Breast Cancer Index (BCI) identifies fewer patients with high risk of late recurrence and high likelihood of benefit from extended endocrine therapy with invasive lobular compared to invasive ductal carcinoma

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INTRODUCTION

- Invasive ductal carcinoma (IDC) and invasive lobular carcinoma (ILC) are the first and second most common histologic subtypes of breast cancer¹. Both IDC and ILC present distinguishing clinicopathologic features that contribute to differences in response to treatment and long-term prognosis.
- Breast Cancer Index (BCI) is a validated gene expression-based assay with two components, the Molecular Grade Index (MGI) and the H/I ratio (HOXB13/IL17BR), that evaluate tumor proliferation and estrogen signaling, respectively.
- Integration of MGI and H/I generates a prognostic BCI score that quantifies the risk of overall (0-10 years) and late (5-10 years) distant recurrence (DR). 4-6
- The H/I ratio is the predictive component of BCI and has been shown to predict endocrine response across various treatment regimens.²⁻⁷
- BCI (H/I) has previously been shown to significantly predict preferential benefit from 5 vs 2.5 years of extended letrozole in the IDEAL (Investigation on the Duration of Extended Letrozole) study designed to directly examine the potential benefit of extended durations of aromatase inhibitor therapy.^{8,9}
- The current analysis compared the predictive and prognostic performance of BCI (H/I) in HR+ lobular and ductal tumor types of the BCI Clinical database and the IDEAL study.

METHODS

- The BCI Clinical Database for Correlative Studies is an IRBapproved de-identified database containing >50 clinicopathologic and molecular variables from cases submitted for BCI testing in clinical practice (N=19,126). Molecular variables include BCI Prognostic score, HOXB13/IL17BR ratio (H/I), and Molecular Grade Index (MGI). Clinicopathologic variables were abstracted from pathology reports when available. Chi-squared tests¹ and Kruskal-Wallis tests² were used to compare categorical and numeric factors, respectively, between IDC and ILC subgroups.
- Out of the 908 patients from the translational IDEAL cohort, 142 were classified as lobular and 720 as ductal.
- Primary endpoints in this analysis were recurrence-free interval (RFI) for the predictive performance and distant recurrence (DR) for the prognostic performance.
- RNA was extracted from formalin-fixed paraffin-embedded (FFPE) blocks of primary tumors from IDEAL patients and BCI testing was performed by RT-PCR blinded to clinical outcome.
- Kaplan-Meier survival analysis and Cox proportional hazards regression were used to analyze BCI Predictive performance in the lobular and ductal patients from the IDEAL study.

