

Table S1. Type and distribution of events over time.

	N
All FUP years	
No event	1352
Loco-regional events	160
Distant metastases	205
Other	155

Alive	1689
Dead	183
First five years from surgery	
DFS events	279
Yearly rate, × 100 PY (95% CI)	3.4 (3.0-3.8)
DM events	116
Yearly rate, × 100 PY (95% CI)	1.4 (1.2-1.7)
Beyond five year after surgery	
DFS events	241
Yearly rate, × 100 PY (95% CI)	4.3 (3.8-4.9)
DM events	89
Yearly rate, × 100 PY (95% CI)	1.6 (1.3-1.9)

Table S2. Prognostic factors of **early** (≤ 5 years) and **late** (>5 years) DFS events in ILCs, univariate and multivariate analysis.

	≤ 5 years					>5 years								Heterogeneity <i>p</i> -value (univariate analyses)
	Univariable analysis					Univariable analysis					Multivariable analysis for late DFS (>5 years)			
	N	Distant events/PY	HR	95% CI	<i>P</i> -value	N	Distant events/PY	HR	95% CI	<i>P</i> -value	HR	95% CI	<i>P</i> -value	
Ki-67 (%)														
<20%	1375	184/6110	Ref.			1060	149/4046	Ref.			Ref.			
$\geq 20\%$	497	95/2165	1.46	1.14-1.87	0.003	366	92/1562	1.56	1.20-2.03	<0.001	1.71	1.26-2.32	<0.001	0.73
HER2^a														
Not expressed	1727	247/7629	Ref.			1318	206/5009	Ref.			Ref.			
Intense and complete	72	23/300	2.40	1.56-3.67	<0.001	45	13/159	1.99	1.13-3.48	0.02	1.79	0.99-3.19	0.05	0.67
pN														
pN0	1103	99/5017	Ref.			901	126/3397	Ref.			Ref.			
pN1/2/3	769	180/3259	2.83	2.21-3.62	<0.001	525	115/2212	1.38	1.07-1.77	0.01	1.20	0.92-1.57	0.17	<0.001
Grade^b														
G1/2	1511	186/6767	Ref.			1190	187/4649	Ref.			Ref.			
G3	209	55/871	2.32	1.72-3.14	<0.001	135	31/568	1.33	0.91-1.94	0.15	0.93	0.61-1.42	0.74	0.04
pT														
pT1/2	1672	224/7447	Ref.			1298	206/5140	Ref.			Ref.			
pT3/4	200	55/828	2.24	1.67-3.00	<0.001	128	35/468	1.90	1.32-2.71	<0.001	1.75	1.19-2.57	0.004	0.49
PgR														
<20%	555	105/2392	Ref.			402	83/1727	Ref.			Ref.			
$\geq 20\%$	1317	174/5883	0.67	0.53-0.85	0.001	1024	158/3881	0.86	0.66-1.13	0.28	0.85	0.64-1.11	0.23	0.16

^a For patients with HER2 unknown 9 events occurred within the first 5 years of FUP and 22 beyond 5 years.

^b For patients with grade unknown 38 events occurred within the first 5 years of FUP and 23 beyond 5 years.

Table S3. Prognostic factors of late (>5 years) DFS in ILCs by lymph-node status.

