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Real-world clinical outcomes of patients with HER2-negative BRCAm early breast cancer treated with adjuvant capecitabine

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Objective

- This retrospective study aimed to assess the real-world clinical benefit of adjuvant capecitabine in patients with HER2-negative early breast cancer (eBC), with and without pathogenic/likely pathogenic mutations in the genes *BRCA1* and/or *BRCA2* (BRCAm)

Conclusions

- Data from this real-world study of patients with known BRCA status who received adjuvant capecitabine for HER2-negative eBC suggest a potential trend for shorter invasive disease-free survival (IDFS) and distant disease-free survival (DDFS) in patients with BRCAm versus non-BRCAm
  - However, these results are descriptive, unadjusted, and were limited by the small number of patients with BRCAm
  - Future work will include confirmatory analyses in larger retrospective cohorts and longer follow-up times to compare the survival of patients with BRCAm or non-BRCAm HER2-negative eBC
- This and future studies will help to inform the personalization of treatments, including targeted therapies, for patients with BRCAm

Plain language summary

Why did we perform this research?

- Capecitabine is sometimes used after surgery in patients with tumors lacking the HER2 protein (HER2–), as this has been shown to improve clinical outcomes compared with a 'watch and wait' approach
- Mutations in *BRCA1* and *BRCA2* genes (BRCAm) can affect how patients with breast cancer respond to some treatments
- To date, there is limited information on how patients with BRCAm respond to capecitabine after surgery to treat their breast cancer
  - Understanding this will help to inform the tailoring of treatments to patients with BRCAm

How did we perform this research?

- This study looked at data collected from routine clinical practice in the USA
- All patients were adults who had early-stage breast cancer that did not have a protein called HER2
  - The tumors of some patients had estrogen/progesterone receptors (hormone receptor–positive), whereas tumors of others had no hormone receptors (triple-negative breast cancer)
- All patients had received capecitabine treatment after surgery and underwent genetic testing that included the *BRCA1* and *BRCA2* genes
- We compared how long patients with and without BRCAm and those with and without hormone receptor-positive tumors survived without their cancer coming back

What were the findings of this research, and what are the implications?

- Patients with BRCAm treated with adjuvant capecitabine tended to not live as long without their cancer spreading than those without BRCAm
- The results of this study were limited by the small number of patients with BRCAm
- Future work will include analyses in a larger cohort of patients, which will help doctors decide how best to treat patients with this type of breast cancer and BRCAm

Poster

Plain language infographic

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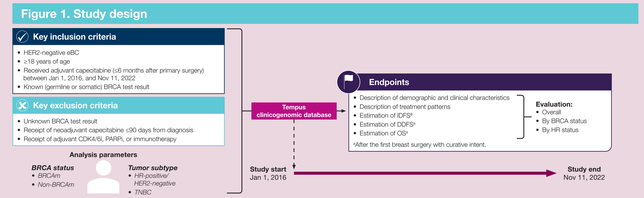
Introduction

- In the CREATE-X trial, addition of adjuvant capecitabine after standard-of-care neoadjuvant chemotherapy improved clinical benefit in patients with early-stage TNBC[1]
- BRCAm can affect how patients with breast cancer respond to treatment.[2,3] However, the effect of adjuvant capecitabine in patients with BRCAm has not been specifically examined
  - The FinXX trial found that the addition of capecitabine to standard-of-care chemotherapy only improved recurrence-free survival in patients with non-*BRCA1*m-like TNBC[2]
  - Some studies have noted a decreased benefit of capecitabine in patients with basal-like tumors, which are enriched in *BRCA1*m breast cancers[3–7]
- This retrospective study explored the effect of adjuvant capecitabine in a real-world cohort of patients with HER2-negative eBC, stratified by BRCA status and tumor subtype (HR-positive/HER2-negative or TNBC)