	Ductal(N=3072)	Lobular(N=504)	Total(N=3576)	P-value	Table 2. Key IDE						2. BCI predictive pe				
Age at Diagnosis				<.001 ¹		Ductol					Lobular, Unselected (N=142)	Lobular, B	CI (H/I)-Low (N=87)	Lobular	, BCI (H/I)-High (N
<=39 years	150 (4.9%)	7 (1.4%)	157 (4.4%)	1.001		Ductal	Lobular	Lobular BC	CI (H/I) groups	8 1	7.5 years		7.5 years	^в] —	7.5 years
40-49 years	675 (22.0%)	91 (18.1%)	766 (21.4%)			(N =720)	(N=142)			- 49	10 years	- 46	10 years	- 40	 10 years
50-59 years	894 (29.1%)	152 (30.2%)	1046 (29.3%)					Low (N=87)	High (N =55)	- 30 ^(%)		- 30 %)		e (%)	
60-69 years	991 (32.3%)	170 (33.7%)	1161 (32.5%)		Age at surgery					Ĕ	Absolute benefit: -2.3% HR: 1.16 (0.48-2.78)	Absolute bend		Ĕ	benefit: 11.9% (0.09-2.14)
70+ years	362 (11.8%)	84 (16.7%)	446 (12.5%)		<50y	233 (32.4%)	46 (32.4%)	28 (32.2%)	18 (32.7%)	a ci	P = 0.742	P = 0.138		P = 0.298	
oT stage		- (/	- ()	<.001 ¹	≥50y	487 (67.6%)	96 (67.6%)	59 (67.8%)	37 (67.3%)	₽ -		₽ -		6 -	
pT1	1843 (75.8%)	215 (54.2%)	2058 (72.8%)		pT stage					∟_ ₀	, ^** ,	。┙┍╾╾ <mark>┍</mark> ┣═		╶┛	۴.,,,
pT2	559 (23.0%)	144 (36.3%)	703 (24.9%)		pT1	352 (48.9%)	33 (23.2%)	14 (16.1%)	19 (34.5%)	0	2 4 6 8 10	0 2	4 6 8 10	0 2	4 6 8
рт з	29 (1.2%)	38 (9.6%)	67 (2.4%)		pT2	335 (46.5%)	80 (56.3%)	54 (62.1%)	26 (47.3%)	No. at risk	Years since randomization	No. at risk	since randomization	No. at risk	ars since randomization
Unknown	641	107	748		pT3	21 (2.9%)	26 (18.3%)	17 (19.5%)	9 (16.4%)	— 76 — 66	76 70 64 44 17 66 60 58 39 18	- 43 43 43 44 44	41 39 26 9 41 40 28 13	— 33 33 22 22	29 25 18 19 18 11
Grade		107	710	<.001 ¹	pT4	12 (1.7%)	3 (2.1%)	2 (2.3%)	1 (1.8%)	00.7					
1	882 (29.9%)	153 (35.4%)	1035 (30.6%)		Grade	105 (15.4%)	16 (14.3%)	11 (15.9%)	5 (11.6%)	• 38.7	% and 61.3% of IL	c patients were	e classified as	S BCI (H/I)-HI	gn and -Lo
2	1456 (49.3%)	250 (57.9%)	1706 (50.4%)		2	300 (44.1%)	76 (67.9%)	49 (71%)	27 (62.8%)						
3	615 (20.8%)	29 (6.7%)	644 (19.0%)		3	276 (40.5%)	20 (17.9%)	9 (13%)	11 (25.6%)	BCI	(H/I)-High showed	a non-significa	nt absolute b	enefit of 11.9	% (HR=0.4
Unknown	119	72	191		Nodal status		20 (17.370)	3 (1370)			BCI (H/I)-Low shov				`
Nodal Status	115	12	191	0.313 ¹	NO	186 (25.9%)	38 (26.8%)	27 (31.0%)	11 (20.0%)	and			(1117 2100, 00		00, p 0110
NO	1589 (70.9%)	274 (73.5%)	1863 (71.3%)	0.315	N1	406 (56.6%)	67 (47.2%)	41 (47.1%)	26 (47.3%)	Table 0					.lt.a
N0 N+		99 (26.5%)			N2	101 (14.1%)	28 (19.7%)	13 (14.9%)	15 (27.3%)	Table 3	. The BCI Clinical I	Jatabase Prog	nostic and Pi	redictive Rest	lits
Unknown	652 (29.1%)		751 (28.7%)		N3	24 (3.3%)	9 (6.3%)	6 (6.9%)	3 (5.5%)			Ductal	Lobular	Total	P-value