	pN0 (N=901)					pN1/2/3 (N=525)					<i>P-value for interaction with pN</i>
	Multivariable analysis					Multivariable analysis					
	N	Events/PY	HR	95% CI	<i>P-value</i>	N	Events/PY	HR	95% CI	<i>P-value</i>	
Ki-67 (%)											
<20%	701	82/2584	Ref.			359	67/1462	Ref.			
≥20%	200	44/812	1.61	1.04-2.50	0.03	166	48/750	1.84	1.20-2.82	0.005	0.61
HER2^a											
Not expressed	846	107/3116	Ref.			472	99/1893	Ref.			
Intense and complete	26	7/85	2.29	1.05-4.98	0.04	19	6/74	1.49	0.63-3.53	0.37	0.12
Grade^b											
G1/2	791	102/2993	Ref.			399	85/1657	Ref.			
G3	72	16/279	1.13	0.63-2.06	0.68	63	15/289	0.77	0.43-1.39	0.38	0.17
pT											
pT1/2	864	118/3272	Ref.			434	88/1868	Ref.			
pT3/4	37	8/125	1.61	0.77-3.37	0.21	91	27/344	1.81	1.15-2.84	0.01	0.88
PgR											
<20%	245	43/1005	Ref.			157	40/722	Ref.			
≥20%	656	83/2391	0.79	0.54-1.15	0.21	368	75/1490	0.83	0.55-1.25	0.37	0.50

^a 29 patients pN0 with missing information (12 events/195 PY), 34 patients pN1/2/3 with missing information (10 events/244 PY).

^b 38 patients pN0 with missing information (8 events/124 PY), 63 patients pN1/2/3 with missing information (15 events/266 PY).

Figure S1. Flowchart for patient's selection and matching.

