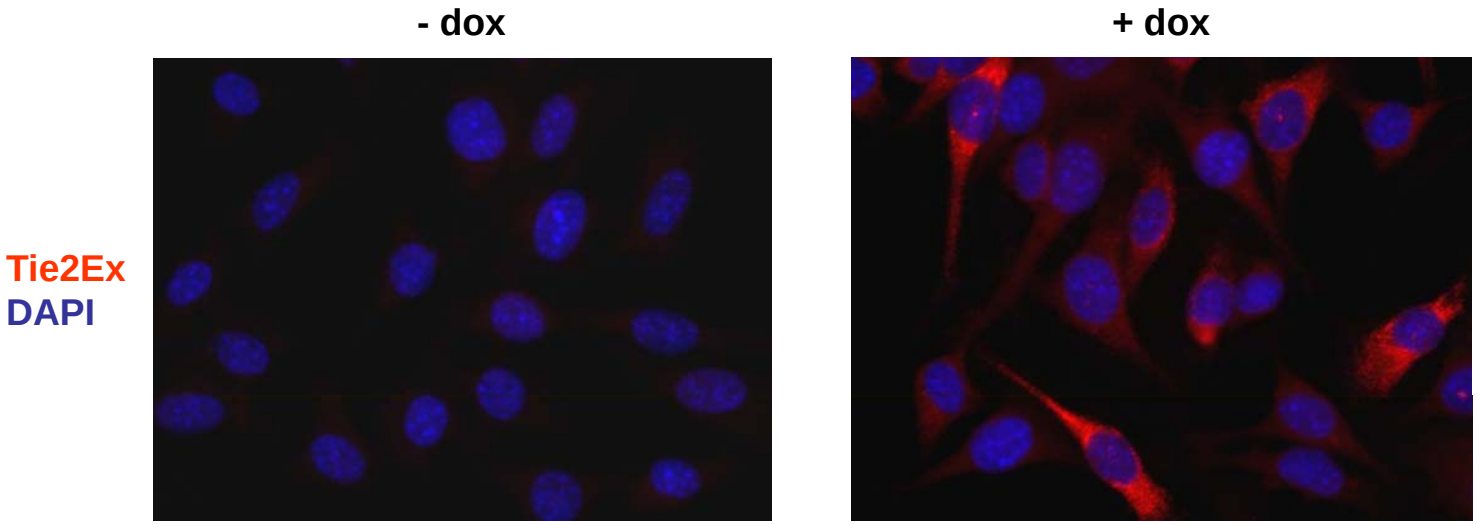
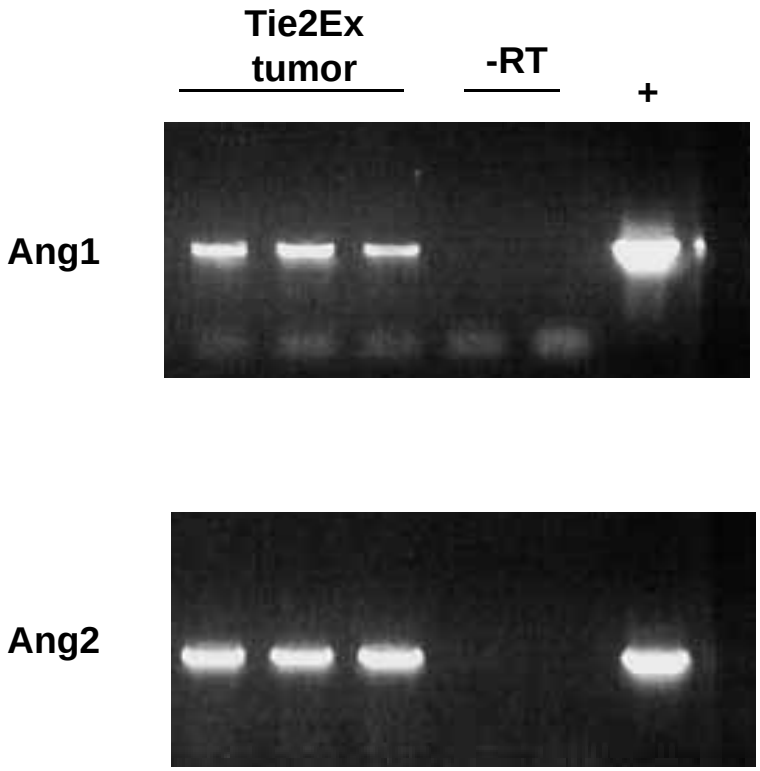