Unknown	831	131	962						3 (3.370)						
				0 1 7 0 1	ER							(N=3072)	(N=504)	(N=3576)	
R		1 (0.20()		0.179 ¹	ER Negative	22 (3.1%)	2 (1.4%)	1 (1.1%)	1 (1.8%)		tic Risk Category (0-10 years)				<.001 ¹
R Negative	22 (1.0%)	1 (0.3%)	23 (0.9%)	0.179 ¹	ER Negative Positive	22 (3.1%) 697 (96.8%)	2 (1.4%) 140 (98.6%)			Low Risk		1396 (45.4%)	288 (57.1%)	1684 (47.1%)	<.001 ¹
Positive	22 (1.0%) 2098 (99.0%)	345 (99.7%)	2443 (99.1%)	0.179 ¹					1 (1.8%)	Low Risk		1396 (45.4%) 136 (4.4%)	288 (57.1%) 25 (5.0%)	1684 (47.1%) 161 (4.5%)	<.001 ¹
	22 (1.0%)				Positive Unknown PR	697 (96.8%) 1	140 (98.6%) 0	86 (98.9%) 0	1 (1.8%) 54 (98.2%) 0	Low Risk Intermediate High Risk	e Risk	1396 (45.4%)	288 (57.1%)	1684 (47.1%)	
Positive Unknown PR	22 (1.0%) 2098 (99.0%) 952	345 (99.7%) 158	2443 (99.1%) 1110	0.179 ¹	Positive Unknown PR Negative	697 (96.8%) 1 133 (19.0%)	140 (98.6%) 0 25 (17.9%)	86 (98.9%) 0 10 (11.6%)	1 (1.8%) 54 (98.2%) 0 15 (27.8%)	Low Risk Intermediate High Risk		1396 (45.4%) 136 (4.4%) 1540 (50.1%)	288 (57.1%) 25 (5.0%) 191 (37.9%)	1684 (47.1%) 161 (4.5%) 1731 (48.4%)	<.001 ¹
Positive Unknown PR Negative	22 (1.0%) 2098 (99.0%) 952 272 (12.9%)	345 (99.7%) 158 36 (10.5%)	2443 (99.1%) 1110 308 (12.6%)		Positive Unknown PR Negative Positive	697 (96.8%) 1 133 (19.0%) 568 (81.0%)	140 (98.6%) 0	86 (98.9%) 0	1 (1.8%) 54 (98.2%) 0	Low Risk Intermediate High Risk BCI Prognost	e Risk	1396 (45.4%) 136 (4.4%) 1540 (50.1%) 1396 (45.4%)	288 (57.1%) 25 (5.0%) 191 (37.9%) 288 (57.1%)	1684 (47.1%) 161 (4.5%) 1731 (48.4%) 1684 (47.1%)	
Positive Unknown PR Negative Positive	22 (1.0%) 2098 (99.0%) 952 272 (12.9%) 1829 (87.1%)	345 (99.7%) 158 36 (10.5%) 307 (89.5%)	2443 (99.1%) 1110 308 (12.6%) 2136 (87.4%)		Positive Unknown PR Negative Positive Unknown	697 (96.8%) 1 133 (19.0%)	140 (98.6%) 0 25 (17.9%)	86 (98.9%) 0 10 (11.6%)	1 (1.8%) 54 (98.2%) 0 15 (27.8%)	Low Risk Intermediate High Risk BCI Prognost Low Risk High Risk	e Risk	1396 (45.4%) 136 (4.4%) 1540 (50.1%)	288 (57.1%) 25 (5.0%) 191 (37.9%)	1684 (47.1%) 161 (4.5%) 1731 (48.4%)	<.001 ¹
Positive Unknown PR Negative Positive Unknown	22 (1.0%) 2098 (99.0%) 952 272 (12.9%)	345 (99.7%) 158 36 (10.5%)	2443 (99.1%) 1110 308 (12.6%)	0.205 ¹	Positive Unknown PR Negative Positive Unknown HER2	697 (96.8%) 1 133 (19.0%) 568 (81.0%) 19	140 (98.6%) 0 25 (17.9%) 115 (82.1%) 2	86 (98.9%) 0 10 (11.6%) 76 (88.4%) 1	1 (1.8%) 54 (98.2%) 0 15 (27.8%) 39 (72.2%) 1	Low Risk Intermediate High Risk BCI Prognost Low Risk High Risk Prognostic a	e Risk tic Risk Category (5-10 years)	1396 (45.4%) 136 (4.4%) 1540 (50.1%) 1396 (45.4%)	288 (57.1%) 25 (5.0%) 191 (37.9%) 288 (57.1%)	1684 (47.1%) 161 (4.5%) 1731 (48.4%) 1684 (47.1%)	<.001 ¹
