SABCS Abstract #441

Genomic analysis of ER+/HER2- metastatic invasive lobular carcinoma (ILC) and clinical outcomes comparison with metastatic invasive carcinoma of no special type (NST)

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BACKGROUND

- Invasive lobular carcinoma (ILC) is the second most common histology of breast cancer after invasive carcinoma of no special type (NST)
- It makes up 10-15% of invasive breast cancers[1]
- There is a significant disparity in our understanding of ILC compared to NST
- ILC has unique pathology, as well as unique patterns of presentation, spread, and progression [2, 3, 4, 5, 6]
- Despite these differences, treatment of ILC does not differ from NST
- Mutational landscape of primary ILC has been described [7, 8, 9]
- Here we aim to describe genomic alterations of patients with metastatic ILC and clinical outcomes for subgroups of patients in a unique cohort from a single cancer center

METHODS

- Metastatic hormone receptor-positive (HR+) HER2-negative breast cancer
- Seen ≥1 time 7/1/2001-8/2/2022 at Dana-Farber Cancer Institute
- Targeted tumor-only DNA sequencing with OncoPanel completed on archival tissue collected within 3 months of time of patients' diagnosis with distant recurrence or de novo metastatic disease
- Clinical information about disease and treatment course was available
- Tested via Fischer enrichment with a Benjamini-Hochberg correction for differences across clinical variables
- Median time to next treatment (TTNT) and median overall survival (mOS) were compared between the ILC and NST cohorts in patients receiving endocrine therapy (ET) + CDK4/6 inhibitor using Kaplan-Meier analysis and Cox proportional hazards models

TABLE 1: Clinical characteristics

	ILC (n=125), no. (%)	IDC (n=408), no. (%)	All (n=533), no. (%)
Age initial dx, median (min-max)	55.55 (33.46-83.80)	49.91 (22.60-84.58)	50.54 (22.60-84.58)
Age metastatic dx, median (min-max)	60.51 (38.73-83.79)	55.16 (24.68-89.16)	56.41 (24.68-89.16)
Race			
African American	1 (0.80)	17 (4.17)	18 (3.38)
Asian or Pacific Islander	0 (0.00)	15 (3.68)	15 (2.81)
Caucasian	119 (95.20)	358 (87.75)	477 (89.49)
Sex			
Female	125 (100.00)	401 (98.28)	526 (98.69)
Male	0 (0.00)	7 (1.72)	7 (1.31)
Stage at initial diagnosis			
I	10 (8.00)	75 (18.38)	85 (15.95)
II	28 (22.40)	124 (30.39)	152 (28.52)
III	34 (27.20)	62 (15.20)	96 (18.01)
IV/DeNovo	51 (40.80)	145 (35.54)	196 (36.77)
Histologic Grade			
I Low Grade	21 (16.80)	23 (5.64)	44 (8.26)
II Intermediate Grade	81 (64.80)	206 (50.49)	287 (53.85)
III High Grade	8 (6.40)	162 (39.71)	170 (31.89)
ER Status Metastatic			
ER Positive	108 (86.40)	358 (87.75)	466 (87.43)
ER Positive Low	7 (5.60)	10 (2.45)	17 (3.19)
ER Negative	0 (0.00)	0 (0.00)	0 (0.00)
PR Status Metastatic			
PR Positive	63 (50.40)	171 (41.91)	234 (43.90)
PR Positive Low	13 (10.40)	49 (12.01)	62 (11.63)
PR Negative	36 (28.80)	133 (32.60)	169 (31.71)
HER2 Status Metastatic			
HER2-0	28 (22.40)	135 (33.09)	163 (30.58)
HER2-Low	45 (36.00)	135 (33.09)	180 (33.77)
HER2 Negative/NOS	37 (29.60)	78 (19.12)	115 (21.58)
Disease free interval in years, median (min-max)	5.40 (1.02, 30.94)	6.21 (0.60, 32.16)	5.93 (0.60, 32.16)
De Novo	51 (40.80)	145 (35.54)	196 (36.77)
Recurrent MBC			
<2 years	8 (10.81)	30 (11.41)	38 (11.28)
2-5 years	28 (37.84)	80 (30.42)	108 (32.05)
5+ years	38 (51.35)	153 (58.17)	191 (56.68)
Prior neo/adjuvant chemotherapy	57 (77.03)	197 (74.90)	254 (75.37)
Prior neo/adjuvant ET	67 (90.54)	225 (85.55)	292 (86.65)
Tam	23 (31.08)	113 (42.97)	136 (40.36)
AI	24 (32.43)	57 (21.67)	81 (24.04)
Tam and AI	20 (27.03)	54 (20.53)	74 (21.96)
Prior neo/adjuvant CDK4/6i	3 (4.05)	4 (1.52)	7 (2.08)

RESULTS

GENOMICS RESULTS

The most common genomic alterations in ILC were CDH1, PIK3CA, TP53, ESR1, CCND1 and PTEN

