Impact of Access to CGP-Guided Recommended Therapies on Overall Survival in Invasive Lobular and Ductal Carcinomas: Insights from theC-CAT Registry

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Abstract

Background/Purpose:
The clinical benefit of accessing comprehensive genomic profiling (CGP)–guided recommended therapies in invasive lobular carcinoma (ILC) remains poorly defined.This study aimed to evaluate the impact of achieving CGP-guided recommended therapy on overall survival (OS) among breast cancer patients enrolled in the nationwide C-CAT registry.

Methods:
We retrospectively analyzed 7,363 breast cancer cases (IDC: 6,902; ILC: 461) registered in the C-CAT database between June 2019 and June 2025 who underwent CGP testing and provided consent for secondary use. Patients were stratified according to receipt of CGP-guided recommended therapy. Kaplan–Meier curves were generated and survival differences were tested by log-rank analysis.

Results:
In ILC, frequent alterations included CDH1 (309 cases), PIK3CA (278), and TP53 (182). Subtype distribution comprised HER2-positive (0.3%), luminal (73.7%), luminal/HER2 (2.2%), and triple-negative (17.7%). A total of 55 ILC patients (12%) achieved recommended therapy, most commonly with pembrolizumab monotherapy (n=11) or capivasertib-based regimens (n=10). These patients demonstrated significantly longer median OS compared with those not receiving recommended therapy (35 vs. 16 months; P=0.019).

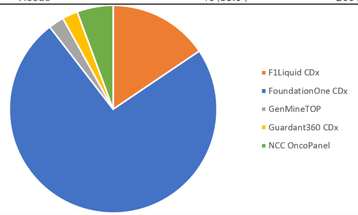
Conclusions:
This large nationwide registry analysis demonstrates that access to CGP-guided recommended therapy is associated with a significant improvement in OS in ILC. Notably, despite limited availability of targetable alterations and trial opportunities in ILC, meaningful survival benefit was observed. These findings underscore the clinical importance of expanding access to CGP-driven recommended therapies for all breast cancer patients, and highlight the value of large-scale real-world evidence in rare subtypes such as ILC.

Methods

Table 3. The types of cancer gene panel

This figure illustrates the data from cancer gene panel testing conducted on metastatic breast cancer patients between June 2019 and February 2024. A total of 7,363 patients underwent testing, were registered with C-CAT (Center for Cancer Genomics and Advanced Therapeutics), and consented to secondary use of their data. The data is based on C-CAT Version 20250617.

Factor	Group	CGP-matched therapy group	Non–CGP-matched group
n		55	318
Panel name(%)	F1Liquid CDx	9 (16.4)	49 (15.4)
	FoundationOne CDx	41 (74.5)	235 (73.9)
	GenMineTOP	0 (0.0)	9 (2.8)
	Guardant360 CDx	0 (0.0)	9 (2.8)
	NCC OncoPanel	5 (9.1)	16 (5.0)
Panel type(%)	Liquid	9 (16.4)	58 (18.2)
	Tissue	46 (83.6)	260 (81.8)



Results

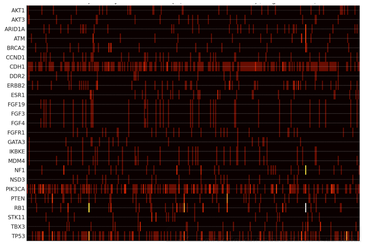
Table 4. Frequency of Genomic Alterations in the CGP-Matched Therapy Group and the Non–CGP-Matched Group

Table4 summarizes the distribution of major genomic alterations detected by comprehensive genomic profiling (CGP) in patients who received CGP-matched therapy compared with those who did not.Among the analyzed genes, PIK3CA mutations were significantly more frequent in the CGP-matched therapy group (p = 0.003), consistent with the clinical availability of PIK3CA-targeted therapies.In contrast, ARID1A mutations were more common in the non–CGP-matched group (p < 0.001), and ATM mutations also showed a significantly higher prevalence in the non-treated group (p = 0.016).GATA3 mutations were modestly enriched in the CGP-matched therapy group (p = 0.025).No other genomic alterations demonstrated statistically significant differences between the two groups.Overall, these findings suggest that specific actionable genomic alterations—particularly PIK3CA—played a major role in determining whether patients received CGP-matched therapy, whereas other mutations such as ARID1A and ATM did not translate into actionable therapeutic opportunities in current clinical practice.