Positive Unknown PR Negative Positive Unknown HER2	 22 (1.0%) 2098 (99.0%) 952 272 (12.9%) 1829 (87.1%) 971 	345 (99.7%) 158 36 (10.5%) 307 (89.5%) 161	2443 (99.1%) 1110 308 (12.6%) 2136 (87.4%) 1132		Positive Unknown PR Negative Positive Unknown HER2 Negative	697 (96.8%) 1 133 (19.0%) 568 (81.0%) 19 226 (76.4%)	140 (98.6%) 0 25 (17.9%) 115 (82.1%) 2 55 (88.7%)	86 (98.9%) 0 10 (11.6%) 76 (88.4%) 1 34 (87.2%)	1 (1.8%) 54 (98.2%) 0 15 (27.8%) 39 (72.2%) 1 1 21 (91.3%)	Low Risk Intermediate High Risk BCI Prognost Low Risk High Risk Prognostic a Low Risk/ Lo	e Risk tic Risk Category (5-10 years) and Predictive Results	1396 (45.4%) 136 (4.4%) 1540 (50.1%) 1396 (45.4%) 1676 (54.6%)	288 (57.1%) 25 (5.0%) 191 (37.9%) 288 (57.1%) 216 (42.9%)	1684 (47.1%) 161 (4.5%) 1731 (48.4%) 1684 (47.1%) 1892 (52.9%)	<.001 ¹
Positive Unknown PR Negative Positive Unknown	22 (1.0%) 2098 (99.0%) 952 272 (12.9%) 1829 (87.1%)	345 (99.7%) 158 36 (10.5%) 307 (89.5%)	2443 (99.1%) 1110 308 (12.6%) 2136 (87.4%)	0.205 ¹	Positive Unknown PR Negative Positive Unknown HER2 Negative Positive	697 (96.8%) 1 133 (19.0%) 568 (81.0%) 19 226 (76.4%) 70 (23.6%)	140 (98.6%) 0 25 (17.9%) 115 (82.1%) 2 55 (88.7%) 7 (11.3%)	86 (98.9%) 0 10 (11.6%) 76 (88.4%) 1 1 34 (87.2%) 5 (12.8%)	1 (1.8%) 54 (98.2%) 0 15 (27.8%) 39 (72.2%) 1 1 21 (91.3%) 2 (8.7%)	Low Risk Intermediate High Risk BCI Prognost Low Risk High Risk Prognostic a Low Risk/ Lo Low Risk/ Hi High Risk/ Lo	e Risk tic Risk Category (5-10 years) and Predictive Results ow Likelihood igh Likelihood ow Likelihood	1396 (45.4%) 136 (4.4%) 1540 (50.1%) 1396 (45.4%) 1676 (54.6%) 1161 (37.8%)	288 (57.1%) 25 (5.0%) 191 (37.9%) 288 (57.1%) 216 (42.9%) 218 (43.3%)	1684 (47.1%) 161 (4.5%) 1731 (48.4%) 1684 (47.1%) 1892 (52.9%) 1379 (38.6%)	
Positive Unknown PR Negative Positive Unknown HER2	 22 (1.0%) 2098 (99.0%) 952 272 (12.9%) 1829 (87.1%) 971 	345 (99.7%) 158 36 (10.5%) 307 (89.5%) 161	2443 (99.1%) 1110 308 (12.6%) 2136 (87.4%) 1132	0.205 ¹	Positive Unknown PR Negative Positive Unknown HER2 Negative Positive Unknown	697 (96.8%) 1 133 (19.0%) 568 (81.0%) 19 226 (76.4%)	140 (98.6%) 0 25 (17.9%) 115 (82.1%) 2 55 (88.7%)	86 (98.9%) 0 10 (11.6%) 76 (88.4%) 1 34 (87.2%)	1 (1.8%) 54 (98.2%) 0 15 (27.8%) 39 (72.2%) 1 1 21 (91.3%)	Low Risk Intermediate High Risk BCI Prognost Low Risk High Risk Prognostic a Low Risk/ Lo Low Risk/ Lo High Risk/ Hi High Risk/ H	e Risk tic Risk Category (5-10 years) and Predictive Results ow Likelihood igh Likelihood igh Likelihood ligh Likelihood	1396 (45.4%) 136 (4.4%) 1540 (50.1%) 1396 (45.4%) 1676 (54.6%) 1161 (37.8%) 235 (7.6%)	288 (57.1%) 25 (5.0%) 191 (37.9%) 288 (57.1%) 216 (42.9%) 218 (43.3%) 70 (13.9%)	1684 (47.1%) 161 (4.5%) 1731 (48.4%) 1684 (47.1%) 1892 (52.9%) 1379 (38.6%) 305 (8.5%)	<.001 ¹ <.001 ¹
