Adjuvant chemotherapy & survival outcomes of early-stage HR-positive HER2-negative lobular vs ductal carcinoma

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Background

- Invasive lobular carcinoma (ILC) represents 10-15% of all breast cancers (BC) and differs biologically and clinically from invasive ductal carcinoma (IDC).
- Conflicting data exist with regard to variation in prognosis and benefit of chemotherapy (CT) between these histologic subtypes.
- Here, we compare the impact of adjuvant CT on survival outcomes in patients (pts) with early-stage (ES) HR+/HER2- ILCand IDC

Methods

- Pts receiving upfront surgical resection for early-stage HR+ HER2- invasive BC
- Study period: 2010-2021
- Cohorts: ILC & IDC
- Cox proportional hazards models assessed the relationship between overall survival (OS) and histology type adjusting for potential confounders including age, race, stage, grade, and treatment variables
- Subgroup analysis based on
  - Receipt of chemo
  - Oncotype DX recurrence score (RS)
    - low (L) 0-15
    - intermediate (I) 16-25
    - high (H) >=26

Results

- Of the 1,101,920 pts included, 14.7% (n= 162,430) had ILC.
- Compared to pts with IDC, the ILC cohort was comprised of a greater proportion of Whites (87.7 vs 85.4%), intermediate-grade (63.7 vs 48.8%), clinical T2 (26.5 vs 22.1%) and N0 disease (89.1 vs 88.3%) (allp<0.001).
- RS scores varied by histologic subtype with a greater proportion of ILC having L (17.9 vs 17.2%) and I RS (15.2 vs 11.9%)compared to IDC, in which H RS was more common (2.8 % ILC vs 5.8% IDC).

Results

Baseline characteristics of ILC & IDC patients

	Total (n=954,934)	Lobular (n=141,949)	Ductal (n=812,985)	P-value
Age				<.0001
Median (IQR)	64 (55, 72)	65 (57, 73)	64 (54, 72)	
Race, n (%)				<.0001
White	820865 (86.6%)	124055 (88.0%)	696810 (86.4%)	
African American / Black	80047 (8.4%)	12036 (8.5%)	68011 (8.4%)	
Asian / Pacific Islander	35223 (3.7%)	3379 (2.4%)	31844 (3.9%)	
Other	11394 (1.2%)	1465 (1.0%)	9929 (1.2%)	
Receipt of Adjuvant Chemotherapy, n (%)				<.0001
Yes	196829 (20.6%)	27857 (19.6%)	168972 (20.8%)	
No	758105 (79.4%)	114092 (80.4%)	644013 (79.2%)	
Receipt of Radiation, n (%)				<.0001
Yes	582303 (63.1%)	82400 (60.1%)	499903 (63.6%)	
No	340512 (36.9%)	54683 (39.9%)	285829 (36.4%)	
Receipt of Hormone Therapy, n (%)				<.0001
Yes	814389 (86.5%)	124254 (88.6%)	690135 (86.1%)	
No	127038 (13.5%)	15942 (11.4%)	111096 (13.9%)	
Oncotype Score, n (%)				<.0001
Low (0 – 15)	183579 (19.2%)	27577 (19.4%)	156002 (19.2%)	
Intermediate (16 – 25)	128647 (13.5%)	23156 (16.3%)	105491 (13.0%)	
High (26+)	52559 (5.5%)	4139 (2.9%)	48420 (6.0%)	
Cancer Stage, n (%)				<.0001
1	768239 (80.4%)	104310 (73.5%)	663929 (81.7%)	
2	172312 (18.0%)	34323 (24.2%)	137989 (17.0%)	
3	14383 (1.5%)	3316 (2.3%)	11067 (1.4%)	
Menopausal, n (%)				<.0001
Pre-menopausal	142765 (15.0%)	16399 (11.6%)	126366 (15.5%)	
Post-menopausal	812169 (85.0%)	125550 (88.4%)	686619 (84.5%)	
Clinical T Stage, n (%)				<.0001
1	742008 (78.0%)	97056 (68.6%)	644952 (79.6%)	
2	187327 (19.7%)	35710 (25.3%)	151617 (18.7%)	
3	17808 (1.9%)	8055 (5.7%)	9753 (1.2%)	
4	4099 (0.4%)	593 (0.4%)	3506 (0.4%)	
Clinical N Stage, n (%)				<.0001
0	887834 (93.7%)	131099 (93.0%)	756735 (93.8%)	
1	53033 (5.6%)	8382 (5.9%)	44651 (5.5%)	
2	5057 (0.5%)	923 (0.7%)	4134 (0.5%)	
3	1783 (0.2%)	512 (0.4%)	1271 (0.2%)	

Lobular has higher number of patients with advanced stages (2, 3) and higher T staging (T2, T3), N staging (N1, 2, 3), however presented with more low and intermediate oncotype scores