Group	CGP-matched therapy group	Non-CGP-matched group	p.value
	55	318	
CDH1	37(67.3)	199(62.6)	0.306
	18(32.7)	119(37.4)	
PIK3CA	42(76.4)	177(55.7)	0.003
	13(23.6)	141(44.3)	
TP53	25(45.5)	135(42.5)	0.393
	30(54.5)	183(57.5)	
ERBB2	13(23.6)	51(16.0)	0.120
	42(76.4)	267(84.0)	
RB1	11(20.0)	53(16.7)	0.331
	44(80.0)	265(83.3)	
PTEN	9(16.4)	47(14.8)	0.447
	46(83.6)	271(85.2)	
ARID1A	22(40.0)	33(10.4)	<0.001
	33(60.0)	285(89.6)	
CCND1	7(12.7)	37(11.6)	0.481
	48(87.3)	281(88.4)	
FGF19	8(14.5)	35(11.0)	0.288
	47(85.5)	283(89.0)	
FGF4	8(14.5)	35(11.0)	0.288
	47(85.5)	283(89.0)	
FGF3	8(14.5)	33(10.4)	0.241
	47(85.5)	285(89.6)	
MDM4	5(9.1)	36(11.3)	0.416
	50(90.9)	282(88.7)	
NF1	9(16.4)	32(10.1)	0.128
	46(83.6)	286(89.9)	
AKT1	9(16.4)	31(9.7)	0.113
	46(83.6)	287(90.3)	
TBX3	8(14.5)	26(8.2)	0.107
	47(85.5)	292(91.8)	
FGFR1	4(7.3)	28(8.8)	0.475
	51(92.7)	290(91.2)	
ESR1	2(3.6)	29(9.1)	0.133
	53(96.4)	289(90.9)	
IKBKE	3(5.5)	28(8.8)	0.299
	52(94.5)	290(91.2)	
ATM	9(16.4)	20(6.3)	0.016
	46(83.6)	298(93.7)	
STK11	7(12.7)	21(6.6)	0.099
	48(87.3)	297(93.4)	
GATA3	8(14.5)	18(5.7)	0.025
	47(85.5)	300(94.3)	
NSD3	3(5.5)	22(6.9)	0.481
	52(94.5)	296(93.1)	
BRCA2	1(1.8)	23(7.2)	0.104
	54(98.2)	295(92.8)	
AKT3	3(5.5)	20(6.3)	0.552
	52(94.5)	298(93.7)	
DDR2	1(1.8)	20(6.3)	0.155
	54(98.2)	298(93.7)	

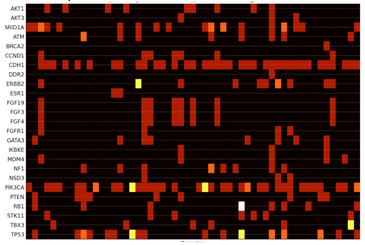
Figures 1. Oncoprint of Genomic Alterations in the CGP-Matched Therapy Group

Figure 1 visually illustrates the distribution of genomic alterations in patients who received CGP-matched therapy.Consistent with the findings in Table 4, actionable alterations such as PIK3CA mutations, which were significantly enriched in the treated group, are clearly observed across multiple samples.The high-contrast heatmap highlights mutation-positive cases, demonstrating that patients who received CGP-matched therapy frequently harbored alterations linked to available targeted treatments.This pattern supports the interpretation that the presence of actionable genomic alterations played a major role in facilitating treatment implementation.