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Positive Unknown PR Negative Positive Unknown HER2 Negative Positive Unknown Symphovascular	 22 (1.0%) 2098 (99.0%) 952 952 272 (12.9%) 1829 (87.1%) 971 1807 (87.3%) 262 (12.7%) 	345 (99.7%) 158 36 (10.5%) 307 (89.5%) 161 338 (97.7%) 8 (2.3%)	2443 (99.1%) 1110 308 (12.6%) 2136 (87.4%) 1132 2145 (88.8%) 270 (11.2%)	0.205 ¹ <.001 ¹	Positive Unknown PR Negative Positive Unknown HER2 Negative Positive Unknown Prior Endocrine therapy 2–3 yrs TAM–> 3–2 yrs AI	697 (96.8%) 1 133 (19.0%) 568 (81.0%) 19 226 (76.4%) 70 (23.6%) 424 432 (60%)	140 (98.6%) 0 25 (17.9%) 115 (82.1%) 2 55 (88.7%) 7 (11.3%) 80 80	 86 (98.9%) 0 10 (11.6%) 76 (88.4%) 76 (88.4%) 34 (87.2%) 34 (87.2%) 5 (12.8%) 48 51 (58.6%) 	1 (1.8%) 54 (98.2%) 0 15 (27.8%) 39 (72.2%) 1 21 (91.3%) 2 (8.7%) 32 29 (52.7%)	Low Risk Intermediate High Risk BCI Prognost Low Risk High Risk Prognostic a Low Risk/ Lo Low Risk/ Lo Low Risk/ Hi High Risk/ Hi High Risk/ H H/I Predictiv Low likelihoo High likelihoo	e Risk tic Risk Category (5-10 years) and Predictive Results ow Likelihood igh Likelihood ow Likelihood ligh Likelihood ve Category od	1396 (45.4%) 136 (4.4%) 1540 (50.1%) 1396 (45.4%) 1676 (54.6%) 1161 (37.8%) 235 (7.6%) 604 (19.7%) 1072 (34.9%) 1765 (57.5%) 1307 (42.5%)	288 (57.1%) 25 (5.0%) 191 (37.9%) 288 (57.1%) 216 (42.9%) 218 (43.3%) 70 (13.9%) 88 (17.5%) 128 (25.4%) 306 (60.7%) 198 (39.3%)	1684 (47.1%) 161 (4.5%) 1731 (48.4%) 1684 (47.1%) 1892 (52.9%) 1379 (38.6%) 305 (8.5%) 692 (19.4%) 1200 (33.6%) 2071 (57.9%) 1505 (42.1%)	<.001 ¹ <.001 ¹ 0.169 ¹
Positive Unknown PR Negative Positive Unknown HER2 Negative Positive Unknown Symphovascular nvasion	 22 (1.0%) 2098 (99.0%) 952 952 272 (12.9%) 1829 (87.1%) 971 1807 (87.3%) 262 (12.7%) 1003 	345 (99.7%) 158 36 (10.5%) 307 (89.5%) 161 338 (97.7%) 8 (2.3%) 158	2443 (99.1%) 1110 308 (12.6%) 2136 (87.4%) 1132 2145 (88.8%) 270 (11.2%) 1161	0.205 ¹ <.001 ¹	Positive Unknown PR Negative Positive Unknown HER2 Negative Positive Unknown Prior Endocrine therapy 2–3 yrs TAM–> 3–2 yrs Al 5 yrs Al	697 (96.8%) 1 133 (19.0%) 568 (81.0%) 19 226 (76.4%) 70 (23.6%) 424 432 (60%) 197 (27.4%)	140 (98.6%) 0 25 (17.9%) 115 (82.1%) 2 2 55 (88.7%) 7 (11.3%) 80 80 80 80 44 (31%)	 86 (98.9%) 0 10 (11.6%) 76 (88.4%) 76 (88.4%) 11 34 (87.2%) 34 (87.2%) 5 (12.8%) 48 51 (58.6%) 25 (28.7%) 	1 (1.8%) 54 (98.2%) 0 15 (27.8%) 39 (72.2%) 1 1 21 (91.3%) 2 (8.7%) 32 29 (52.7%) 19 (34.5%)	Low Risk Intermediate High Risk BCI Prognost Low Risk High Risk Prognostic a Low Risk/ Lo Low Risk/ Lo Low Risk/ Hi High Risk/ Hi High Risk/ H H/I Predictiv Low likelihoo High likeliho	e Risk tic Risk Category (5-10 years) and Predictive Results ow Likelihood igh Likelihood ow Likelihood ligh Likelihood ve Category od ood Prognostic and BCI	1396 (45.4%) 136 (4.4%) 1540 (50.1%) 1396 (45.4%) 1676 (54.6%) 1161 (37.8%) 235 (7.6%) 604 (19.7%) 1072 (34.9%) 1765 (57.5%) 1307 (42.5%) Predictive resu	288 (57.1%) 25 (5.0%) 191 (37.9%) 288 (57.1%) 216 (42.9%) 218 (43.3%) 70 (13.9%) 88 (17.5%) 128 (25.4%) 306 (60.7%) 198 (39.3%) Ults reveal a la	1684 (47.1%) 161 (4.5%) 1731 (48.4%) 1684 (47.1%) 1892 (52.9%) 1379 (38.6%) 305 (8.5%) 692 (19.4%) 1200 (33.6%) 2071 (57.9%) 1505 (42.1%) arger number	<.001 ¹ <.001 ¹ 0.169 ¹
Positive Unknown PR Negative Positive Unknown HER2 Negative Positive Unknown Symphovascular nvasion No	 22 (1.0%) 2098 (99.0%) 952 952 272 (12.9%) 272 (12.9%) 1829 (87.1%) 971 971 1807 (87.3%) 262 (12.7%) 1003 1488 (76.2%) 	345 (99.7%) 158 36 (10.5%) 307 (89.5%) 161 338 (97.7%) 8 (2.3%) 158 274 (89.3%)	2443 (99.1%) 1110 308 (12.6%) 2136 (87.4%) 1132 2145 (88.8%) 270 (11.2%) 1161 1161 1762 (78.0%)	0.205 ¹ <.001 ¹	Positive Unknown PR Negative Positive Unknown HER2 Negative Positive Unknown Prior Endocrine therapy 2–3 yrs TAM–> 3–2 yrs Al 5 yrs TAM	697 (96.8%) 1 133 (19.0%) 568 (81.0%) 19 226 (76.4%) 70 (23.6%) 424 432 (60%) 197 (27.4%)	140 (98.6%) 0 25 (17.9%) 115 (82.1%) 2 2 55 (88.7%) 7 (11.3%) 80 80 80 80 44 (31%)	 86 (98.9%) 0 10 (11.6%) 76 (88.4%) 76 (88.4%) 11 34 (87.2%) 34 (87.2%) 5 (12.8%) 48 51 (58.6%) 25 (28.7%) 	1 (1.8%) 54 (98.2%) 0 15 (27.8%) 39 (72.2%) 1 21 (91.3%) 2 (8.7%) 32 29 (52.7%) 19 (34.5%) 7 (12.7%)	Low Risk Intermediate High Risk BCI Prognost Low Risk High Risk Prognostic a Low Risk/ Lo Low Risk/ Lo Low Risk/ Hi High Risk/ Hi High Risk/ H H/I Predictiv Low likelihoo High likelihoo	e Risk tic Risk Category (5-10 years) and Predictive Results ow Likelihood igh Likelihood ow Likelihood ligh Likelihood ve Category od ood	1396 (45.4%) 136 (4.4%) 1540 (50.1%) 1396 (45.4%) 1676 (54.6%) 1167 (54.6%) 1161 (37.8%) 235 (7.6%) 604 (19.7%) 1072 (34.9%) 1765 (57.5%) 1307 (42.5%) Predictive results of benefit (43°)	288 (57.1%) 25 (5.0%) 191 (37.9%) 288 (57.1%) 216 (42.9%) 218 (43.3%) 70 (13.9%) 88 (17.5%) 128 (25.4%) 306 (60.7%) 198 (39.3%) ults reveal a la % vs 38%) ar	1684 (47.1%) 161 (4.5%) 1731 (48.4%) 1684 (47.1%) 1892 (52.9%) 1379 (38.6%) 305 (8.5%) 692 (19.4%) 1200 (33.6%) 2071 (57.9%) 1505 (42.1%) arger number nd fewer were	<.001 ¹ <.001 ¹ 0.169 ¹

