Clinical and pathological variables associated with brain metastases development among patients receiving neoadjuvant chemotherapy for breast cancer

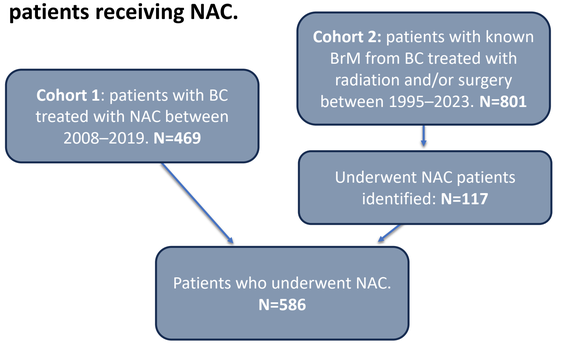
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Background

- Overall, 25% of patients with early breast cancer (BC) receive neoadjuvant chemotherapy (NAC); however, most patients with HER2+ and triple negative (TN) BC are treated with this approach.[1]
- Nearly 15% of patients with high-risk HER2+ or TNBC will develop brain metastasis (BrM) within 5 years of initial diagnosis.[2] In the KATHERINE trial, BrM as 1st site of distant relapse occurred in 7.0% (T-DM1) & 5.1% (control) of patients.[3]
- In the KEYNOTE-522 trial, central nervous system (CNS) recurrences represented > 50% of distant events in patients with a residual cancer burden (RCB) index of 0-1.[4]
- However, **risk factors of BrM in patients receiving NAC for BC remain poorly defined.**

Methods

Retrospective study of two BC cohorts at Sunnybrook Odette Cancer Centre to evaluate **clinical and pathological variables associated with the development of BrM in patients receiving NAC.**



Descriptive statistics summarized patient and treatment characteristics. Cox proportional hazards models estimated Hazard Ratios (HR) and identified predictors of BrM. Statistical significance set at p<.05.

Results

Table 2. Descriptive characteristics of patients who underwent NAC.

Categorical Variables	All patients[1] (%)	BrM	No BrM	P-value
Total	586 (100)	152 (100)	434 (100)	
Age				
<50	296 (50.5)	217 (50)	79 (52)	0.4064[2]
50-59	164 (28)	118 (27.2)	46 (30.3)	
≥60	126 (21.5)	99 (22.8)	27 (17.8)	
BC Subtype				
HER2+	225 (39.5)	56 (40.3)	169 (39.2)	0.0568[2]
HR+	213 (37.4)	42 (30.2)	171 (39.7)	
TN	132 (23.2)	41 (29.5)	91 (21.1)	
Pre-treatment tumor size				
<=2 cm	53 (10.3)	13 (14.6)	40 (9.3)	0.2227[2]
2.1-5 cm	266 (51.5)	40 (44.9)	226 (52.8)	
>5 cm	198 (38.3)	36 (40.4)	162 (37.9)	
Post-treatment lymph nodes				
Negative	268 (49.3)	27 (24.5)	241 (55.5)	**<0.0001[2]**
Positive	276 (50.7)	83 (75.5)	193 (44.5)	
Not known		42 (NA)	0 (NA)	
Inflammatory breast cancer				
No	495 (86.5)	97 (70.3)	398 (91.7)	**<0.0001[2]**
Yes	77 (13.5)	41 (29.7)	36 (8.3)	
Not known		14 (NA)	0 (NA)	
Lymphovascular invasion				
No	336 (67.3)	33 (42.3)	303 (72)	**<0.0001[3]**
Yes	163 (32.7)	45 (57.7)	118 (28)	
Not known		74 (NA)	13 (NA)	
Response to NAC				
noPCR[4]	409 (75.3)	101 (92.7)	308 (71)	**<0.0001[2]**
pCR	134 (24.7)	8 (7.3)	126 (29)	
Not known		43 (NA)	0 (NA)	

[1]. Excluding patients with missing data. [2]. Chi-square test. [3]. Fischer's exact test. [4]. Including residual microinvasive disease
Legend: HR = hormone receptor; NAC = neoadjuvant chemotherapy; pCR = pathological complete response; TN = triple negative.

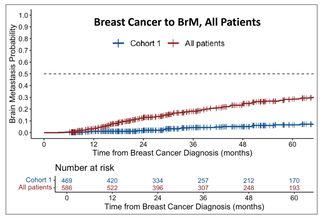
Results

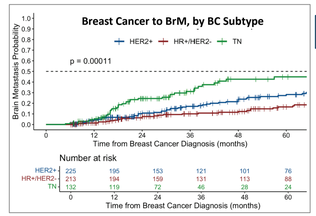
Table 2. Median follow-up time from primary breast cancer diagnosis to the development of BrM or death (months).

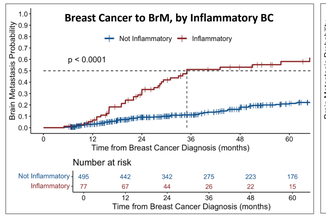
Characteristic	N (%)	Median TTBM (IQR)
All Patients	152 (100)	29.6 (16 – 50.5)
HER2+	56 (40.3)	32.0 (19.4 - 51.1)
HR+/HER2-	42 (30.2)	49.1 (19.8 – 76.3)
TNBC	41 (29.5)	18.0 (15.0 – 31.0)

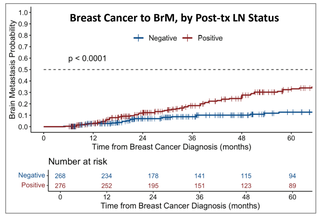
TTBM = Time to brain metastasis; IQR = Interquartile range.

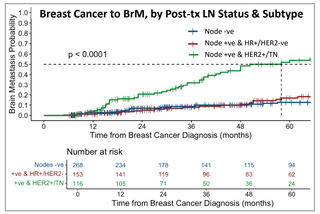
Figure 1. Time to BrM in (a) All patients, and according to (b) BC subtype, (c) inflammatory BC, (d) post-treatment lymph node (LN) status and (e) both post-treatment LN status and subtype.





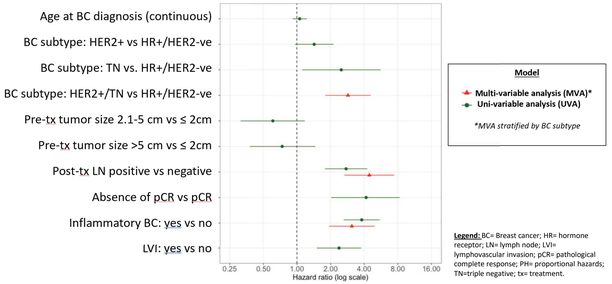






Results

Figure 2. Forest plot for uni- and multi-variable Cox PH Hazard Ratios (HRs) for BrM development.



Legend: BC= Breast cancer; HR= hormone receptor; LN= lymph node; LVI= lymphovascular invasion; pCR= pathological complete response; PH= proportional hazards; TN=triple negative; tx= treatment.

Conclusions

BrM risk was significantly higher among patients with **inflammatory breast cancer** and those with **residual nodal involvement after NAC**.

Among patients with TNBC who developed BrM, the median **time to BrM was <24 months *in the absence of screening***.

Further evaluation of **brain metastasis screening studies** in select NAC-treated populations is warranted.

References

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2. Chehade R. *ESMO Open*, 2024.
3. Mamounas EP. *Annals of Oncology*, 2021.
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Contacts

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