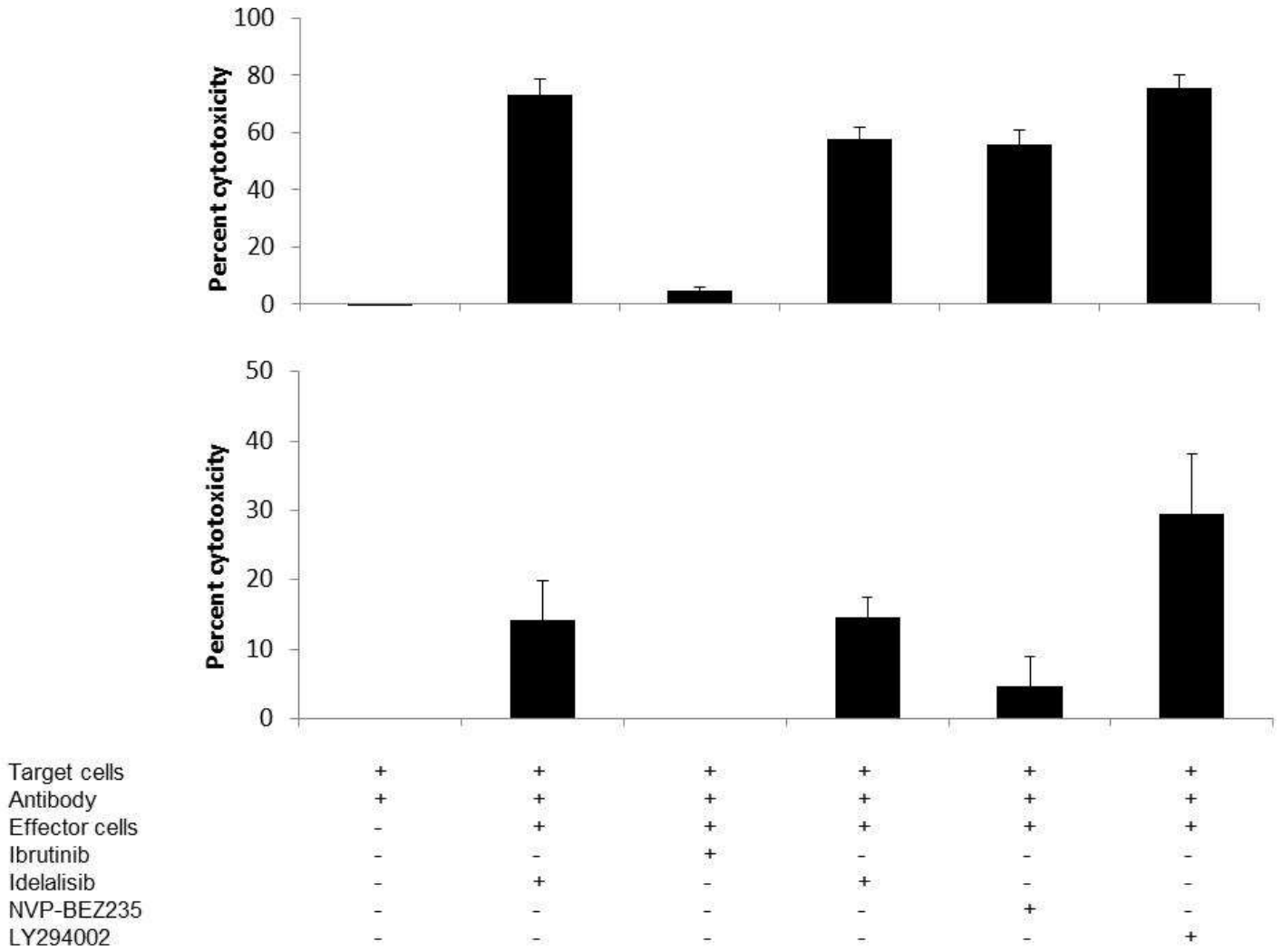