- Low derived no benefit from EET.

1. https://www.cancer.org/cancer/breast-cancer/about/types-of-breast-cancer/invasive-breast-cancer.html. 2. Sgroi D et al. J Natl Cancer Inst 2013;105:1036-42. 4. Zhang Y et al. Clin Cancer Res 2013;19:4196-205. 5. Sgroi D et al. Cancer Res 2013;14(11):1067-76. 3. Sgroi D et al. J Natl Cancer Res 2013;14(11):1067-76. 3. Sgroi D et al. J Natl Cancer Inst 2013;105:1036-42. 4. Zhang Y et al. Clin Cancer Res 2013;19:4196-205. 5. Sgroi D et al. Cancer Res 2013;19:4196-205. 5. Sgroi D et al. Cancer Res 2013;14(11):1067-76. 3. Sgroi D et al. J Natl Cancer Inst 2013;105:1036-42. 4. Zhang Y et al. Clin Cancer Res 2013;19:4196-205. 5. Sgroi D et al. Cancer Res 2013;105:1036-42. 4. Zhang Y et al. Clin Cancer Res 2013;19:4196-205. 5. Sgroi D et al. Cancer Res 2013;105:1036-42. 4. Zhang Y et al. Clin Cancer Res 2013;19:4196-205. 5. Sgroi D et al. Cancer Res 2013;105:1036-42. 4. Zhang Y et al. Clin Cancer Res 2013;19:4196-205. 5. Sgroi D et al. Cancer Res 2013;105:1036-42. 4. Zhang Y et al. Clin Cancer Res 2013;19:4196-205. 5. Sgroi D et al. Cancer Res 2013;105:1036-42. 4. Zhang Y et al. Clin Cancer Res 2013;19:4196-205. 5. Sgroi D et al. Cancer Res 2013;105:1036-42. 4. Zhang Y et al. Clin Cancer Res 2013;19:4196-205. 5. Sgroi D et al. Cancer Res 2013;105:1036-42. 4. Zhang Y et al. Clin Cancer Res 2013;19:4196-205. 5. Sgroi D et al. 2012;72(Suppl):abstract P2-10-15. 6. Bartlett JMS, et al. Clin Cancer Res. 2022; 28(9):1871-1880. 7. Noordhoek I et al. Clin Cancer Res 2021;27:311-9.



