**Supplementary Table 1**: Patient characteristics, unadjusted univariate model and adjusted analysis with multivariate model analyses of overall survival (months) in patients without resection due to metastatic disease. Chemo=chemotherapy, HTN=hypertension, ASI=angiotensin system inhibitors.

**Supplementary Table 2**: Patient characteristics, unadjusted univariate model and adjusted analysis with multivariate model analyses of overall survival (months) in patients without resection due to locally advanced disease. RT=radiotherapy, Chemo=chemotherapy, HTN=hypertension, ASI=angiotensin system inhibitors.

**Supplementary Table 3:** Unadjusted Univariate Analysis of Resected Patients with Hypertension, Stratified by ASI and Chemotherapy

**Supplementary Table 3A**: Case processing summary of patients with hypertension and resected primary tumor

**Supplementary Table 3B**: Medians for overall survival of patients with hypertension and resected primary tumor

**Supplementary Table 3C**: Pairwise comparison of overall survival in patients with hypertension and resected primary tumor

**Supplementary Table 4:** Propensity score analysis:

**Supplementary Table 4A**: Propensity score adjusted analysis in Cox model

**Supplementary Table 4B**: Inverse probability weighted analysis

**Supplementary Table 5:** Competing risk analysis in resected patients

**Supplementary Table 6**: Multivariate model analysis of time to recurrence in the liver (A), lung (B), and local recurrence (C) in patients with resected disease. BMI=Body Mass Index, LNR=lymph node ratio, LVI=lymphovascular invasion, PNI=perineural invasion, Naj=neoadjuvant, Adj=adjuvant, Tx=treatment, RT=radiotherapy, Chemo=chemotherapy, HTN=hypertension, ASI=angiotensin system inhibitors.

**Supplementary Table 7**: Genes differentially expressed in ACEi alone treated group compared to control group.

**Supplementary Table 8:** Complete results for GO analysis on differentially expressed genes comparing lisinopril vs. control PDAC tumors.

**Supplementary Table 9**: Complete results for REACTOME analysis on differentially expressed genes comparing lisinopril vs. control PDAC tumors.

**Supplementary Table 10:** Selected key pathways up-regulated or down-regulated by ACEi treatment alone in Gene Set Enrichment Analysis. ES=Enrichment Score, NES=Normalized Enrichment Score, NOM p-val=Nominal p value, FDR q-val=False Discovery Rate q value

**Supplementary Table 11**: Complete results for GSEA analysis on GO, BIOCARTA, KEGG, PID, and REACTOME curated gene sets on canonical pathways. ES=Enrichment Score, NES=Normalized Enrichment Score, NOM p-val=Nominal p value, FDR q-val=False Discovery Rate q value

**Supplementary Table 12:** Adjusted Analysis with Multivariate Model on TCGA PDAC dataset to test for independent factors. LNR=lymph node ratio, RT=radiotherapy, Chemo=chemotherapy, ASI=angiotensin system inhibitors.

**Supplementary Figure 1**: Clinical status of patients included in the analysis: Group A patients (n=310) did not receive resection due to metastatic disease; Group B patients (n=185) did not receive resection due to locally advanced disease; Group C patients (n=299) presented with resectable disease and successfully underwent primary tumor resection.

**Supplementary Figure 2**: Unadjusted Kaplan Meier survival curves of patients who received ACEi (green), ARB (yellow) vs. control group (blue). The survival benefit from ACEi (green) and ARB (yellow) is not distuishable (p=0.9).

**Supplementary Figure 3**: Chronic ASI use in resected patients with hypertension. left: patients who did not receive chemotherapy or radiation therapy (blue: non-ASI, green: ASI); middle: patients with resected tumor who received chemotherapy (blue: non-ASI, green: ASI); right: overlay of the previous two survival curves. (Detailed pair-wise comparison, see supplementary table 3)

**Supplementary Figure 4**: Supplementary Figure 4: Unadjusted Kaplan Meier survival curve of all resected patients stratified by BMI and chemotherapy. Upper row: BMI < 25; Lower row: BMI > 25. Left column: No chemotherapy; mid column: with Chemotherapy. Green: chronic ASI use; Blue: control.

**Supplementary Figure 5**: Unadjusted Kaplan Meier curves for disease recurrence. A: time to distant metastasis, B: Recurrence free survival, C: time to liver metastasis as index recurrence, D: time to lung metastasis as index recurrence, E: time to metastasis at other body sites as index recurrence, F: time to local recurrence.