

**Table S1. Patient Characteristics and PPI Usage**

<b>Patient Characteristics</b>	<b>Total/Death Events</b>	<b>PPI Users/Death Events</b>
<b>All</b>	6754/1220	840/137
<b>Mean age of diagnosis</b>	58.7 (range 19-102)	
<b>Gender</b>		
<b>Male</b>	48/12	5/1
<b>Female</b>	6706/1211	835/136
<b>Race</b>		
<b>Caucasian</b>	5297/817	540/71
<b>Africa American</b>	1340/397	288/65
<b>Others</b>	117/6	12/1
<b>Types</b>		
<b>TNBC</b>	500/122	65/13
<b>Others</b>	3450/574	458/61
<b>Unknown</b>	2804/137	317/63
<b>Tumor stages</b>		
<b>Stage 0</b>	593/28	60/1
<b>Stage 1</b>	1805/180	159/16
<b>Stage 2</b>	1215/197	121/14
<b>Stage 3</b>	280/70	25/7
<b>Stage 4</b>	75/35	7/4
<b>Unknown</b>	2786/710	468/95
<b>Metastatic disease at diagnosis</b>		
<b>Yes</b>	217/108	479/58
<b>No</b>	3397/270	18/11
<b>Unknown</b>	3140/842	343/68
<b>Treatments</b>		
<b>Hormone only*</b>	747/165	125/31
<b>Chemotherapeutics only**</b>	540/141	64/16
<b>DNA-damaging drugs</b>	108/28	12/5
<b>Non-DNA-damaging drugs</b>	133/33	12/3
<b>Radiation only</b>	964/132	147/14

\*Hormone therapeutites include ER modulators (fulvestrant and tamoxifen), GnRH agonist (goserelin and leuprolide), aromatase inhibitor (anastrozole, exemestane, and letrozole), and HER2 inhibitor (Trastuzumb)

\*\*Chemotherapeutics include DNA-damaging drugs such as anthracyclines (epirubicin, doxorubicin, and liposomal doxorubicin) and cross-linkers (carboplatin, cisplatin, and cyclophosphamide) and other non-DNA-damaging drugs such as anti-mitotic drugs (docetaxel, paclitaxel, vinorelbine) and antimetabolites (capecitabine, gemcitabine, fluorouracil, and methotrexate).

**Table S2. Univariate and multivariate Cox regression analyses of survival**

Variates	Univariate		Multivariate	
	HR (95% CI)	P	HR(95% CI)	P
<b>PPI Usage</b>				
Users vs Non-Users	0.44 (0.37-0.53)	$<2 \times 10^{-16}$	0.40 (0.34-0.48)	$<2 \times 10^{-16}$
<b>Diagnosis Age</b>				
$58 \geq$ vs $\leq 57$	1.03 (1.03-1.04)	$<2 \times 10^{-16}$	1.04 (1.03-1.04)	$<2 \times 10^{-16}$
<b>Race</b>				
AA vs CA	1.42 (1.26-1.60)	$1.09 \times 10^{-8}$	1.38 (1.22-1.56)	$2.70 \times 10^{-7}$
Others vs CA	0.42 (0.19-0.94)	0.034	0.46 (0.21-1.03)	0.058
<b>Tumor Stage</b>				
Stage 1 vs 0	1.84 (1.24-2.74)	0.0027	1.70 (1.13-2.54)	0.010
Stage 2 vs 0	2.92 (1.97-4.34)	$1.10 \times 10^{-7}$	2.87 (1.92-4.28)	$2.70 \times 10^{-7}$
Stage 3 vs 0	5.57 (3.59-8.64)	$1.62 \times 10^{-14}$	5.92 (3.81- 9.22)	$3.33 \times 10^{-15}$
Stage 4 vs 0	15.56 (9.46-25.60)	$<2 \times 10^{-16}$	6.17 (3.66-10.42)	$9.06 \times 10^{-12}$
Unknown vs 0	3.93 (2.70-5.74)	$1.23 \times 10^{-12}$	3.86 (2.64-5.65)	$3.15 \times 10^{-12}$
<b>Metastasis</b>				
Metastasis vs non-metastasis	10.00 (7.99-12.51)	$<2 \times 10^{-16}$	8.40 (6.58-10.75)	$< 2 \times 10^{-16}$
Unknown vs non-metastasis	1.54 (1.33-1.77)	$3.62 \times 10^{-9}$	1.61 (1.39-1.87)	$3.06 \times 10^{-10}$
<b>Types</b>				
TNBC vs Non-TNBC	1.74 (1.43-2.12)	$3.35 \times 10^{-8}$	Stratified Variable	