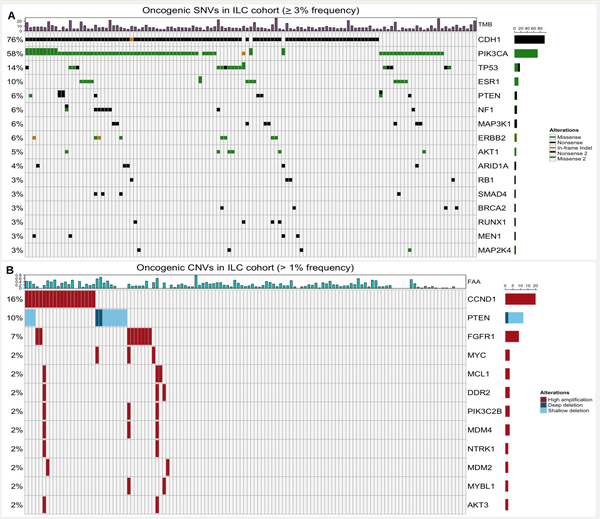


FIG. 1: A) Oncogenic single nucleotide variants (SNVs) in ILC cohort with ≥ 3% frequency. B) Oncogenic copy number variants (CNVs) in ILC cohort with >1% frequency.

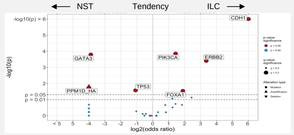
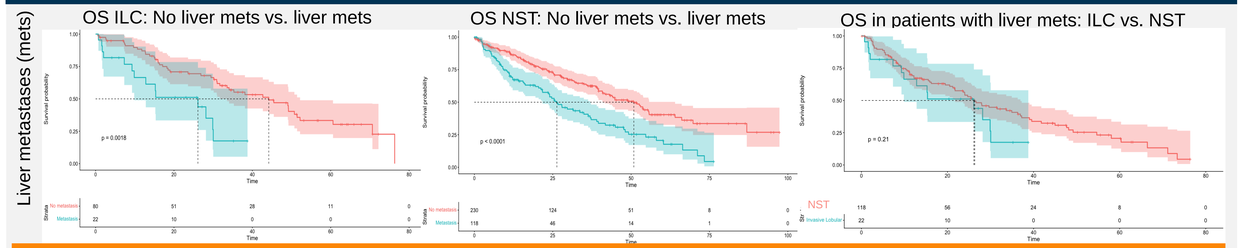


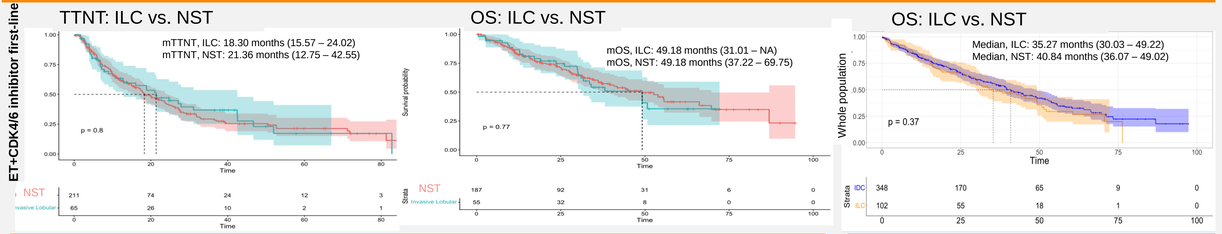
FIG. 2: Alterations with significantly different frequencies comparing tumors from patients with ILC to NST

Alterations in GATA3 and TP53 are more common in NST. Alterations in CDH1, ERBB2, PIK3CA, and FOXA1 are more common in ILC.

OUTCOMES RESULTS



Patients with liver metastases at baseline have shorter mOS. mOS is similar between patients with ILC and NST who have liver metastases at baseline.



TTNT and mOS are similar between ILC and NST in patients treated with ET + CDK4/6 inhibitor in the first line

mOS is similar in patients with ILC and NST

TABLE 2: SNV association with clinical variables for patients with ILC.

	0-5 years recurrence, n=36 n (%)	>5 years recurrence, n=38 n (%)	Odds ratio	Tendency	P-value	Adjusted p values
CDH1	32 (88.9)	22 (57.9)	0.176	0-5 years	0.0037	0.0371
ERBB2	7 (0.194)	0 (0)	0	0-5 years	0.0046	0.0371
	No liver mets, n=100, n (%)	**Liver mets n=26, n (%)**	**Odds Ratio**	**Tendency**	**P-value**	**Adjusted p-values**
ERBB2	2 (2.0)	6 (23.1)	14.1	Liver mets	0.001	0.0171

In ILC: CDH1 and ERBB2 were associated with early recurrence. ERBB2 was more common in patients with liver metastases.

CONCLUSIONS

- **Metastatic ILC has a unique genomic landscape**
- **Patients with metastatic ILC have similar clinical outcomes to patients with NST**
- **ILC genomics highlight paths for development of histology-specific treatments**

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