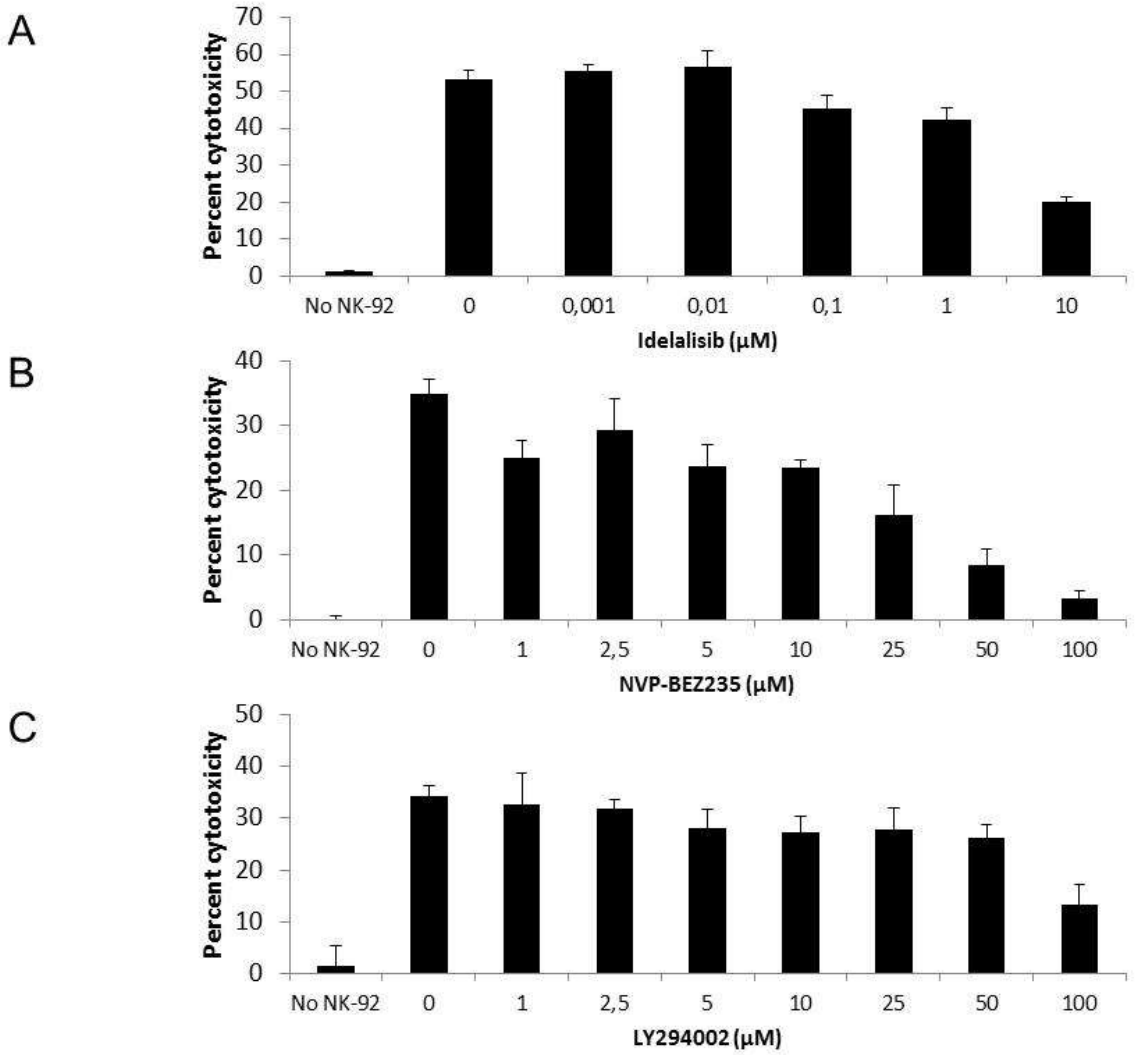
Supplementary Figure S1



