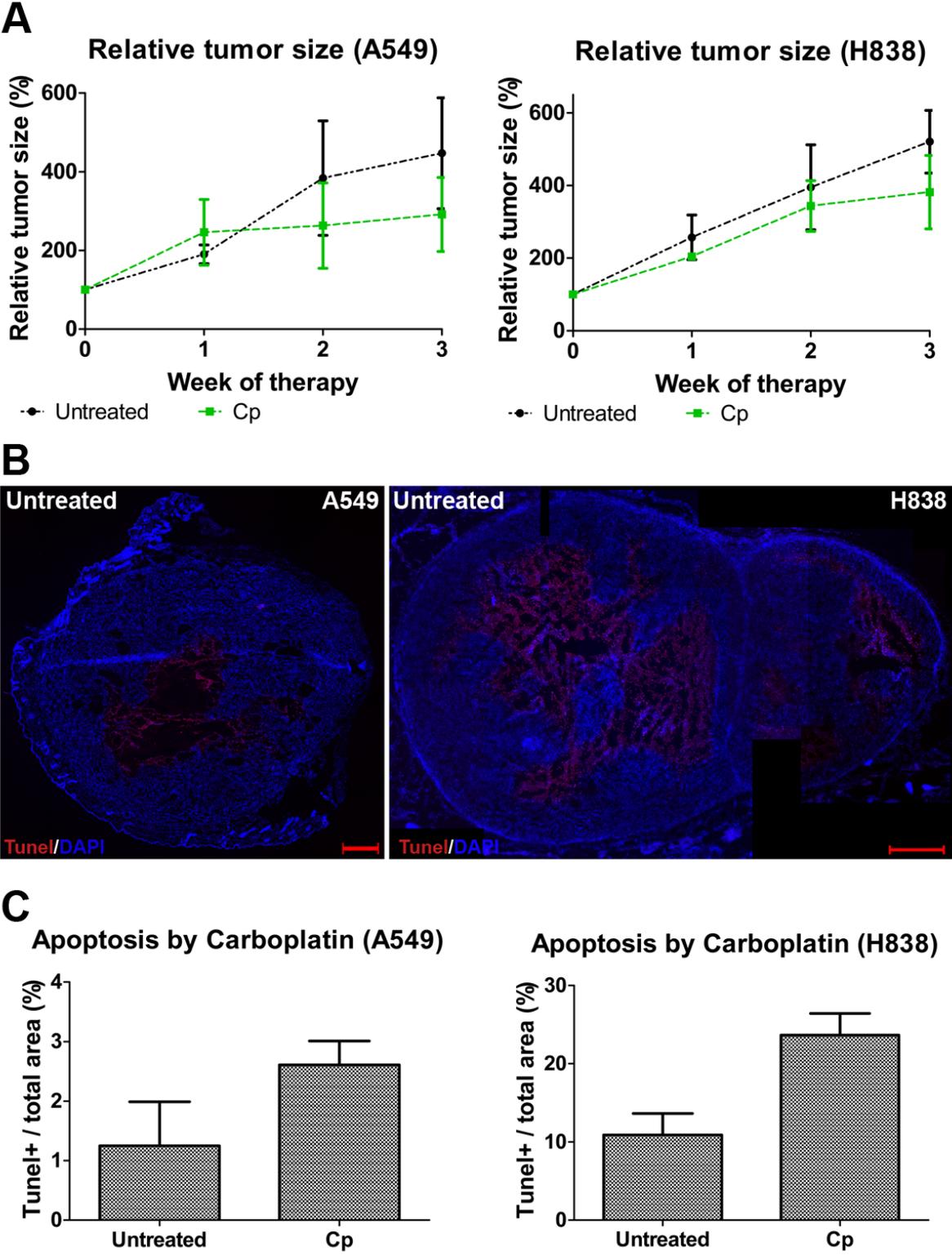


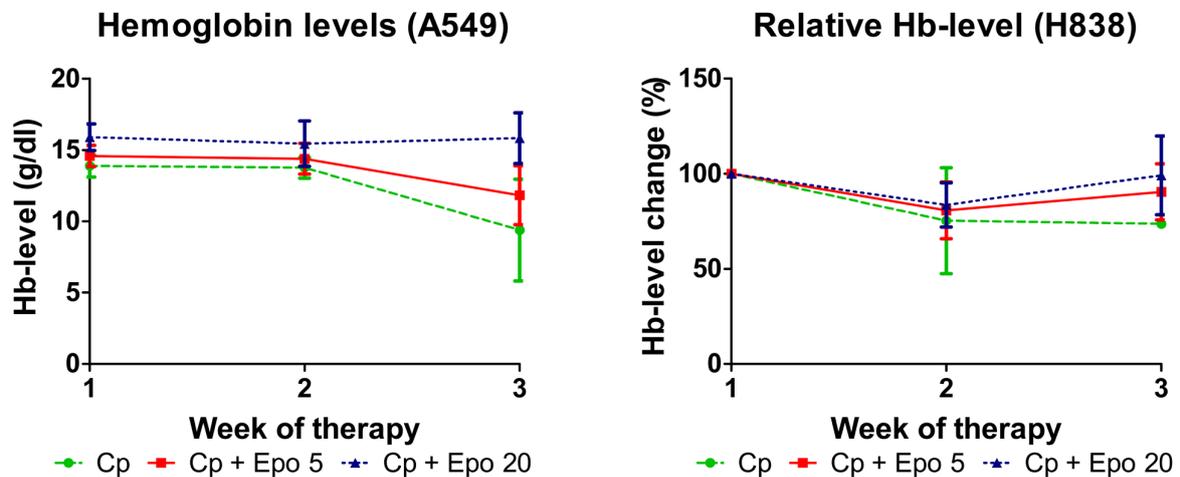
Supplementary Material:



Supplementary Figure 1. Effect of carboplatin-treatment on A549 and H838 tumors

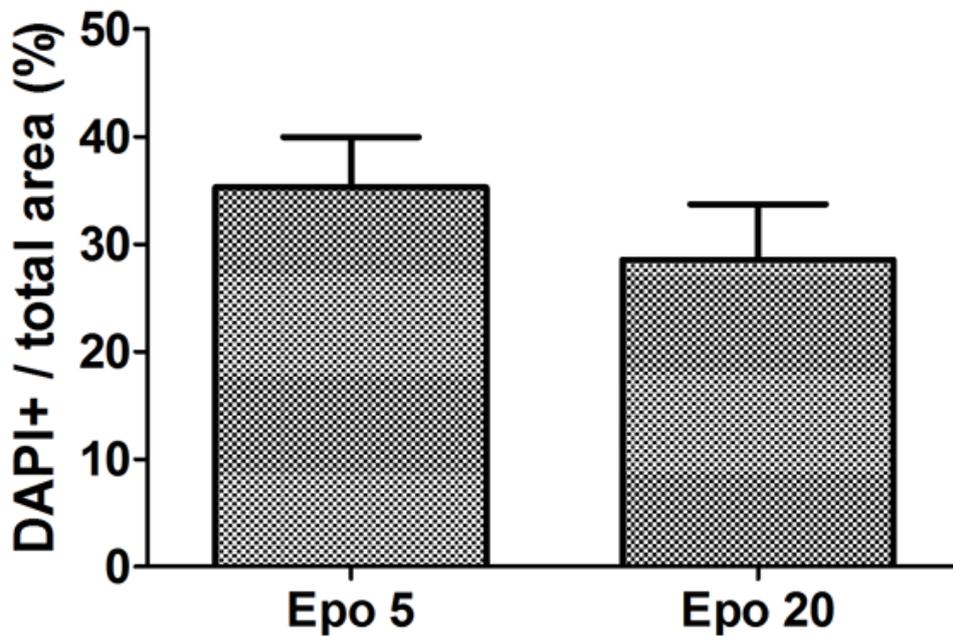
A: Increase in tumor size of untreated A549 (left) and H838 (right) animals in comparison to carboplatin-treated (Cp) animals. B: Representative staining (TUNEL in red, cell nuclei in

blue) of untreated A549 (left) and H838 (right) tumors, showing the degree of apoptosis in the untreated tumors (scale bars: 500  $\mu\text{m}$ ). C: Quantification of the TUNEL+ area fraction for A549 (left) and H838 (right) shows stronger apoptosis in carboplatin-treated (Cp) tumors (n=5).