Methods

- Data were extracted from the Tempus database, a library of de-identified, real-world clinical and molecular data derived from US patients
- Included patients were ≥18 years of age; had received adjuvant capecitabine (administered within 6 months after primary surgery) for HER2-negative eBC between January 1, 2016, and November 11, 2022; and had known BRCA test results (germline or somatic BRCAm or non-BRCAm, determined by germline or tumor testing) (**Figure 1**)
  - All patients underwent either Tempus or third-party molecular testing
  - Patients who had received neoadjuvant capecitabine ≤90 days from diagnosis were excluded
  - Patients who had received adjuvant CDK4/6 inhibitor, PARP inhibitor, or immunotherapy were also excluded
- Demographics, clinical characteristics, and treatment patterns were described
- As measures of real-world survival, IDFS, DDFS, and OS were estimated using a Kaplan–Meier approach after the first breast surgery with curative intent

Figure 1. Study design



Results

- In total, 269 patients receiving adjuvant capecitabine with known BRCA status were followed for a median of 23 months (**Table 1**)
  - Most patients had TNBC (n=192/269, 71.4%); approximately a quarter (n=71/269, 26.4%) had HR-positive/HER2-negative eBC, and six had unknown subtype
- BRCAm were reported in 8.2% (n=22/269) of patients (TNBC: n=15/192, 7.8%; HR-positive/HER2-negative: n=7/71, 9.9%)
- The median age at eBC diagnosis was 53 years, and was lower among patients with BRCAm versus non-BRCAm (44 vs 54 years, respectively)

Table 1. Demographics and clinical characteristics[a]

	Overall	BRCA status		Tumor subtype[b]	
	(N=269)	BRCAm (n=22)	Non-BRCAm (n=247)	HR+/HER2– (n=71)	TNBC (n=192)
Age at eBC diagnosis, years, median (IQR)	53 (43–61)	44 (39–57)	54 (44–62)	56 (43–61)	51 (43–62)
Race, n (%)					
Asian	14 (5.2)	0	14 (5.7)	4 (5.6)	9 (4.7)
Black	36 (13.4)	7 (31.8)	29 (11.7)	10 (14.1)	25 (13.0)
White	126 (46.8)	6 (27.3)	120 (48.6)	37 (52.1)	86 (44.8)
Other	29 (10.8)	1 (4.5)	28 (11.3)	5 (7.0)	24 (12.5)
Unknown	64 (23.8)	8 (36.4)	56 (22.7)	15 (21.1)	48 (25.0)
Months of follow-up, median (IQR)	23 (14–34)	24 (18–32)	22 (13–34)	27 (16–35)	21 (13–34)
Prior history of cancer, n (%)					
Yes	10 (3.7)	1 (4.5)	9 (3.6)	3 (4.2)	7 (3.6)
Stage at primary diagnosis, n (%)					
I	13 (4.8)	2 (9.1)	11 (4.5)	2 (2.8)	11 (5.7)
II	120 (44.6)	10 (45.5)	110 (44.5)	30 (42.3)	87 (45.3)
III [including A, B, and C]	93 (34.5)	8 (36.4)	85 (34.4)	30 (42.3)	61 (31.8)
Unknown	43 (16.0)	2 (9.1)	41 (16.6)	9 (12.7)	33 (17.2)
BRCAm present, n (%)	22 (8.2)	22 (100)	0	7 (9.9)	15 (7.8)

[a]Categories with >75% missing data not included. [b]Six patients with unknown tumor subtype are not shown.

- Most patients (n=245/269, 91.1%) had received ≥1 neoadjuvant therapy for a median of 133 days (**Table 2**)
  - Among patients who had received neoadjuvant therapy, n=232/245 (94.7%) received chemotherapy only
- The median duration of adjuvant therapy was 168 days
  - Most patients with TNBC received capecitabine monotherapy as adjuvant therapy (n=176/192, 91.7%), whereas patients who had HR-positive/HER2-negative tumors primarily received either capecitabine monotherapy (n=37/71, 52.1%) or capecitabine plus hormone therapy (n=29/71, 40.8%)
  - A slightly higher proportion of patients with BRCAm versus non-BRCAm received capecitabine monotherapy as adjuvant therapy (n=20/22, 90.9% vs n=199/247, 80.6%)