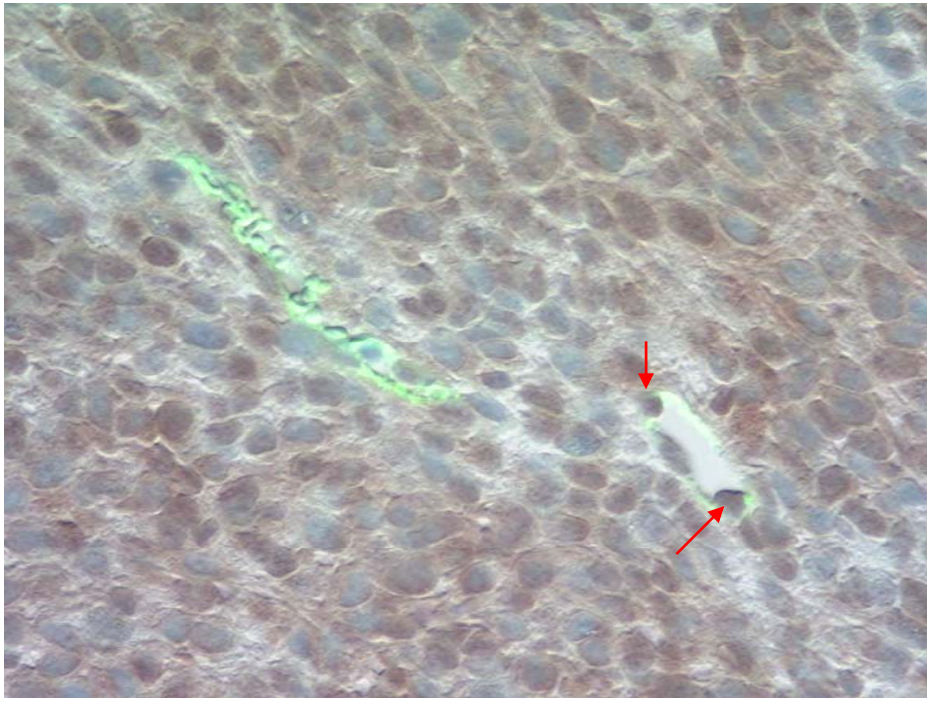
Supplemental Figure 1

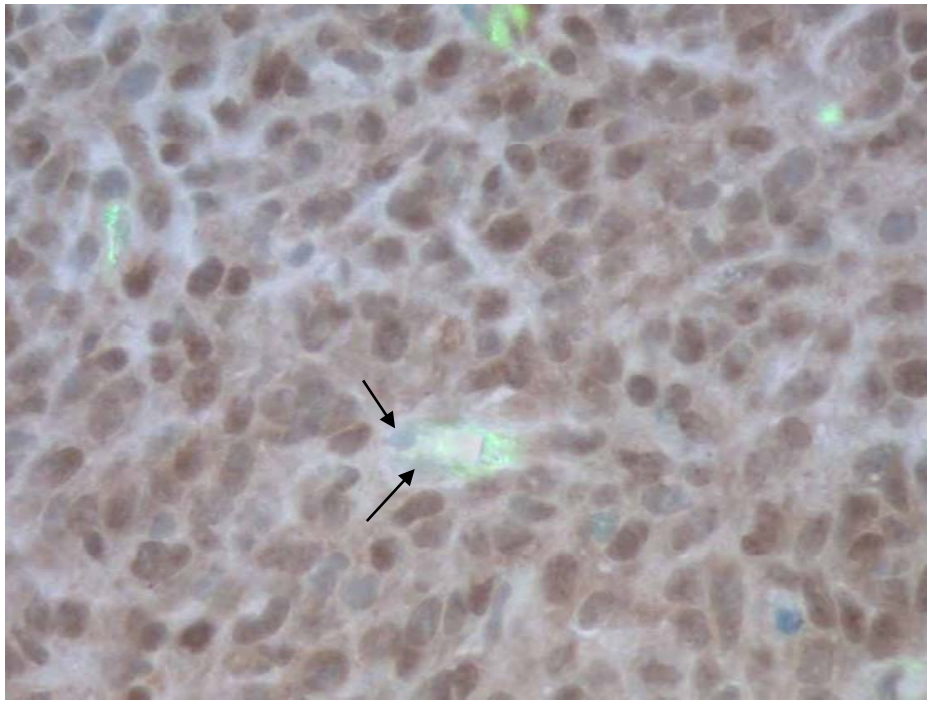


Supplemental Figure 2

