S8 Table. Cox proportional hazards model of survival for patients with and without insulin and/or metformin exposure before the diagnosis of ER-positive breast cancer

Variable	Univariable analysis Hazard ratio (95% CI)	p-value	Multivariable analysis Hazard ratio (95% CI)	p-value
Histologic type				
IDC	1		1	
ILC	2.264 (0.894-5.729)	0.085	1.298 (0.431-3.267)	0.617
Others	0.111 (0.015-0.809)	0.030	0.279 (0.031-1.082)	0.068
Stage: T				
T1	1		1	
T0	1.657 (0.013-12.743)	0.746	1.141 (0.008-12.813)	0.934
T2	3.513 (1.834-7.220)	< 0.001	3.287 (1.636-7.020)	0.001
T3	9.811 (3.898-23.729)	< 0.001	7.440 (2.410-23.115)	0.001
T4	2.474 (0.019-19.073)	0.583	0.793 (0.005-10.176)	0.883
Tis	0.294 (0.002-2.259)	0.303	1.297 (0.009-26.020)	0.879
Stage: N				
N0	1		1	
N1	2.086 (1.080-4.030)	0.029	1.138 (0.560-2.287)	0.718
N2	1.830 (0.543-6.161)	0.330	1.120 (0.275-3.396)	0.858
N3	11.555 (5.405-24.704)	< 0.001	3.697 (1.380-9.098)	0.011
Stage: M				
M0	1		1	
M1	20.536 (6.263-67.330)	< 0.001	3.258 (0.743-11.337)	0.109
PR				
Negative	1		1	
Positive	0.472 (0.265-0.838)	0.010	0.522 (0.295-0.946)	0.033
Age at diagnosis (yr)				

< 40	1		1	
≥ 40 and < 50	1.236 (0.149-10.281)	0.845	1.001 (0.200-9.887)	0.999
≥ 50	2.369 (0.325-17.249)	0.394	1.567 (0.380-14.501)	0.584
CCI	1.128 (1.004-1.266)	0.043	1.055 (0.923-1.202)	0.429
Exposure before breast cancer				
Reference: no exposure to either drug	1		1	
Exposure to insulin	2.130 (0.503-9.016)	0.305	3.260 (0.595-11.394)	0.150
Exposure to metformin	1.265 (0.671-2.384)	0.468	1.169 (0.589-2.270)	0.650
Exposure to insulin and metformin	1.691 (0.728-3.927)	0.222	1.505 (0.598-3.384)	0.365

CCI, Charlson comorbidity index; CI, confidence interval; DM, diabetes mellitus; ER, estrogen receptor; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; M, metastasis; N, node; PR, progesterone receptor; T, tumor.