

S1 Table. Characteristics of patients with and without insulin and/or metformin exposure before the diagnosis of ER-positive breast cancer

	No exposure to either drug (n=377)	Exposure to insulin (n=17)	Exposure to metformin (n=184)	Exposure to both drugs (n=71)	Total (n=649)	p-value
Histologic type						
IDC	307 (81.43)	17 (100.00)	150 (81.52)	51 (71.83)	525 (80.89)	0.009 ^{a)}
ILC	18 (4.77)	0	6 (3.26)	10 (14.08)	34 (5.24)	
Others	52 (13.79)	0	28 (15.22)	10 (14.08)	90 (13.87)	
Stage: T						
T0	2 (0.53)	2 (11.76)	0	2 (2.82)	6 (0.92)	< 0.001 ^{a)}
T1	194 (51.46)	11 (64.71)	95 (51.63)	26 (36.62)	326 (50.23)	
T2	136 (36.07)	4 (23.53)	75 (40.76)	35 (49.30)	250 (38.52)	
T3	21 (5.57)	0	4 (2.17)	3 (4.23)	28 (4.31)	
T4	1 (0.27)	0	2 (1.09)	1 (1.41)	4 (0.62)	
Tis	23 (6.10)	0	8 (4.35)	4 (5.63)	35 (5.39)	
Stage: N						
N0	251 (66.58)	15 (88.24)	116 (63.04)	43 (60.56)	425 (65.49)	0.041 ^{a)}
N1	95 (25.20)	0	54 (29.35)	18 (25.35)	167 (25.73)	
N2	23 (6.10)	0	8 (4.35)	5 (7.04)	36 (5.55)	
N3	8 (2.12)	2 (11.76)	6 (3.26)	5 (7.04)	21 (3.24)	
Stage: M						
M0	376 (99.73)	16 (94.12)	182 (98.91)	71 (100.00)	645 (99.38)	0.077 ^{b)}
M1	1 (0.27)	1 (5.88)	2 (1.09)	0	4 (0.62)	
PR						
Negative	91 (24.14)	4 (23.53)	43 (23.37)	17 (23.94)	155 (23.88)	0.998 ^{a)}
Positive	286 (75.86)	13 (76.47)	141 (76.63)	54 (76.06)	494 (76.12)	
Age at diagnosis (yr)						
< 40	26 (6.90)	1 (5.88)	1 (0.54)	0	28 (4.31)	< 0.001 ^{a)}
≥ 40 and < 50	95 (25.20)	0	25 (13.59)	13 (18.31)	133 (20.49)	

≥ 50	256 (67.90)	16 (94.12)	158 (85.87)	58 (81.69)	488 (75.19)	
CCI						
Mean±SD	5.29±1.82	7.47±3.08	6.31±2.22	6.86±2.57	5.81±2.16	< 0.001 ^{c)}
Median (min-max)	5 (3-13)	8 (2-12)	6 (3-13)	7 (3-14)	5 (2-14)	

Values are presented as number (%). CCI, Charlson comorbidity index; ER, estrogen receptor; 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.