- dox

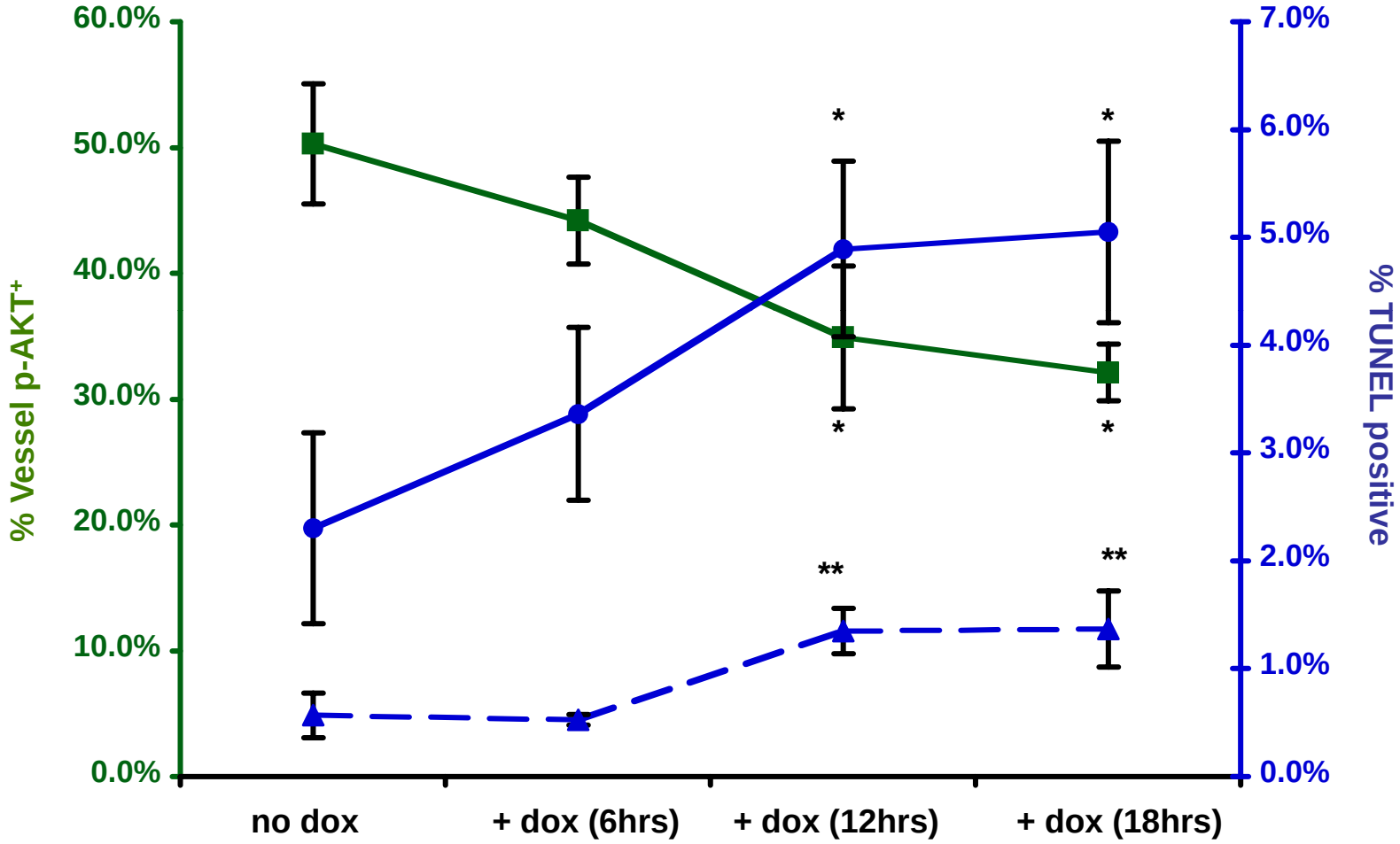
+ dox



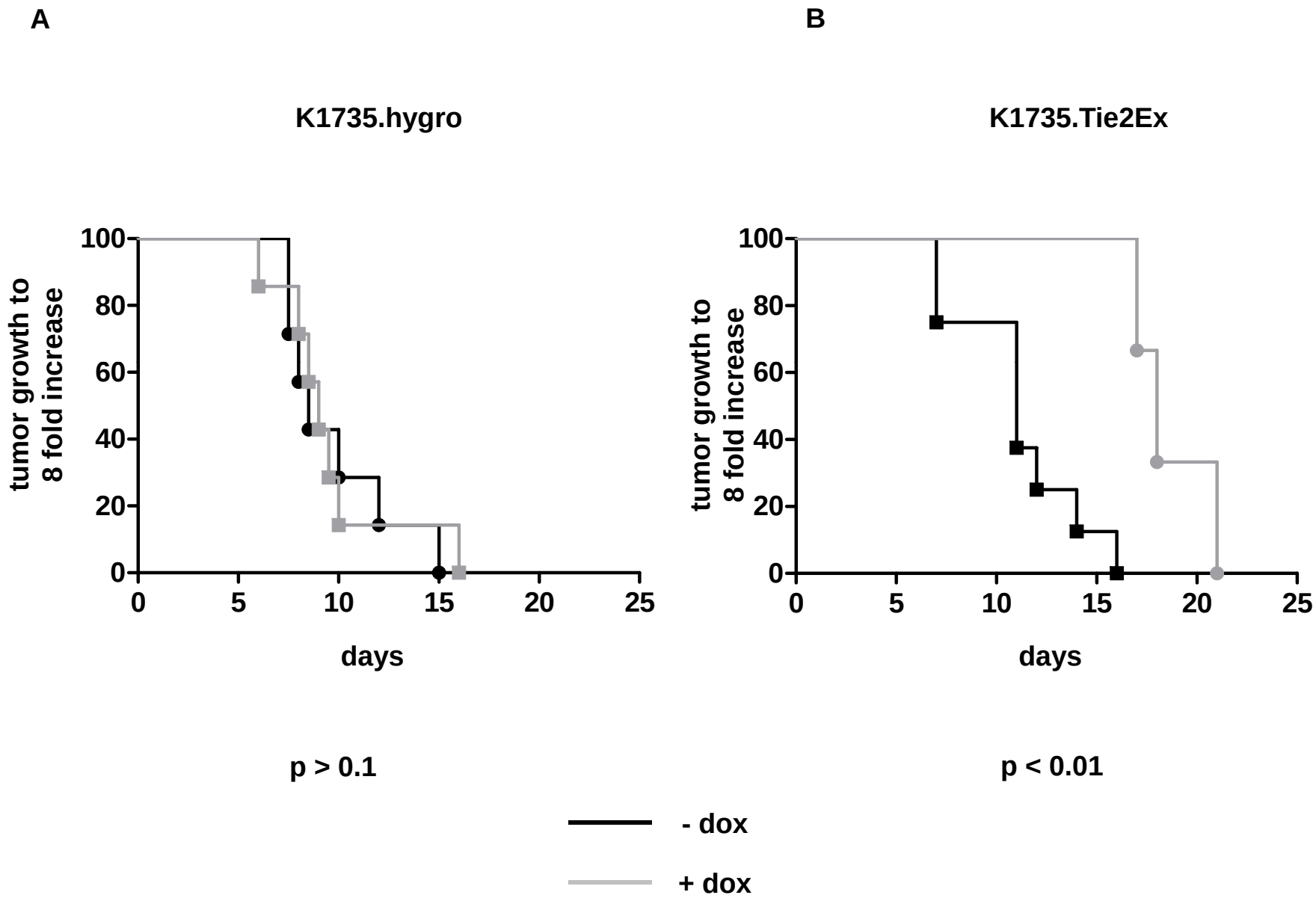


p-AKT
CD34