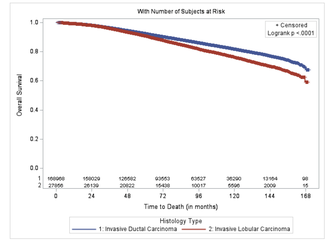
Providers rely more on tumor staging than Oncotype DX scores when making chemotherapy decisions for ILC

Baseline characteristics of ILC & IDC patients who received adjuvant chemotherapy

	Total (n=196,829)	Lobular (n=27,857)	Ductal (n=168,972)	P-value
Oncotype Score, n (%)				<.0001
Low (0 – 15)	6091 (3.1%)	1199 (4.3%)	4892 (2.9%)	
Moderate (16 – 25)	20507 (10.4%)	3088 (11.1%)	17419 (10.3%)	
High (26+)	38368 (19.5%)	2555 (9.2%)	35813 (21.2%)	
Unknown	131863 (67.0%)	21015 (75.4%)	110848 (65.6%)	
Cancer Stage, n (%)				<.0001
1	111375 (56.6%)	12844 (46.1%)	98531 (58.3%)	
2	76574 (38.9%)	12813 (46.0%)	63761 (37.7%)	
3	8880 (4.5%)	2200 (7.9%)	6680 (4.0%)	
Menopausal, n (%)				<.0001
Pre-menopausal	57632 (29.3%)	6085 (21.8%)	51547 (30.5%)	
Post-menopausal	139197 (70.7%)	21772 (78.2%)	117425 (69.5%)	
Clinical T Stage, n (%)				<.0001
1	113356 (57.8%)	12474 (45.0%)	100882 (60.0%)	
2	71923 (36.7%)	10914 (39.4%)	61009 (36.3%)	
3	9267 (4.7%)	4140 (14.9%)	5127 (3.0%)	
4	1407 (0.7%)	194 (0.7%)	1213 (0.7%)	
Clinical N Stage, n (%)				<.0001
0	158310 (81.2%)	21452 (77.8%)	136858 (81.8%)	
1	31668 (16.2%)	5065 (18.4%)	26603 (15.9%)	
2	3650 (1.9%)	664 (2.4%)	2986 (1.8%)	
3	1341 (0.7%)	398 (1.4%)	943 (0.6%)	

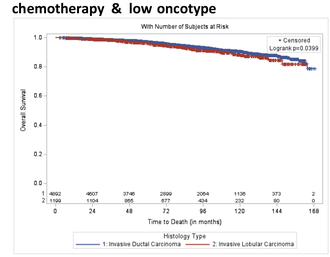
Results

Survival analysis of ILC & IDC patients who received adjuvant chemotherapy



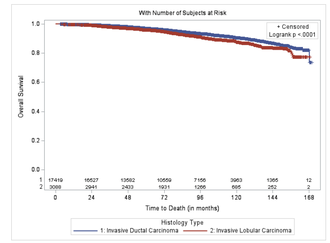
	ILC	IDC
5-year OS	90.8% (90.4%-91.2%)	92.4% (92.3%-92.6%)
10-year OS	76.2% (75.5%-76.9%)	81.8% (81.6%-82.1%)

ILC vs IDC patients who received adjuvant chemotherapy & low oncotype



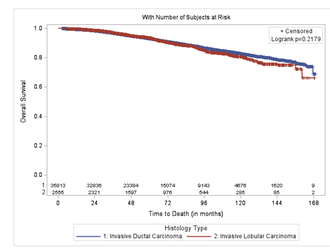
	ILC	IDC
5-year OS	96.1% (94.7%-97.2%)	97.1% (96.5%-97.6%)
10-year OS	88.1% (85.1%-90.5%)	90.4% (89.2%-91.5%)

ILC vs IDC patients who received adjuvant chemotherapy & intermediate oncotype



	ILC	IDC
5-year OS	96.0% (95.1%-96.6%)	97.0% (96.8%-97.3%)
10-year OS	87.6% (85.9%-89.1%)	90.6% (90.0%-91.2%)

ILC vs IDC patients who received adjuvant chemotherapy & high oncotype



	ILC	IDC
5-year OS	93.6% (92.4%-94.6%)	93.1% (92.8%-93.4%)
10-year OS	80.7% (77.9%-83.2%)	82.9% (82.2%-83.5%)

Conclusions

- Our study suggests that while 5-year survival may be comparable, early-stage ILC pts receiving adjuvant CT may experience worse long-term outcomes compared to IDC, particularly among those with higher genomic risk.
- Further research is needed to personalize treatment strategies for ILC by identifying underlying molecular differences that drive this disparity

Please contact aryamariam.roy@osumc.edu if any questions