

**S9 Table.** Cox proportional hazards model of survival for patients with and without insulin and/or metformin exposure before the diagnosis of ER-negative breast cancer

<b>Variable</b>	<b>Univariable analysis Hazard ratio (95% CI)</b>	<b>p-value</b>	<b>Multivariable analysis Hazard ratio (95% CI)</b>	<b>p-value</b>
<b>Histologic type</b>				
IDC	1		1	
ILC	2.889 (0.023-20.888)	0.526	18.872 (0.139-193.840)	0.166
Others	0.523 (0.142-1.388)	0.212	0.301 (0.048-1.381)	0.129
<b>Stage: T</b>				
T1	1		1	
T0	5.970 (0.046-50.738)	0.336	30.241 (0.178-730.438)	0.141
T2	2.316 (0.995-6.140)	0.051	2.377 (0.955-6.759)	0.063
T3	5.260 (1.725-16.037)	0.005	2.700 (0.700-10.406)	0.147
T4	5.715 (0.595-27.150)	0.111	1.872 ((0.157-13.781)	0.575
Tis	1.135 (0.209-4.438)	0.866	5.054 (0.613-33.979)	0.126
<b>Stage: N</b>				
N0	1		1	
N1	1.896 (0.774-4.644)	0.161	1.982 (0.745-5.199)	0.166
N2	5.875 (2.312-14.930)	< 0.001	5.156 (1.782-14.366)	0.003
N3	5.054 (1.896-13.475)	0.001	4.771 (1.360-15.272)	0.016
<b>Stage: M</b>				
M0	1		1	
M1	3.245 (0.442-23.830)	0.247	8.787 (0.842-42.101)	0.065
<b>PR</b>				
Negative	1		1	
Positive	0.922 (0.007-6.516)	0.954	0.788 (0.006-6.850)	0.868
<b>Age at diagnosis (yr)</b>				
< 40	1		1	
≥ 40 and < 50	0.596 (0.133-2.664)	0.498	0.449 (0.105-2.077)	0.287

≥ 50	0.614 (0.186-2.034)	0.425	0.325 (0.099-1.342)	0.111
CCI	1.176 (1.017-1.361)	0.029	1.142 (0.983-1.314)	0.082
Exposure before breast cancer				
Reference: no exposure to either drug	1		1	
Exposure to insulin	5.729 (1.921-17.087)	0.002	17.884 (4.660-61.172)	< 0.001
Exposure to metformin	1.042 (0.449-2.416)	0.924	0.845 (0.332-1.995)	0.707
Exposure to insulin and metformin	1.372 (0.461-4.078)	0.570	1.293 (0.357-3.918)	0.674

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