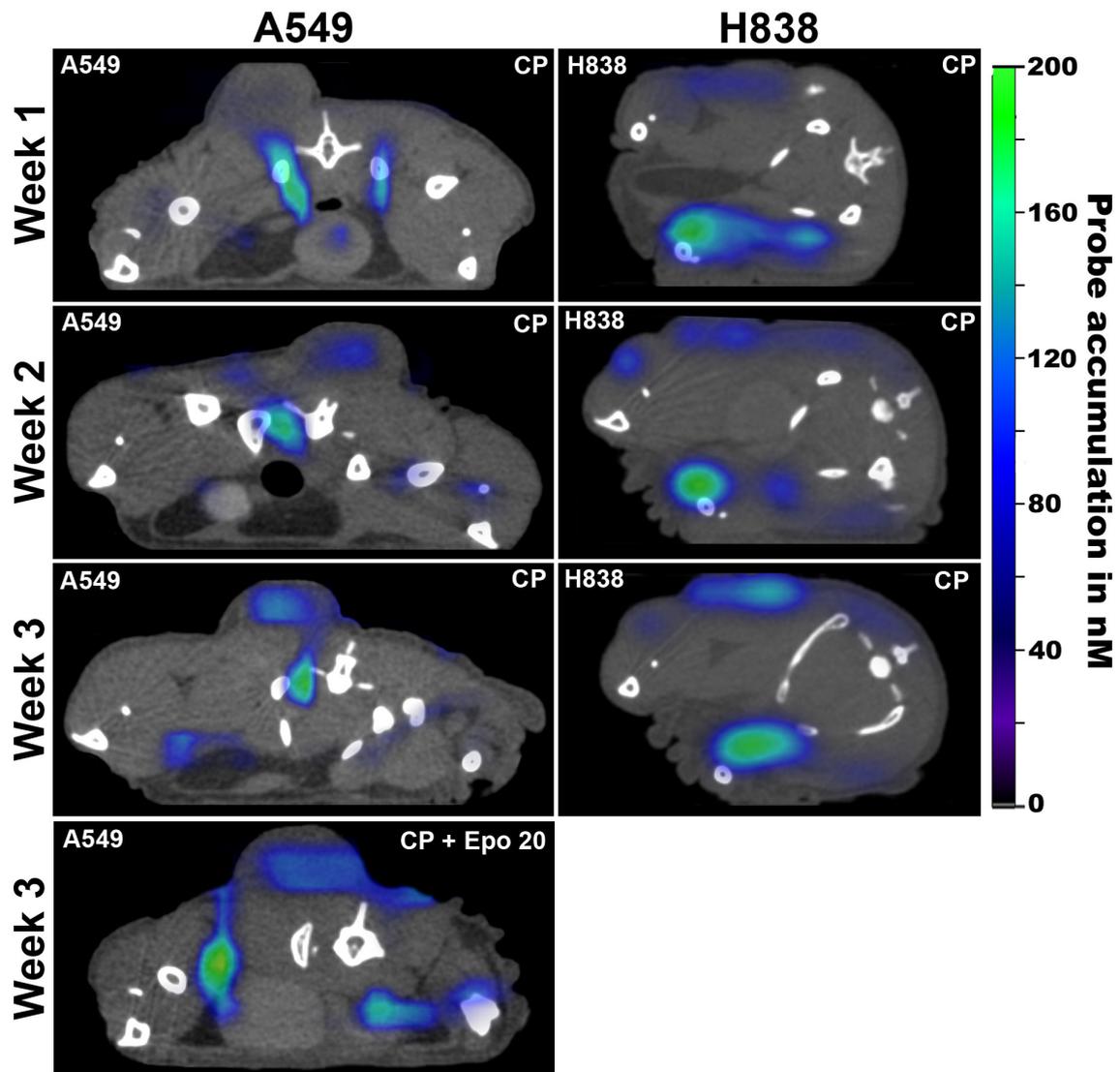
**Supplementary Figure 2.** Analysis of the hemoglobin (Hb) levels of the NSCLC-tumor-bearing animals (A549 left and H838 right) demonstrates a decrease in the group only receiving carboplatin (Cp). Note the dose-dependent normalizing effect of Epo on the Hb-levels, as obvious by the lower decrease in combination with 5  $\mu\text{g}/\text{kg}$  (Cp + Epo 5) and the physiological levels in combination with 20  $\mu\text{g}/\text{kg}$  (Cp + Epo 20) at week three of therapy (n = 5 per group). Cp: carboplatin, Epo 5: rhuEpo 5  $\mu\text{g}/\text{kg}$ , Epo 20: rhuEpo 20  $\mu\text{g}/\text{kg}$ .

