 pts were treated per dose level. Ejection fractions were performed at base line and after every second cycle., BNP and troponin after every cycle.

Results:

9 pts were treated, 3 level I, 6 level II. Dose level I was declared the maximum tolerated dose following 2 occurrences of dose-limiting toxicity in Level II. 1 pt experienced febrile neutropenia, 1 had > 20% decrease in LVEF. To date there have been 3 PRs by RECIST out of 8 evaluable patients which represents a response rate of 37.5%.

Conclusions: Using classic phase I criteria, the combination of L 1250 mg together with Epi 75 mg/m² combination is relatively well tolerated and suitable for further investigation in a phase II study of Her2+veTopo+ve MBC patients. We will conduct such a study in pts with HER2+Topo+ metastatic BC.