Supplementary Figure S1. Effect of kinase inhibitors on ADCC induced by trastuzumab with PBMC and purified NK cells as effector cells.

ADCC was performed with BT474 cells as target cells, 1µg/mL trastuzumab, and peripheral blood mononuclear cells (E:T = 50 :1, top panel) or purified human NK cells (E:T = 5:1, bottom panel) as effector cells. Ibrutinib, idelalisib, NVP-BEZ235 and LY294002 were used at 10 µM.

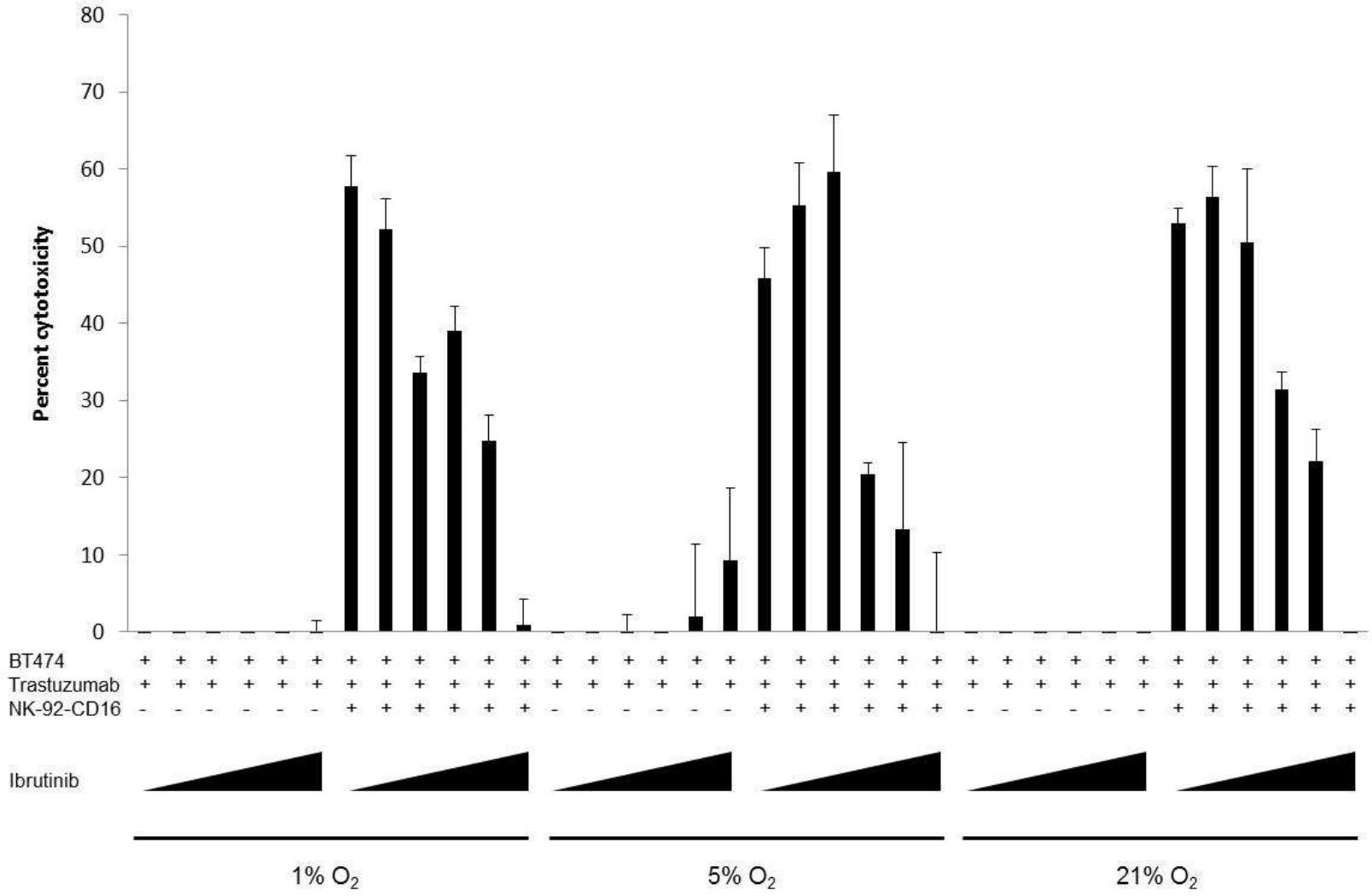
Supplementary Figure S2



Supplementary Figure S2. Dose-response of idelalisib, NVP-BEZ235 and LY294002 on ADCC induced by trastuzumab.

ADCC assays were performed with BT474 cells as target cells, 1 µg/mL trastuzumab, and NK-92 cells as effector cells (E:T=5:1), in the presence of idelalisib, NVP-BEZ235 or LY294002 at indicated concentrations.