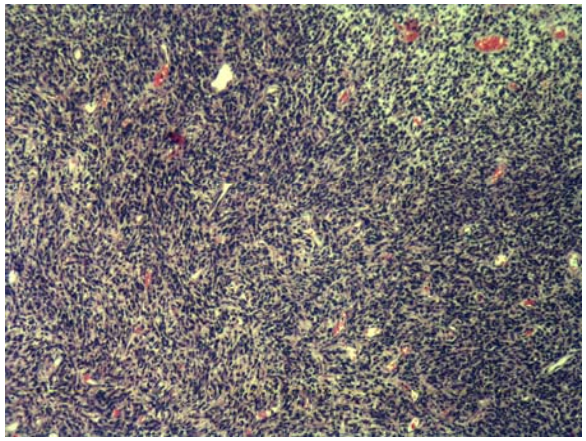
Supplemental Figure 3



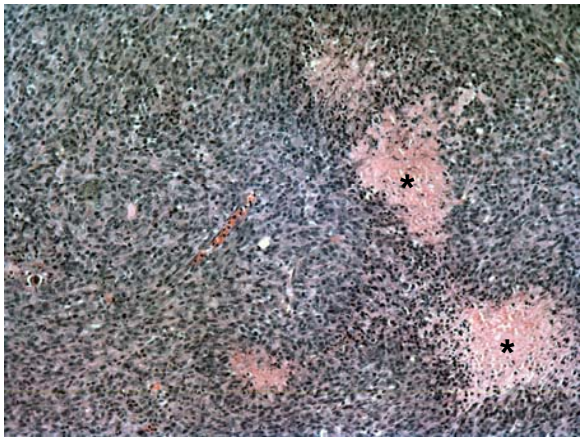
Supplemental Figure 4