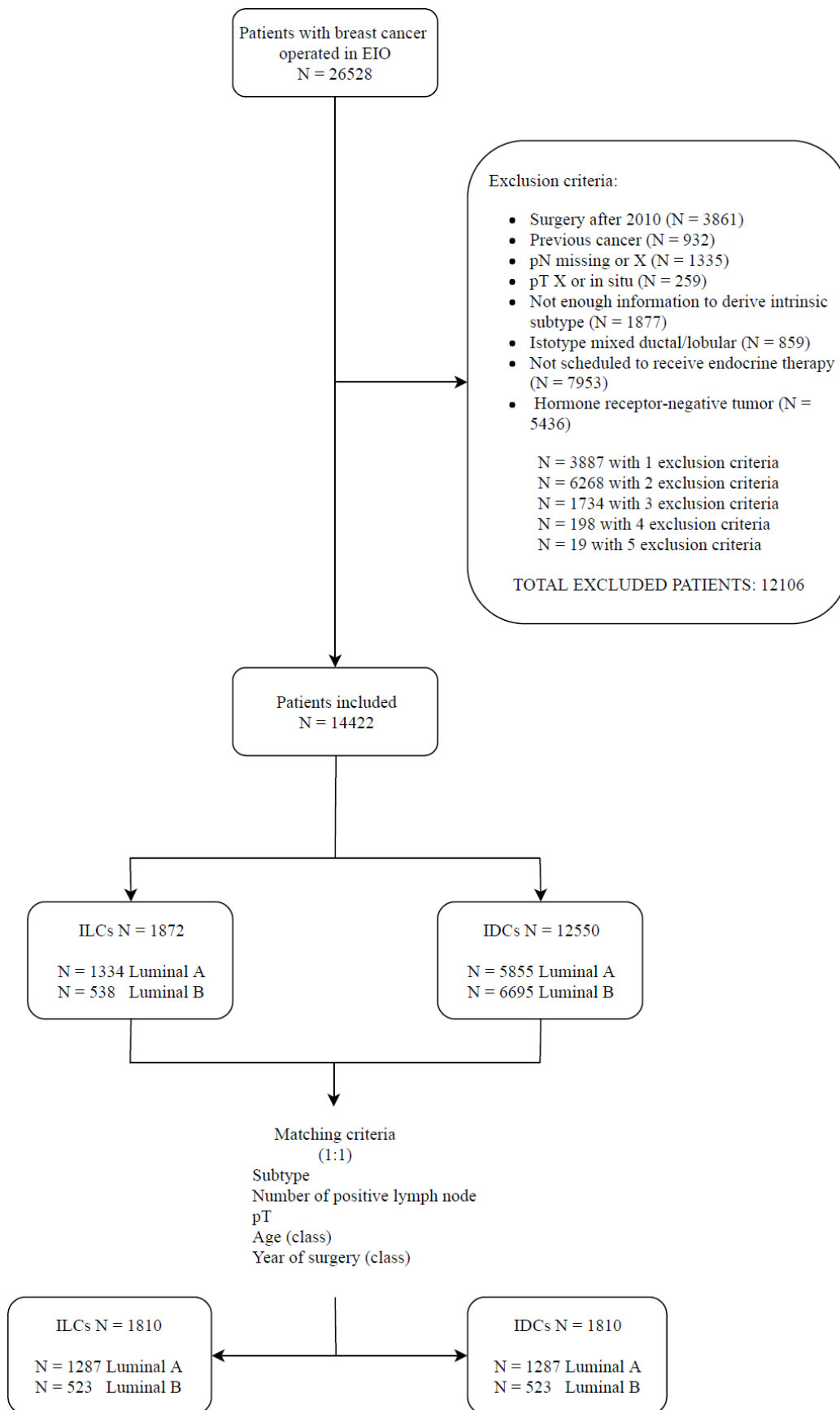


Table S4. Distribution of patient baseline characteristics according to intrinsic and histological subtype – matched groups

	Lobular (N=1810)		Ductal (N=1810)		P-value
	N	%	N	%	
Matching variables					
Subtype					
Luminal A	1287	71	1287	71	
Luminal B	523	29	523	29	
pN					
pN0	1076	60	1076	60	
pN1	439	24	439	24	
pN2	129	7	129	7	
pN3	166	9	166	9	
pT					
pT1	1055	58	1055	58	
pT2	608	34	608	34	
pT3/4	147	8	147	8	
Age group					
<50	638	35	638	35	
50-59	519	29	519	29	
60+	653	36	653	36	
Year of surgery					
Before 2003	520	29	520	29	
2003-2006	641	35	641	35	
2007-2010	649	36	649	36	
Other variables					
Menopausal status					0.31
Premenopausal	777	43	747	41	
Postmenopausal	1033	57	1063	59	
Tumor grade^a					<0.001
G1	276	15	423	23	
G2	1201	66	923	51	
G3	196	11	275	15	
Unknown	137	8	189	11	
Vessel invasion					<0.001
No	1739	96	1281	71	
Yes	71	4	529	29	
Local treatment					<0.001
Mastectomy w/o RT	322	18	242	14	
Mastectomy w RT	230	13	217	12	
Quadrantectomy w/o RT	35	2	25	1	
Quadrantectomy w RT	1223	67	1326	73	
Adjuvant treatment					0.01
ET	1440	80	1379	76	
CT+ET	370	20	431	24	
Receptor status					0.33
Incompletely expressed (ER<50 or PgR<50)	807	45	778	43	
Highly expressed (ER≥50 and PgR≥50)	1003	55	1032	57	
Ki-67					0.35
<20%	1327	73	1302	72	
≥20%	483	27	508	28	
ER Mean (SD) / Median (IQR)					<0.001
83 (17) / 90 (80-95) 86 (15) / 90 (85-95)					
PgR Mean (SD) / Median (IQR)					0.01
51 (37) / 60 (10-90) 53 (37) / 60 (10-90)					
Ki67 Mean (SD) / Median (IQR)					<0.001
15 (9) / 14 (9-20) 17 (11) / 15 (10-21)					

^aMissing values are not considered in the p-value calculation

Table S5. Prognostic factors of **early** (≤ 5 years) and **late** (> 5 years) **distant recurrences** in **IDCs** and **ILCs**, univariable analysis.

