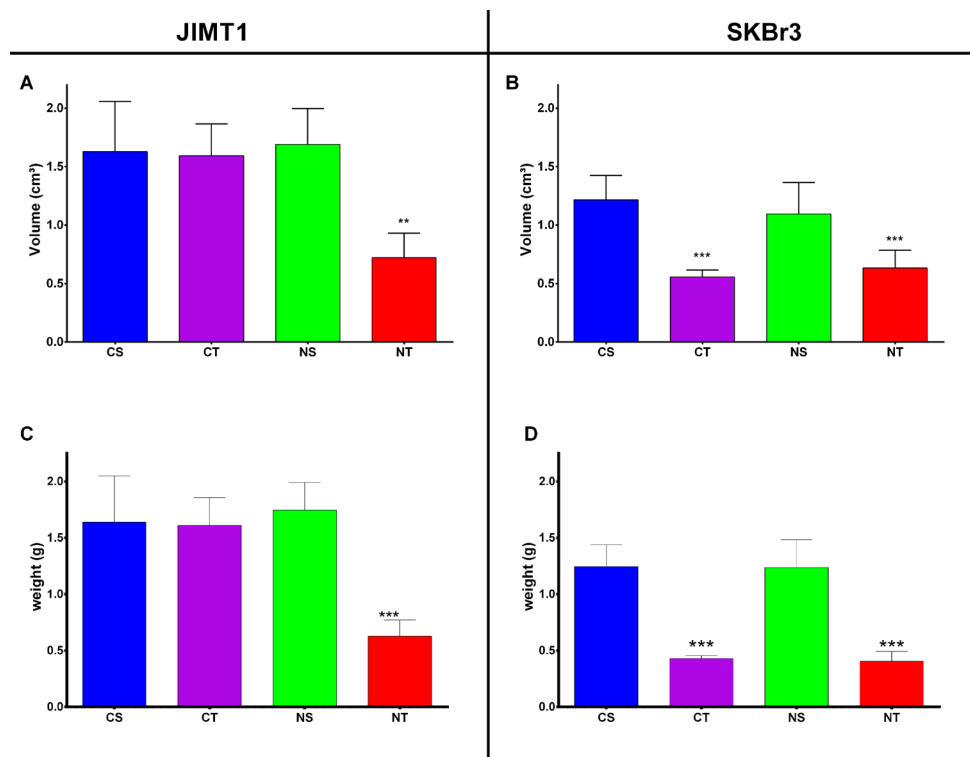
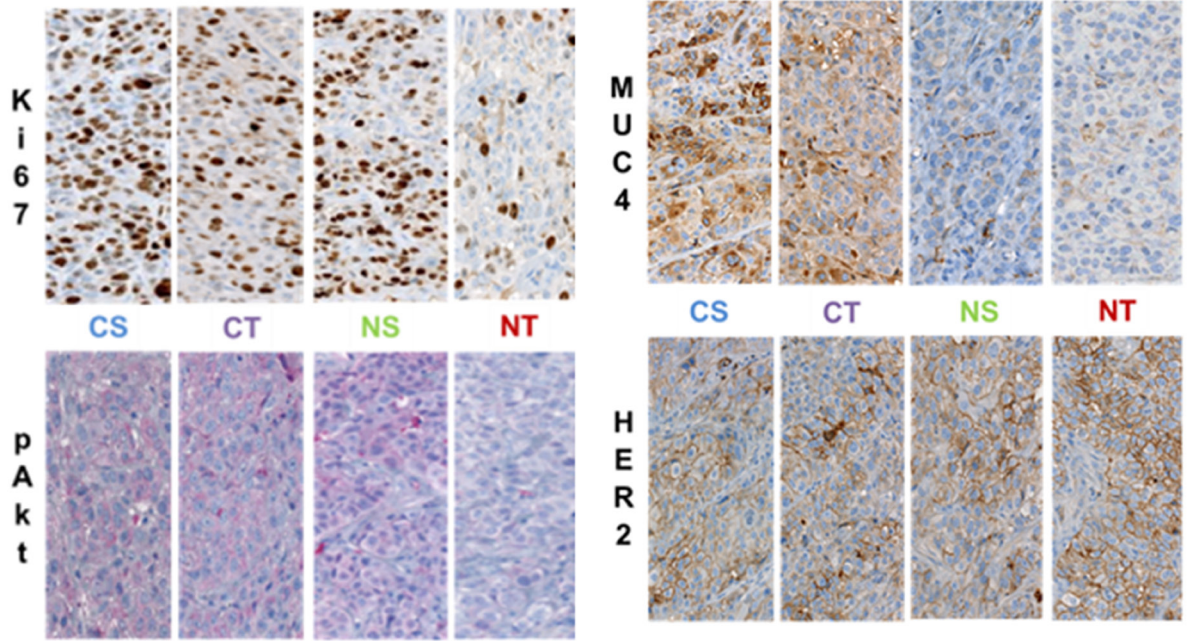
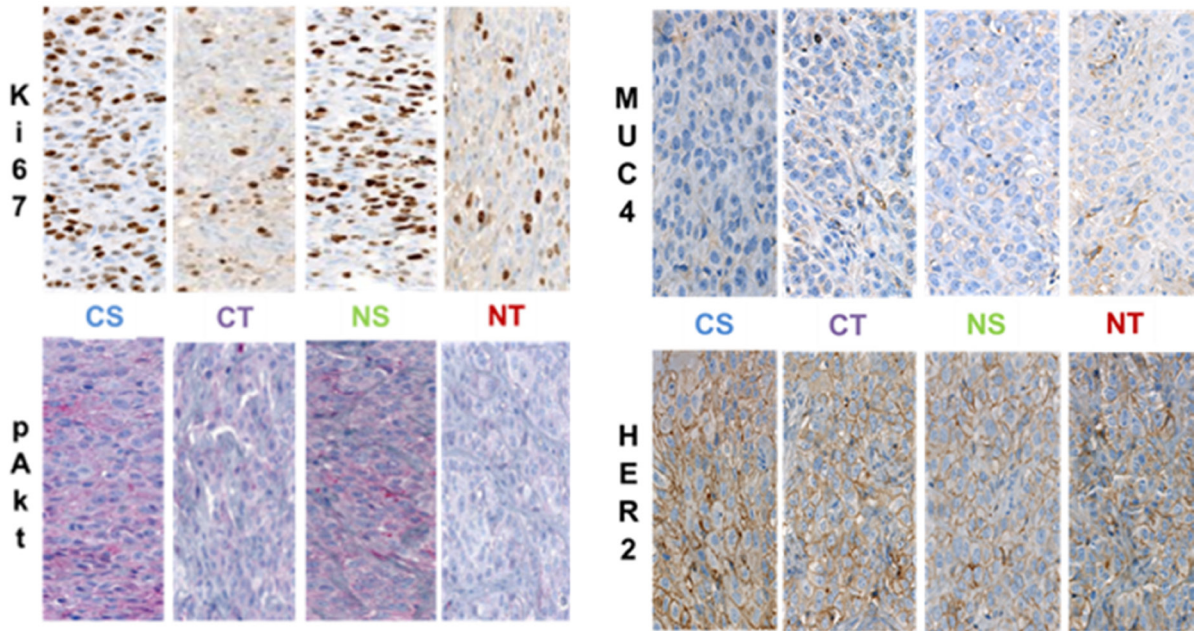