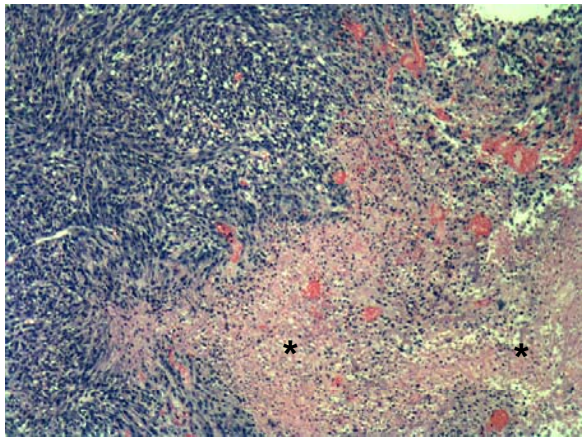
Supplemental Figure 5



- dox



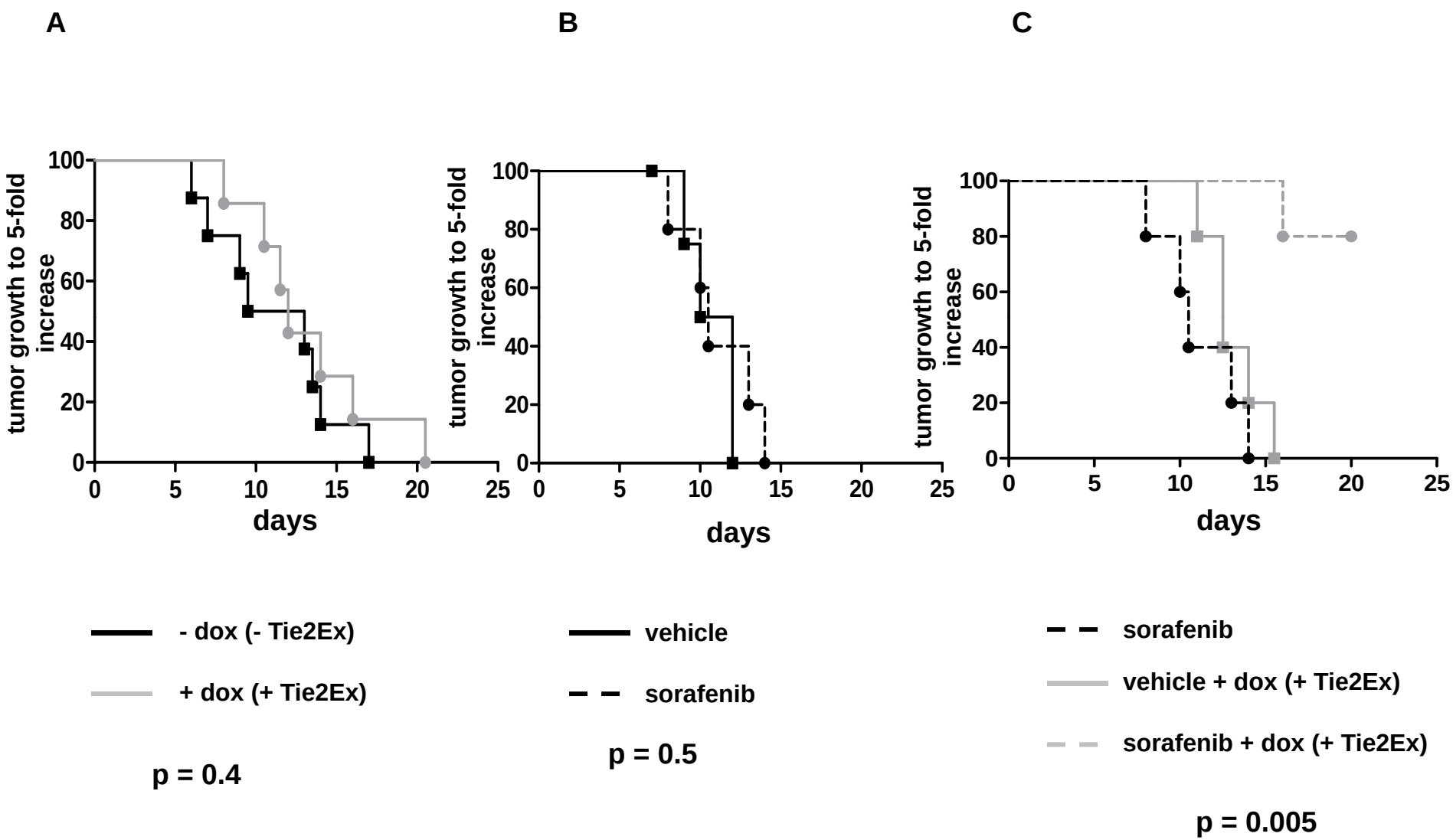
+ dox (24hrs)