Table 2. Treatment patterns

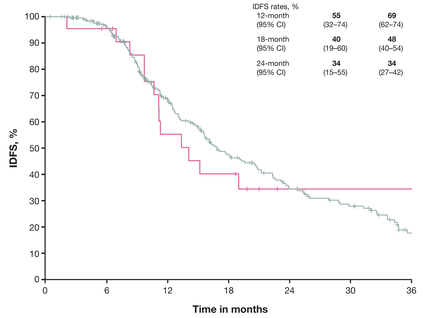
	Overall	BRCA status		Tumor subtype[b]	
		BRCAm	Non-BRCAm	HR+/HER2–	TNBC
Patients who received ≥1 neoadjuvant treatment, n	245	21	224	67	174
Neoadjuvant treatment type, n (%)[a]					
ChT	232 (94.7)	19 (90.5)	213 (95.1)	64 (95.5)	164 (94.3)
ChT + hormone therapy	4 (1.6)	2 (9.5)	2 (0.9)	2 (3.0)	2 (1.1)
ChT + IO	12 (4.9)	1 (4.8)	11 (4.9)	1 (1.5)	11 (6.3)
Hormone therapy	7 (2.9)	-	7 (3.1)	6 (9.0)	1 (0.6)
Other	3 (1.2)	-	3 (1.3)	-	3 (1.7)
Duration of neoadjuvant treatment, median (IQR), days	133 (105–148)	138 (129–155)	133 (105–148)	133 (112–140)	133 (105–148)
Patients who received ≥1 adjuvant treatment, n	269	22	247	71	192
Adjuvant treatment type, n (%)					
Capecitabine monotherapy	219 (81.4)	20 (90.9)	199 (80.6)	37 (52.1)	176 (91.7)
Capecitabine + ChT	16 (5.9)	-	16 (6.5)	4 (5.6)	12 (6.3)
Capecitabine + hormone therapy	31 (11.5)	2 (9.1)	29 (11.7)	29 (40.8)	2 (1.0)
Capecitabine + other	3 (1.1)	-	3 (1.2)	1 (1.4)	2 (1.0)
Duration of adjuvant treatment, median (IQR), days	168 (126–210)	171 (129–190)	167 (126–210)	195 (138–346)	162 (120–197)

[a]Some patients received more than one neoadjuvant treatment. [b]Six patients with unknown tumor subtype are not shown.

Figure 2. IDFS

A. IDFS by BRCA status[a]

	BRCAm (n=22)	Non-BRCAm (n=247)
Events, n (%)	14 (63.6)	148 (59.9)
mIDFS, months (95% CI)	14.1 (10.7–NE)	16.9 (15.1–20.8)
IDFS rates, %		
12-month (95% CI)	55 (32–74)	69 (62–74)
18-month (95% CI)	40 (19–60)	48 (40–54)
24-month (95% CI)	34 (15–55)	34 (27–42)

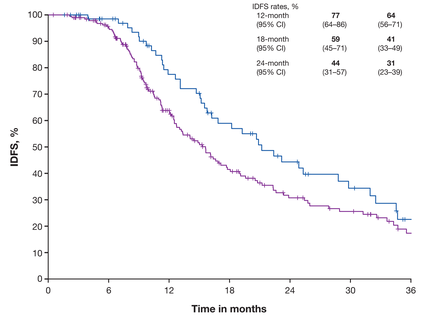


Number at risk

BRCAm	22	20	11	8	3	2	2
Non-BRCAm	247	215	127	78	51	37	15

B. IDFS by tumor subtype[a,b]

	HR+/HER2– (n=71)	TNBC (n=192)
Events, n (%)	39 (54.9)	118 (61.5)
mIDFS, months (95% CI)	21.2 (15.8–29.8)	15.6 (12.8–17.8)
IDFS rates, %		
12-month (95% CI)	77 (64–86)	64 (56–71)
18-month (95% CI)	59 (45–71)	41 (33–49)
24-month (95% CI)	44 (31–57)	31 (23–39)



Number at risk

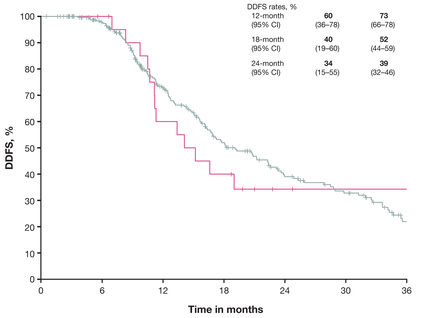
HR+/HER2–	71	61	43	30	20	13	5
TNBC	192	168	91	52	32	24	11

[a]IDFS: The length of time from the index date to the date of recurrence, second invasive cancer, or death. Excludes *in situ* cancers.[4] [b]Six patients with unknown tumor subtype are not shown.