Figures 2. Oncoprint of Genomic Alterations in the Non–CGP-Matched Group

Figure 2 presents the genomic alteration profile of patients who did not receive CGP-matched therapy.In accordance with Table 4, alterations such as ARID1A and ATM, which were significantly more frequent in the non-treated group, are distributed across many samples; however, these mutations currently lack approved targeted therapeutic options.Compared with the treated cohort, fewer actionable alterations such as PIK3CA are observed in this group, which likely contributed to the limited uptake of CGP-guided therapy.These findings collectively suggest that the absence of clinically actionable mutations—rather than the absence of mutations per se—was a key barrier to treatment implementation.



Patients

Table 1. Baseline Characteristics of Patients in the CGP-Matched Therapy Group and the Non-CGP-Matched Group

Baseline characteristics were generally balanced between the CGP-matched therapy group and the non-CGP-matched group. Age, gender distribution, ECOG performance status, intrinsic subtype, ER/PgR status, HER2 IHC results, and family history showed no statistically significant differences. These findings indicate that patient background factors were unlikely to bias treatment allocation, and that the decision to implement CGP-guided therapy likely depended on actionable genomic alterations, therapeutic accessibility, or clinical considerations at the time of CGP reporting.

Factor	Group	CGP-matched therapy group	Non–CGP-matched group	p.value
n		55	318	
Age(mean, range)		60.8,62(41–82)	58.6,57(27–85)	
	<50	5(9.1)	36(11.3)	0.940
	50–69	36(65.5)	208(65.4)	
	≥70	14(25.5)	74(23.3)	
Gender(%)	Woman	54(98.2)	317(99.7)	0.274
	Man	1(1.8)	1(0.3)	
PS(%)	0	32(58.2)	191(60.1)	0.820
	1	23(41.8)	108(34.0)	
	2	0(0.0)	9(2.8)	
	3	0(0.0)	1(0.3)	
	4	0(0.0)	1(0.3)	
	Unknown	0(0.0)	4(1.3)	
Subtype(%)	Luminal	47(85.5)	231(72.6)	0.600
	Luminal-HER2	0(0.0)	8(2.5)	
	HER2	2(0.4)	2(0.6)	
	Triple negative	6(10.9)	56(17.6)	
	Unknown	2(3.6)	21(6.6)	
ER(%)	Positive	6(10.9)	62(19.5)	0.065
	Negative	49(89.1)	241(75.8)	
	Unknown or uninspected	0(0.0)	15(4.7)	
PgR(%)	Positive	20(36.4)	133(41.8)	0.210
	Negative	34(61.8)	169(53.1)	
	Unknown or uninspected	1(1.8)	11(3.5)	
HER2 IHC(%)	Positive(score 3+)	0(0.0)	8(2.5)	0.620
	Boundary area(score 2+)	12(21.8)	62(19.5)	
	Negative(score 1+)	21(38.2)	103(32.4)	
	Negative(score 0)	20(36.4)	132(41.5)	
	Unknown or uninspected	2(3.6)	13(4.1)	
Family history(%)	Yes	49(89.1)	250(78.6)	0.115
	No	6(10.9)	57(17.9)	
	Unknown or uninspected	0(0.0)	11(3.5)	

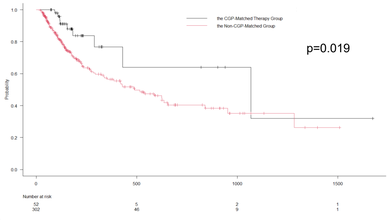
Table 2. Distribution of Metastatic Sites in the CGP-Matched Therapy Group and the Non-CGP-Matched Group

The distribution of metastatic sites showed no significant imbalance between the CGP-matched and non–CGP-matched groups. The number of metastatic organs, as well as the frequencies of bone, brain, lung, lymph node, peritoneal, pleural, skin, and stomach metastases, were similar between groups. Although liver metastases tended to be more common in patients who did not receive CGP-matched therapy and skin metastases showed a trend toward higher frequency in the treated group, these differences did not reach statistical significance. These findings indicate that the extent and pattern of metastatic disease were not major determinants of access to CGP-guided therapies.