+ dox (1wk)

% necrosis:	1% ± 1%	17.6 ± 4.7%	43.1% ± 17.3%

Supplemental Figure 6



Supplemental Figure 7

Supplemental figure 1. Dox induction of Tie2Ex in K1735.Tie2Ex tumor cells. K1735.Tie2Ex cells were cultured in the presence or absence of dox. K1735.Tie2Ex cells were stained for Tie2Ex expression (red) using an anti-Tie2 antibody and counterstained with DAPI (blue), 400X total magnification.

Supplemental figure 2. RT-PCR analysis of K1735.Tie2Ex tumors reveal Ang1 and Ang2 expression. Total RNA was isolated from lysates of 3 independent tumors followed by RT-PCR analysis for Ang1 (top) or Ang2 (bottom). Plasmids of Ang1 or Ang2 were used as positive control and a sample not treated with RT as negative control.

Supplemental figure 3. Endothelial cell phospho-AKT expression in K1735.Tie2Ex tumors. K1735.Tie2Ex tumors were untreated or treated with dox. Paraffin-embedded tumor sections were stained for p-AKT (brown) and CD34 (green) to identify EC p-AKT. Red arrows identify positive EC staining for p-AKT, and black arrows identify negative EC staining for p-AKT, 400X total magnification.

Supplemental figure 4. Endothelial cell phospho-AKT expression and endothelial and tumor cell apoptosis in K1735.Tie2Ex tumors. K1735.Tie2Ex tumors were created in C3H mice. Tumor bearing mice were untreated or treated with dox by administering dox via oral gavage and tumors were excised at 6, 12, and 18 hours after treatment. EC p-AKT expression (solid green), EC apoptosis (solid blue), and tumor cell apoptosis (dashed blue) were plotted on scatter plot over time. Values were obtained

from at least 3 different tumors in each group. The standard deviations of the mean are shown as vertical lines. * $p < 0.01$, ** $p = 0.02$, *t* test.

Supplemental figure 5. Survival analysis of K1735.hygro and K1735.Tie2Ex tumor growth. Tumor growth of K1735.hygro (A) and K1735.Tie2Ex (B) tumors untreated (black line) or treated with dox (gray line) were plotted on Kaplan-Meier curve. Analysis was performed on time for tumor growth to reach 8-fold increase in tumor volume. $p > 0.1$ log-rank test (A) and $p < 0.01$ log-rank test (B).

Supplemental figure 6. Histology of K1735.Tie2Ex tumors. Hematoxylin and eosin staining of K1735.Tie2Ex tumor sections from untreated or dox-treated tumors, 100X total magnification. The percentage of tumor necrosis was calculated and indicated below each condition. * denotes regions of cell loss or necrosis

Supplemental figure 7. Survival analysis of K1735.Tie2Ex tumor growth treated starting at a larger size. Tumor growth K1735.Tie2Ex tumors untreated or treated with dox (A), treated with vehicle or sorafenib (B), and treated with sorafenib alone, vehicle plus dox or sorafenib plus dox (C) were plotted on Kaplan-Meier curves. Analysis was performed on time for tumor growth to reach 5-fold increase in tumor volume. $p = 0.4$ (A), $p = 0.5$ (B), and $p = 0.005$ (C) log-rank test.