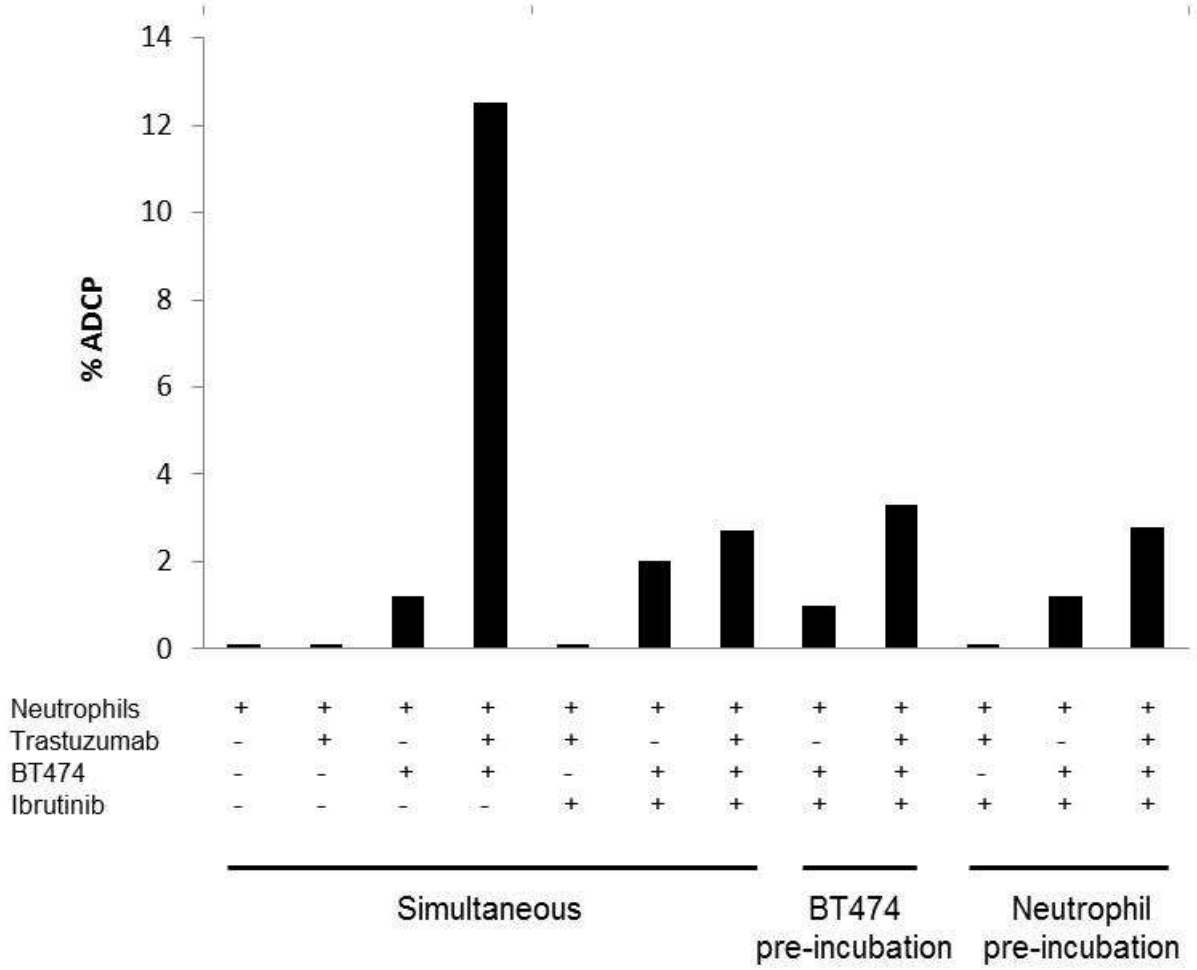
Supplementary Figure S3



Supplementary Figure S3. Effect of ibrutinib on ADCC induced by trastuzumab in hypoxic and normoxic conditions.

ADCC assays were performed with BT474 cells as target cells, 1 µg/mL trastuzumab, and NK-92 cells as effector cells (E:T=5:1), in normoxic (21% O_2) or hypoxic (5% or 1% O_2) conditions. Ibrutinib was used at 0, 0.001, 0.01, 0.1, 1 and 10 µM.

Supplementary Figure S4



Supplementary Figure S4. Effect of pre-incubation of effector or target cells with ibrutinib on ADCC induced by trastuzumab.

Phagocytosis study was performed in the absence or the presence of 10 µM ibrutinib, either added simultaneously or pre-incubated with BT474 cells or neutrophils.