Figure 3. DDFS

A. DDFS by BRCA status[a]

	BRCAm (n=22)	Non-BRCAm (n=247)
Events, n (%)	14 (63.6)	135 (54.7)
mDDFS, months (95% CI)	14.6 (10.7–NE)	19.1 (16.4–22.6)
DDFS rates, %		
12-month (95% CI)	60 (36–78)	73 (66–78)
18-month (95% CI)	40 (19–60)	52 (44–59)
24-month (95% CI)	34 (15–55)	39 (32–46)

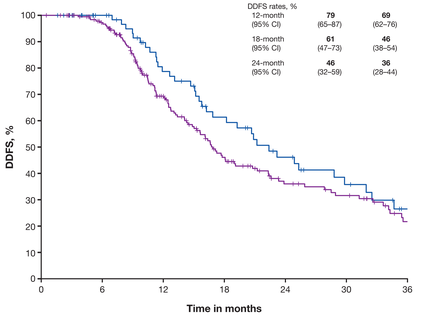


Number at risk

BRCAm	22	21	12	8	3	2	2
Non-BRCAm	247	218	134	84	54	41	18

B. DDFS by tumor subtype[a,b]

	HR+/HER2– (n=71)	TNBC (n=192)
Events, n (%)	36 (50.7)	106 (56.3)
mDDFS, months (95% CI)	22.4 (16.2–29.8)	16.9 (14.9–20.8)
DDFS rates, %		
12-month (95% CI)	79 (65–87)	69 (62–76)
18-month (95% CI)	61 (47–73)	46 (38–54)
24-month (95% CI)	46 (32–59)	36 (28–44)



Number at risk

HR+/HER2–	71	61	43	30	20	13	5
TNBC	192	172	99	58	35	28	14

[a]DDFS: The length of time from index date to the date of distant recurrence, second invasive cancer, or death.[5] [b]Six patients with unknown tumor subtype are not shown.

- The median IDFS was 16.6 months (95% CI: 15.0–20.5) in the overall population (n=269)
- The median IDFS was higher in patients with HR-positive/HER2-negative tumors than in patients with TNBC, and lower in patients with BRCAm than in patients with non-BRCAm (**Figure 2**)
- The median DDFS was 18.1 months (95% CI: 16.1–22.4) in the overall population (n=269)
- The median DDFS was higher in patients with HR-positive/HER2-negative tumors than in patients with TNBC, and lower in patients with BRCAm than in patients with non-BRCAm (**Figure 3**)
- OS by BRCA status and tumor subtype is shown in **Table 3**
  - Data reported are descriptive, unadjusted, and were limited by the small number of OS events recorded in the database

Table 3. OS

	BRCA status		Tumor subtype[a]	
	BRCAm (n=22)	Non-BRCAm (n=247)	HR+/HER2– (n=71)	TNBC (n=192)
Events, n (%)	5 (22.7)	71 (28.7)	16 (22.5)	58 (30.2)
OS rates, % (95% CI)				
12-month	100 (NE)	96 (92–98)	98 (90–100)	95 (90–98)
18-month	100 (NE)	89 (83–92)	95 (85–98)	87 (81–92)
24-month	86 (54–96)	81 (74–86)	91 (80–96)	78 (70–84)

[a]Six patients with unknown tumor subtype are not shown.

Abbreviations

BRCA(m), *BRCA1* or *BRCA2* gene (mutation); CDK4/6(i), cyclin-dependent kinase 4/6 (inhibitor); ChT, chemotherapy; (m)DDFS, (median) distant disease-free survival; eBC, early breast cancer; HER2(–), human epidermal growth factor receptor 2(-negative); HR(+), hormone receptor(-positive); (m)IDFS, (median) invasive disease-free survival; IQR, interquartile range; NE, not estimable; (m)OS, (median) overall survival; PARP(i), poly(ADP-ribose) polymerase (inhibitor); TNBC, triple-negative breast cancer; US, United States.

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