## Cell density (A549)



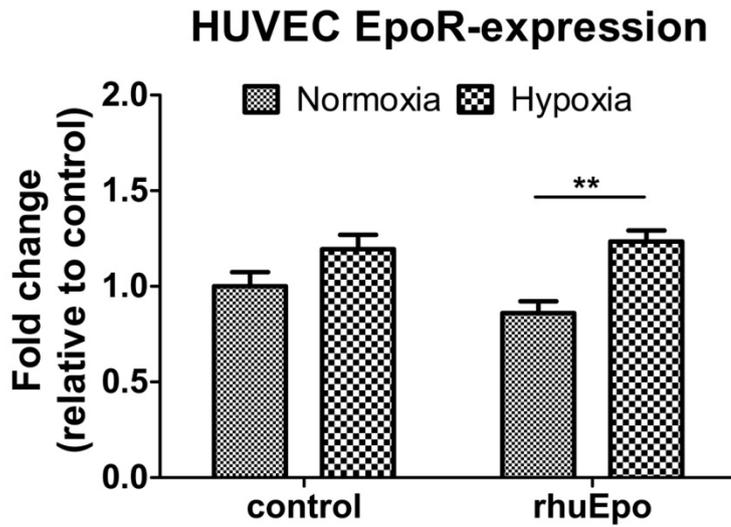
**Supplementary Figure 3.** Lower cell density in A549 tumors co-medicated with 20 µg/ kg of Epo.

Quantification of the DAPI+ area fraction in TUNEL- and DAPI-stained A549 tumors reveals a lower cell density in A549 tumors co-medicated with 20 µg/ kg (Cp + Epo 20) compared to 5 µg/ kg (Cp + Epo 5) of Epo (n = 5 per group), pointing to a marked tumor cell loss at the higher Epo-dose.



**Supplementary Figure 4.** Altered Epo-Cy5.5 levels in tumors during carboplatin-treatment.

$\mu$ CT/FMT fusion images of carboplatin-treated (Cp) A549 (left) and H838 (right) animals show continuously increasing Epo-Cy5.5 levels in the tumors during therapy, pointing to an increase in EpoR-expression. Co-medication of A549 tumors with 20  $\mu$ g/kg of Epo leads to marginally lower Epo-Cy5.5 accumulation (Cp + Epo 20) compared with the solely carboplatin-treated A549 tumor (Cp) at week 3 of therapy.



**Supplementary Figure 5.** EpoR mRNA-expression in HUVECs is up-regulated by hypoxia.

EpoR mRNA-expression was assessed in HUVECs after two days of daily stimulation with Epo (150 ng/ml) under normoxic and hypoxic (2% O<sub>2</sub>) conditions by qPCR. Untreated HUVECs were used as controls. Both, in untreated and Epo-treated HUVECs, the EpoR mRNA-levels were higher under hypoxic conditions. Differences between normoxia and hypoxia were significant upon Epo-stimulation (n = 3, \*\*p < 0.01).