

# Patterns of Treatment and Outcomes of Patients with Brain-only Metastatic Breast Cancer



Badr Id Said<sup>a</sup>, Hany Soliman<sup>a</sup>, Veronika Moravan<sup>b</sup>, Sten Myrehaug<sup>a</sup>, Chia-Lin Tseng<sup>a</sup>, Jay Detsky<sup>a</sup>, Arjun Sahgal<sup>a</sup>, Ellen Warner<sup>c</sup>, Katarzyna J. Jerzak<sup>c</sup>

<sup>a</sup>Department of Radiation Oncology, Odette Cancer Centre, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada, <sup>b</sup>Applied Statistician, VM Stats, Toronto, Ontario, Canada

<sup>c</sup>Department of Medical Oncology, Odette Cancer Centre, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada



## OBJECTIVE

To characterize the risk factors and survival of metastatic breast cancer (MBC) patients with brain metastases as the first and only site of disease in a large, retrospective cohort.

## METHODS

### Study Design

- Retrospective study of patients (≥18yo) with diagnosis of metastatic breast cancer with BrM treated with SRS and/or WBRT at the Odette Cancer Centre between 2005 and 2019
- Clinical and treatment factors were recorded through direct review of the electronic patient record (SunnyCare): Age at diagnosis of breast cancer and BrM, features of the primary breast cancer, performance status at time of BrM, breast cancer subtype (HR+/HER2-negative, HER2+, TNBC), number, location and size of BrM, presence versus absence of extracranial metastases (ECM) and treatments delivered at BrM diagnosis (i.e surgery, SRS, FSRT, WBRT, and systemic agent).

### Study Outcomes

- Brain-only MBC was defined as the presence of BrM without concurrent extracranial or leptomeningeal involvement as determined clinically and on review of imaging.
- Overall survival (OS) was defined from the time of diagnosis of BrM until the date of death.
- Brain-progression free survival (bsPFS) was defined from the time of BrM diagnosis until the date of radiographic brain-specific disease progression.

### Statistical Analysis

- Logistic regression was used to investigate predictors of brain-only MBC. Cox proportional hazard regression was used to estimate hazard ratios (HR) and identify predictors of OS and bsPFS
- MVA excluded treatment covariates as clinical characteristics form the basis for decisions about therapy
- Kaplan Meier method was used to analyse OS and bsPFS

## RESULTS

### PATIENT CHARACTERISTICS

Table 1: Patient and treatment characteristics in overall cohort and brain-only metastatic breast cancer patients.					
	Full cohort N=691 (%)	Brain-only without subsequent ECM/LMD N=40 (%)	Brain-only with subsequent ECM N=10 (%)	Brain-only +/- subsequent ECM/LMD N=67 (%)	p-value
Age at BC <sup>a</sup> (n=600) Median (IQR)	50 (44-60)	55 (45-67)	52 (40-65)	55 (43-66)	0.06
Age at MBC Median (IQR)	56 (48-65)	57.5 (47-72)	59 (48-70)	58 (46-67)	0.3
Age at brain metastases (BrM)					0.7
<50 years	201 (29)	13 (32.5)	3 (30.0)	23 (34.3)	
≥50 years	490 (71)	27 (67.5)	7 (70.0)	44 (65.7)	
Time from BC to brain metastases (mths) Median (IQR)	39 (19-77)	23 (12-40.5)	46 (19-67)	23 (12-40)	0.0007
Breast cancer subtype					0.01
HR+HER2-	229 (33.1)	7 (17.5)	4 (40.0)	18 (26.9)	
HER2+	175 (25.3)	15 (37.5)	4 (40.0)	23 (34.3)	
Triple negative	156 (22.6)	16 (40.0)	2 (20.0)	24 (35.8)	
Not known	131 (19.0)	2 (5.0)	0 (0)	2 (0.3)	
Leptomenigneal disease (LMD)	161 (23.3)	0 (0)	0 (0.0)	17 (25.4)	NA
Karnofsky Performance Scale (KPS)					0.2
60 or higher	322 (46.6)	11 (27.5)	8 (80.0)	8 (11.9)	
Less than 60	84 (12.2)	6 (15.0)	0 (0)	24 (35.8)	
Not known	285 (41.2)	23 (57.5)	2 (20.0)	35 (52.2)	
No. of brain metastases (BrM)					0.003
Single	110 (15.9)	15 (37.5)	2 (20.0)	23 (34.3)	
2 - 10 metastases	141 (20.4)	8 (20.0)	3 (30.0)	13 (19.4)	
>10 metastases	245 (35.5)	11 (27.5)	5 (50.0)	19 (28.4)	
Not known	195 (28.2)	6 (15.0)	0 (0.0)	12 (17.9)	
Extracranial metastases (ECM) sites					NA
Bone	471 (62.8)	0 (0)	6 (60.0)	6 (9.0)	
Lung	389 (56.3)	0 (0)	2 (20.0)	2 (3.0)	
Liver	373 (54.0)	0 (0)	2 (20.0)	2 (3.0)	
Surgery for BrM	104 (15.1)	15 (37.5)	2 (20.0)	24 (35.8)	0.0001
Whole brain radiotherapy	548 (79.3)	26 (65.0)	7 (70.0)	47 (70.1)	0.03
Stereotactic radiosurgery	178 (25.8)	14 (35.0)	4 (40.0)	23 (34.3)	0.2
Systemic therapy at BrM Dx					0.001
Chemotherapy +/- endocrine therapy	221 (32)	1 (2.5)	0 (0)	4 (6.0)	
HER2-targeted agent +/- chemotherapy	96 (13.9)	6 (15.0)	1 (10.0)	8 (11.9)	
Endocrine therapy alone	93 (13.5)	6 (15.0)	2 (20.0)	12 (17.9)	
Other	3 (0.4)	0 (0)	0 (0)	0 (0)	
None	6 (0.9)	1 (2.5)	0 (0)	2 (3.0)	
Not known	272 (39.4)	26 (65)	7 (70.0)	41 (61.2)	