Histological subtype		≤ 5 years					> 5 years					Heterogeneity p-value
		N	Distant events/PY	HR	95% CI	P-value	N	Distant events/PY	HR	95% CI	P-value	
ER⁺												
$< 20\%$	Lobular	1327	61/5913	Ref.			1035	50/3958	Ref.			
$\geq 20\%$	Lobular	483	43/2111	1.96	1.33-2.90	<0.001	358	35/1535	1.79	1.17-2.75	0.008	0.73
$< 20\%$	Ductal	1302	56/5700	Ref.			921	35/3228	Ref.			
$\geq 20\%$	Ductal	508	58/2098	2.73	1.89-3.94	<0.001	314	21/1249	1.57	0.91-2.70	0.11	0.10
Heterogeneity p-value						0.23					0.70	
ER⁻												
HER2⁺												
Not expressed	Lobular	1671	91/7399	Ref.			1288	75/4908	Ref.			
Incomplete	Lobular	69	10/291	2.68	1.40-5.09	0.003	44	3/155	1.19	0.37-3.80	0.77	0.23
Not expressed	Ductal	1691	99/7322	Ref.			1164	45/4120	Ref.			
Incomplete	Ductal	69	7/275	1.88	0.87-4.04	0.11	39	5/149	3.18	1.27-7.99	0.01	0.42
Heterogeneity p-value						0.49					0.19	
HER2⁻												
$\leq N0$	Lobular	1076	14/4900	Ref.			883	26/3336	Ref.			
$> N1/2/3$	Lobular	734	90/3123	10.0	5.70-17.6	<0.001	510	59/2157	3.58	2.26-5.67	<0.001	0.005
$\leq N0$	Ductal	1076	24/4767	Ref.			778	11/2840	Ref.			
$> N1/2/3$	Ductal	734	90/3031	5.80	3.70-9.08	<0.001	457	45/1637	7.13	3.69-13.8	<0.001	0.61
Heterogeneity p-value						0.14					0.09	
Grade												
$\leq 1/2$	Lobular	1477	56/6629	Ref.			1173	68/4590	Ref.			
≥ 3	Lobular	196	24/824	3.40	2.11-5.49	<0.001	130	8/550	0.96	0.47-1.97	0.91	0.004
$\leq 1/2$	Ductal	1346	37/5897	Ref.			959	28/3479	Ref.			
≥ 3	Ductal	275	42/1132	5.77	3.71-8.97	<0.001	159	14/615	2.77	1.43-5.33	0.002	0.08
Heterogeneity p-value						0.11					0.03	
Stage												
$\leq T1/2$	Lobular	1663	82/7414	Ref.			1295	67/5131	Ref.			
$> T3/4$	Lobular	147	22/609	3.21	1.99-5.17	<0.001	98	18/363	3.77	2.28-6.26	<0.001	0.62
$\leq T1/2$	Ductal	1663	83/7213	Ref.			1157	45/4201	Ref.			
$> T3/4$	Ductal	147	31/584	4.61	3.05-6.98	<0.001	78	11/276	3.65	1.89-7.03	<0.001	0.52
Heterogeneity p-value						0.26					0.94	
Receptor												
$< 20\%$	Lobular	534	50/2324	Ref.			396	26/1703	Ref.			
$\geq 20\%$	Lobular	1276	54/5700	0.44	0.30-0.65	<0.001	997	59/3791	1.03	0.65-1.63	0.91	0.005
$< 20\%$	Ductal	509	49/2187	Ref.			350	28/1322	Ref.			
$\geq 20\%$	Ductal	1301	65/5611	0.52	0.36-0.75	<0.001	885	28/3155	0.41	0.24-0.69	<0.001	0.45
Heterogeneity p-value						0.54					0.01	

[‡] For patients with HER2 unknown 11 events (3 ILCs, 8 IDCs) occurred within the first 5 years of FUP and 13 beyond 5 years (7 ILCs, 6 IDCs).

[§] For patients with grade unknown 59 events (24 ILCs, 35 IDCs) occurred within the first 5 years of FUP and 23 beyond 5 years (9 ILCs, 14 IDCs).

Table S6.

	-2 log L	Likelihood- ratio test P-value
CTS5	980.675	
CTS5 + HER2	980.670	0.94
CTS5 + ER	980.541	0.71
CTS5 + PgR	980.611	0.80
CTS5 + ln(Ki-67)[*]	976.784	0.04

^{*}ln: logarithmic transformation