RESULTS

• The BCI clinical database included 3814 patients submitted for BCI testing during years 4-7 post-diagnosis with available histologic subtype data (80.5% IDC; 13.2% ILC; 3.0% mixed; 3.3% other) • Among those with either ductal (n=3072) or lobular (n=504) cancers (70.9% node-negative and 29.1% node-positive), patients with ILC were older than those with IDC (>70 y: 16.7% vs 11.8%) • Clinically, ILC was generally less aggressive than IDC (Grade 3: 6.7% vs 20.8%; lymphovascular invasion: 8.5% vs 20.0%; HER2+: 2.3% vs 12.7%; Ki67 Low: 27.9% vs 44.7%; p<0.001 for all comparisons), with the exception that ILC had larger tumors than IDC (T2/T3: 45.9% vs 24.2%)

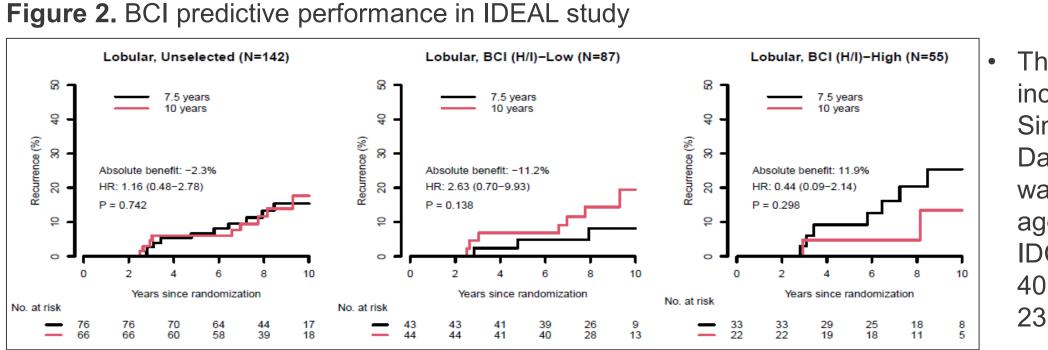
CONCLUSION

BCI identified a smaller proportion of patients with ILC at high risk of late DR and high likelihood of EET benefit compared to IDC. • Preliminary data from the IDEAL study showed that while fewer ILC patients were classified as high likelihood of EET benefit, they still derived similar absolute benefit compared to the overall cohort, while those classified as BCI (H/I)-

• Albeit the small sample size, the results suggests that patients with ILC classified as low likelihood of EET benefit may experience potential harm from longer duration of endocrine treatment.

REFERENCES

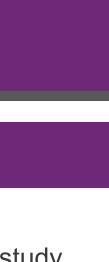
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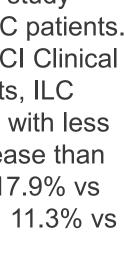


The IDEAL BCI study included 142 ILC patients. Similar to the BCI Clinical Database results, ILC was associated with less aggressive disease than IDC (Grade 3: 17.9% vs 40.5%; HER2+: 11.3% vs 23.6%).

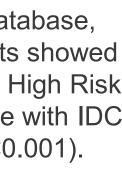
- Low, respectively.
- 0.44, 95% CI 0.09-2.14; p=0.298) 38).

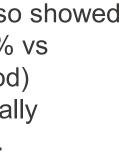
- In the BCI Clinical Database, **BCI** Prognostic results showed fewer ILC patients at High Risk for late DR than those with IDC (42.9% vs 54.6%, p<0.001).
- BCI H/I Predictive also showed a similar trend (39.3% vs 42.5% High Likelihood) although not statistically significant (p=0.169).
- atients, who were associated with ligh Risk/High Likelihood of benefit

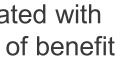
















Abstract Number