Supplementary Figure 1. Effects of single agent of tamoxifen, everolimus, or PI3K inhibitors (LY294002 or BKM120, BEZ-235) on MCF-7 and BT474 breast cancer cell lines after 48h and 72h treatment.

After a 24 h serum withdrawal, MCF-7 (A) and BT474 (B) cells were digested and washed three times in PBS, and 1×10^4 cells were plated into 96-well flat-bottomed tissue culture plates in 0.1 ml in complete growth medium. 24 hours later, treated them with a range of tamoxifen (10 μM), everolimus (20 nM), LY294002 (10 μM), BKM120 (10 μM) and BEZ-235 (10 μM). Proliferation was evaluated by CCK-8 assay over a two-day (blank bar) and 3-day (dark bar) period. The results repeated independently at least three times. * presents statistically significant differences between control and treatment, p < 0.05. ** presents statistically significant differences between control and T+L or T+E+L treatment, p < 0.01.

Supplementary Figure 2. Growth-inhibitory effects of tamoxifen, everolimus, and various PI3K inhibitors on breast cancer cell lines.


After a 24 h serum withdrawal, MCF-7 cells were digested and washed three times in PBS, and 1×10^4 cells were plated into 96-well flat-bottomed tissue culture plates in 0.1 ml in complete growth medium. 24 hours later, treated them with tamoxifen (10 μM), everolimus (20 nM), LY294002 (10 μM), BKM120 (10 μM), BEZ-235 (10 μM) alone or combination. Proliferation was evaluated by CCK-8 assay in a range of 1 to 5 days. Data are presented as means ± s.d. The results repeated independently at least three times. * presents statistically significant differences between control and treatment, p < 0.05. ** presents statistically significant differences between control and T+L or T+E+L treatment, p < 0.01.

(B). Growth inhibition of BT474 cells by different agents combination treatment;

After a 24 h serum withdrawal, BT474 cells were digested and washed three times in PBS, and 1×10^4 cells were plated into 96-well flat-bottomed tissue culture plates in 0.1 ml in complete growth medium. 24 hours later, treated them with tamoxifen (10 μM), everolimus (20 nM), LY294002 (10 μM), BKM120 (10 μM), BEZ235 (10 μM) alone or combination. Proliferation was evaluated by CCK-8 assay in a range of 1 to 5 days. Data
are presented as means ± s.d. The results repeated independently at least three times. * presents statistically significant differences between control and treatment, p < 0.05. ** presents statistically significant differences between control and T+L or T+E+L treatment, p < 0.01.

**Abbreviation:** Ctrl: Control; T: tamoxifen; E: everolimus; L: LY294002; BKM: BKM120; BEZ: BEZ235

**Supplementary Figure 3. Efficacy of PI3K inhibitors on pAkt cross-talk activation on the basis of tamoxifen and everolimus treatment in MCF-7 (left) and BT474 (right) cell lines.**

Cell extracts were prepared from MCF-7 and BT474 cells with the pretreatment of tamoxifen (10 μM) alone or combined with everolimus (20 nM), BKM120 (10 μM), BEZ235 (10 μM) for 30 minutes. Then whole cell protein were used to detect the expressions of total p-P70S6K, T-P70S6K, p-Akt(Thr473), T-Akt, p-4EBP1, T-4EBP1 and GAPDH by Western blot assays. The results repeated independently at least three times.

**Abbreviation:** Ctrl: Control; T: tamoxifen; E: everolimus; L: LY294002; BKM: BKM120; BEZ: BEZ235