N-Acetylcysteine breaks resistance to trastuzumab caused by MUC4 overexpression in human HER2 positive BC-bearing nude mice monitored by ^{89}Zr -Trastuzumab and ^{18}F -FDG PET imaging

Supplementary Materials



Supplementary Figure 1: The combination of trastuzumab with NAC supplementation results in smaller tumor volumes and weights of trastuzumab resistant tumors. The effect of the different treatment on JIMT1 (HER2+/MUC4+) and SKBr3 (HER2+/MUC4) tumors in dual-tumor-bearing mice randomized to the four treatment arms CS (Control+Saline; blue, $n = 10$), CT (Control+Trastuzumab; purple, $n = 10$), NS (NAC+Saline; green, $n = 9$) and NT (NAC+Trastuzumab; red $n = 10$) is represented per methodologies as follows: tumor volume of JIMT1 (A) and SKBr3 (B) tumors monitored by means of computed tomography images and tumor weight of JIMT1 (C) and SKBr3 (D) tumors at dissection. Data are represented as mean \pm SEM, expressed in cm³ for tumor volume and in grams (g) for tumor weight, with ** $p < 0.01$ and *** $p < 0.001$.

A**B**

Supplementary Figure 2: Effect of combining trastuzumab with NAC supplementation on proliferation, the molecular Pi3K/Akt signaling pathway, MUC4 and HER2 expression in HER2 positive tumors. Representative FFPE stained sections of the pathological examination are shown as illustration for the proliferation index Ki67, pAkt, MUC4 and HER2 expression levels for (A) JIMT1 (HER2+/MUC4+) and (B) SKBr3 (HER2+/MUC4-) tumors in dual-tumor-bearing mice randomized to the four treatment arms CS (Control+Saline; blue, $n = 5$), CT (Control+Trastuzumab; purple, $n = 5$), NS (NAC+Saline; green, $n = 5$) and NT (NAC+Trastuzumab; red $n = 5$).