

S3 Table. Characteristics of patients with and without insulin and/or metformin exposure before the diagnosis of breast cancer (included HER2-avaliable patients only)

	No exposure to either drug (n=345)	Exposure to insulin (n=14)	Exposure to metformin (n=170)	Exposure to both drugs (n=74)	Total (n=603)	p-value
Histologic type						
IDC	289 (83.77)	13 (92.86)	142 (83.53)	52 (70.27)	496 (82.26)	0.009 ^{a)}
ILC	10 (2.90)	0	3 (1.76)	8 (10.81)	21 (3.48)	
Others	46 (13.33)	1 (7.14)	25 (14.71)	14 (18.92)	86 (14.26)	
Stage: T						
T0	1 (0.29)	2 (14.29)	1 (0.59)	0	4 (0.66)	< 0.001 ^{a)}
T1	155 (44.93)	6 (42.86)	75 (44.12)	22 (29.73)	258 (42.79)	
T2	151 (43.77)	4 (28.57)	73 (42.94)	37 (50.00)	265 (43.95)	
T3	14 (4.06)	1 (7.14)	10 (5.88)	6 (8.11)	31 (5.14)	
T4	2 (0.58)	0	2 (1.18)	1 (1.35)	5 (0.83)	
Tis	22 (6.38)	1 (7.14)	9 (5.29)	8 (10.81)	40 (6.63)	
Stage: N						
N0	212 (61.45)	10 (71.43)	97 (57.06)	43 (58.11)	362 (60.03)	0.066 ^{a)}
N1	92 (26.67)	0	52 (30.59)	17 (22.97)	161 (26.70)	
N2	26 (7.54)	1 (7.14)	9 (5.29)	8 (10.81)	44 (7.30)	
N3	15 (4.35)	3 (21.43)	12 (7.06)	6 (8.11)	36 (5.97)	
Stage: M						
M0	343 (99.42)	13 (92.86)	167 (98.24)	74 (100.00)	597 (99.00)	0.092 ^{b)}
M1	2 (0.58)	1 (7.14)	3 (1.76)	0	6 (1.00)	
ER						
Negative	118 (34.20)	5 (35.71)	59 (34.71)	23 (31.08)	205 (34.00)	0.952 ^{a)}
Positive	227 (65.80)	9 (64.29)	111 (65.29)	51 (68.92)	398 (66.00)	
PR						
Negative	173 (50.14)	7 (50.00)	88 (51.76)	34 (45.95)	302 (50.08)	0.873 ^{a)}

HER2						
Positive	172 (49.86)	7 (50.00)	82 (48.24)	40 (54.05)	301 (49.92)	
Negative	243 (70.43)	10 (71.43)	126 (74.12)	52 (70.27)	431 (71.48)	0.845 ^{a)}
PR						
Positive	102 (29.57)	4 (28.57)	44 (25.88)	22 (29.73)	172 (28.52)	
Age at diagnosis (yr)						
< 40	23 (6.67)	1 (7.14)	2 (1.18)	0	26 (4.31)	< 0.001 ^{a)}
≥ 40 and < 50	91 (26.38)	0	25 (14.71)	11 (14.86)	127 (21.06)	
≥ 50	231 (66.96)	13 (92.86)	143 (84.12)	63 (85.14)	450 (74.63)	
CCI						
Mean±SD	5.42±1.92	6.86±3.48	6.23±2.13	7±2.55	5.88±2.18	< 0.001 ^{c)}
Median (min-max)	5 (1-13)	7 (1-12)	6 (1-13)	7 (3-14)	5 (1-14)	

Values are presented as number (%). CCI, Charlson comorbidity index; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; M, metastasis; N, node; PR, progesterone receptor; SD, standard deviation; T, tumor. ^{a)}Chi-square test, ^{b)}Fisher exact test, ^{c)}Kruskal-Wallis test.