Group	CGP-matched therapy group	Non–CGP-matched group	p.value
	55	318	
1	14(25.5)	100(31.4)	0.300
2	15(27.3)	96(30.2)	
3	11(20.0)	78(24.5)	
≧4	15(27.3)	34(10.7)	
Yes	35(63.6)	185(58.2)	0.272
No	20(36.4)	133(41.8)	
Yes	4(7.3)	13(4.1)	0.231
No	51(92.7)	305(95.9)	
Yes	12(21.8)	105(33.0)	0.065
No	43(78.2)	213(67.0)	
Yes	6(10.9)	16(5.0)	0.087
No	49(89.1)	302(95.0)	
Yes	18(32.7)	106(33.3)	0.532
No	37(67.3)	212(66.7)	
Yes	1(1.8)	8(2.5)	0.608
No	54(98.2)	310(97.5)	
Yes	14(25.5)	67(21.1)	0.285
No	41(74.5)	251(78.9)	
Yes	6(10.9)	26(8.2)	0.327
No	49(89.1)	292(91.8)	
Yes	10(18.2)	31(9.7)	0.059
No	45(81.8)	287(90.3)	
Yes	6(10.9)	26(8.2)	0.327
No	49(89.1)	292(91.8)	

Figure 3. Survival According to Receipt of CGP-Matched Recommended Therapy in Patients with Invasive Lobular Carcinoma

Figure 3 summarizes the overall survival (OS) outcomes for patients with invasive lobular carcinoma (ILC) according to whether they received CGP-matched recommended therapy.Consistent with the genomic patterns demonstrated in Table 4 and Figures 1 and 2, only 12% of ILC patients (55/461) ultimately received CGP-recommended therapy, most frequently pembrolizumab monotherapy (n=11) or capivasertib-based regimens (n=10). Kaplan–Meier analysis (Figure 3) shows that patients who received CGP-matched therapy experienced a significantly longer median OS compared with non-treated patients (35 vs. 16 months; P = 0.019).



These findings support the notion that the presence of actionable genomic alterations—particularly those highlighted in the treated cohort—translated into meaningful clinical benefit when matched therapies were implemented.Together with the results of Tables 1–4, these data indicate that while actionable alterations are relatively infrequent in ILC, appropriate application of CGP-guided therapy has the potential to substantially improve survival outcomes in this population.

Discussions&Conclusions

In this nationwide ILC cohort, clinically actionable genomic alterations were uncommon, and only 12% of patients ultimately received CGP-matched recommended therapy, most often pembrolizumab monotherapy or capivasertib-based regimens. As shown in Tables 1–4 and Figures 1–2, baseline characteristics and metastatic patterns were similar between treated and untreated patients, indicating that treatment implementation was primarily driven by the presence of actionable alterations—particularly PIK3CA—rather than differences in patient background.Non-actionable variants such as ARID1A and ATM were more frequent in the non-treated cohort, underscoring the limited availability of effective targeted options for ILC. Despite multiple genomic alterations, many do not translate into therapeutic opportunities in current practice.Kaplan–Meier analysis (Table 5) demonstrated a substantial survival advantage for patients receiving CGP-matched therapy (median OS 35 vs. 16 months; P=0.019), supporting the real-world clinical benefit of precision oncology even in a genomically “low-actionability” disease. These findings highlight the need to expand the therapeutic landscape for ILC—potentially through agents targeting non-classical or epigenetic alterations—and emphasize the importance of early CGP testing and improved access to matched therapies.