**Table S3. Univariate and multivariate survival analyses of PPI users in different subgroups**

Patient Subgroups	Univariate		Multivariate	
	HR (95% CI)	P	HR (95% CI)	P
<b>Caucasian American</b>				
PPI Users vs Non-Users	0.38 (0.29-0.48)	3.8×10 <sup>-15</sup>	0.34 (0.27-0.44)	<2×10 <sup>-16</sup>
<b>African American</b>				
PPI Users vs Non-Users	0.50 (0.38-0.65)	2.7×10 <sup>-7</sup>	0.49 (0.37-0.64)	1.5×10 <sup>-7</sup>
<b>Molecular Subtypes</b>				
TNBC (PPI Users vs Non-Users)	0.50 (0.28-0.88)	0.017	0.49 (0.27-0.87)	0.015
Luminal A (PPI Users vs Non-Users)	0.52 (0.65-0.76)	6.0×10 <sup>-4</sup>	0.46 (0.31-0.68)	8.61×10 <sup>-4</sup>
Luminal B (PPI Users vs Non-Users)	0.34 (0.10-1.16)	0.072	0.29 (0.076-1.11)	0.070
HER2+ (PPI Users vs Non-Users)	0.49 (0.22-1.01)	0.068	0.48 (0.21-1.08)	0.076
<b>Hormone</b>				
PPI Users vs Non-Users	0.60 (0.41-0.89)	0.011	0.65 (0.44-0.97)	0.037
<b>Chemotherapy</b>				
PPI Users vs Non-Users	0.53 (0.37-0.75)	0.00029	0.46 (0.33-0.66)	1.6×10 <sup>-5</sup>
<b>DNA-Damaging Drugs</b>				
PPI Users vs Non-Users	1.00 (0.97-1.04)	0.80	1.00 (0.97-1.04)	0.80
<b>Non-DNA-Damaging Drugs</b>				
PPI Users vs Non-Users	0.62 (0.19-2.05)	0.44	1.11 (0.30-4.10)	0.87
<b>Radiation</b>				
PPI Users vs Non-Users	0.33 (0.19-0.58)	9.9×10 <sup>-5</sup>	0.30 (0.17-0.53)	2.5×10 <sup>-5</sup>
<b>Recurrence Free Disease</b>				
PPI Users vs Non-Users	0.087 (0.039-0.20)	3.5×10 <sup>-9</sup>	0.088 (0.039-0.20)	4.1×10 <sup>-9</sup>
<b>5-Year Survival After Recurrence</b>				
PPI Users vs Non-Users	0.47 (0.20-1.06)	0.069	0.41 (0.17-0.95)	0.038

**Table S4. Univariate and multivariate analyses of different PPIs and dosage on survival**

PPI Types and Dosing*	Univariate		Multivariate***	
	HR (95% CI)	P	HR (95% CI)	P
<b>Omeprazole Users vs Non-PPI Users</b>	0.33 (0.23-0.49)	3.03×10 <sup>-8</sup>	0.27 (0.18-0.40)	3.91×10 <sup>-11</sup>
<b>Lansoprazole Users vs Non-PPI Users</b>	0.20 (0.074-0.53)	0.0013	0.25 (0.094-0.67)	0.006
<b>Pantoprazole Users vs Non-PPI Users</b>	0.43 (0.25-0.74)	0.0025	0.41 (0.24-0.71)	0.0014
<b>Esomeprazole Users vs Non-PPI Users</b>	0.52 (0.39-0.70)	1.39×10 <sup>-5</sup>	0.48 (0.36-0.64)	9.75×10 <sup>-7</sup>
<b>Other PPIs** vs Non-PPI Users</b>	0.31 (0.044-2.23)	0.25	0.49 (0.070-3.51)	0.48
<b>Multi-PPI Users vs Non-PPI Users</b>	0.53 (0.39-0.71)	1.89×10 <sup>-5</sup>	0.48 (0.36-0.65)	1.49×10 <sup>-6</sup>
<b>40 mg Omeprazole vs Non-PPI users</b>	0.21 (0.03-1.53)	0.09	0.12 (0.02-0.89)	0.038
<b>10-20 mg Omeprazole vs No PPI</b>	0.33 (0.21-0.51)	2.1×10 <sup>-7</sup>	0.28 (0.18-0.43)	1.49×10 <sup>-8</sup>
<b>40 mg Esomeprazole vs No PPI</b>	0.30 (0.21-0.52)	4.2×10 <sup>-7</sup>	0.33 (0.21-0.52)	1.8×10 <sup>-6</sup>
<b>20 mg Esomeprazole vs No PPI</b>	1.0 (0.62-1.61)	0.98	0.72 (0.44-1.16)	0.18

\*For single PPI analysis, patients who took only one PPI type were used. Patients who took more than one PPI were grouped as multi-PPI users.

\*\*Other PPI users are patients who used either rabeprazole or dexlansoprazole only.

\*\*\*Multivariate includes PPI types, diagnostic age, race, molecular marker (non-TNBC or TNBC), and tumor stage and metastasis upon diagnosis. Values for other variables except PPI types are similar to overall survival analysis as displayed in Table 1 and therefore are omitted here to avoid repeated information.