- N=67 patients (9.7%, n=67/691) with brain-only MBC
- Median age at BrM diagnosis 55 yo
- Most common subtypes: TNBC (35.8%, n=24), HER2+ (34.3%, n=23)
- A third of brain-only MBC patients (34.3%, n=23) had a single BrM
- Median FUP 8 months (IQR 2-35)

### PREDICTORS OF BRAIN-ONLY MBC

Table 2: Predictors of brain-only metastatic breast cancer without subsequent extracranial metastases or leptomeningeal disease				
	Univariable		Multivariable	
	OR (95% CI)	p-value	OR (95% CI)	p-value <sup>a</sup>
Age at initial breast cancer diagnosis	1.323(1.04, 1.69)	0.02		
Age at MBC diagnosis	1.17 (0.91,1.51)	0.2		
Time from BC to brain metastases (mths)	0.98 (0.97, 0.99)	0.006		
Breast cancer subtype				
HR+HER2-	Ref		Ref	
HER2+	2.96 (1.18, 7.43)	0.02	3.30 (1.13, 9.65)	0.03
Triple negative	3.61 (1.45, 9.0)	0.006	4.09 (1.42, 11.74)	0.009
Karnofsky Performance Scale (KPS)				
60 or higher	Ref			
Less than 60	0.46 (0.16, 1.28)	0.1	NA	NA
No. of brain metastases (BrM)				
>1 metastases	Ref			
Single	3.05 (1.49, 6.21)	0.002	3.41 (1.62, 7.19)	0.001
Surgery for BrM	3.73 (1.89, 7.34)	0.0001	NA	NA
Whole brain radiotherapy	0.46 (0.23, 0.90)	0.02	NA	NA
Stereotactic radiosurgery	1.60 (0.81, 3.13)	0.2	NA	NA

In patients with brain-only MBC, there was a higher likelihood of

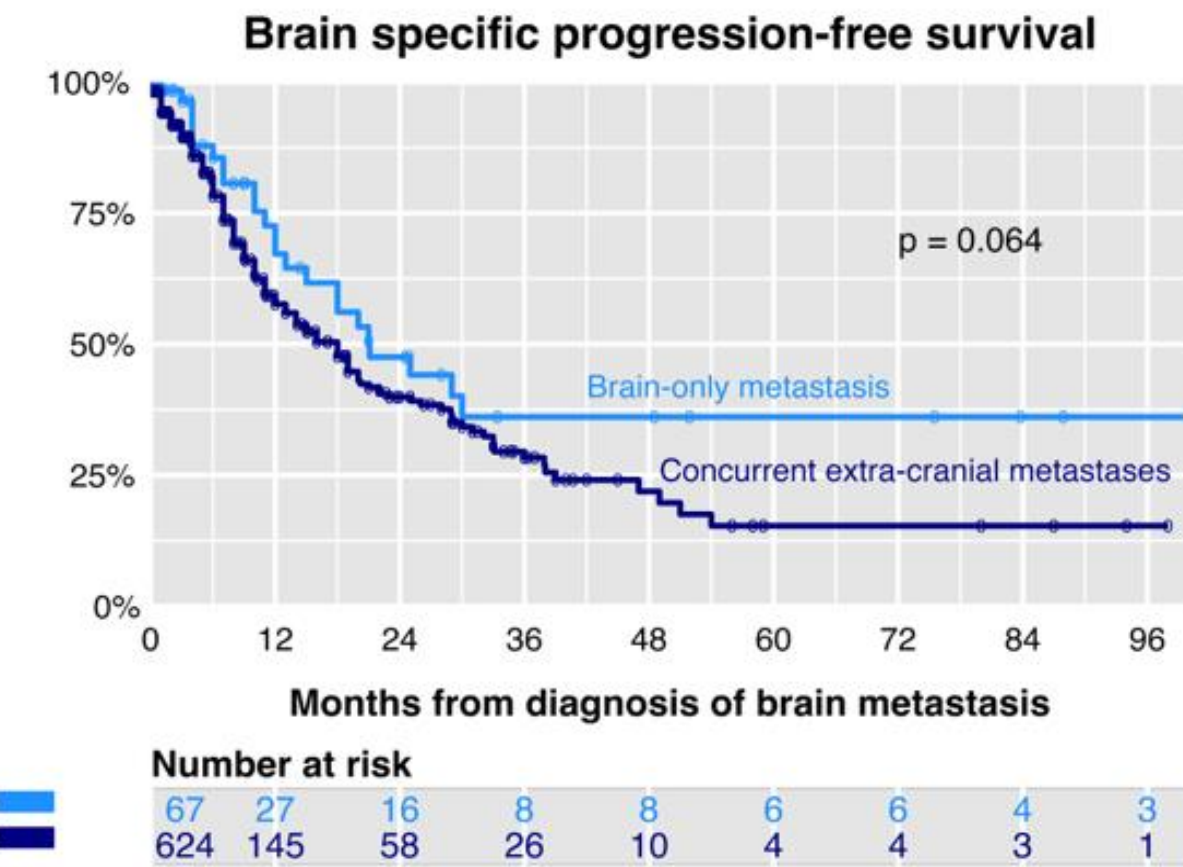
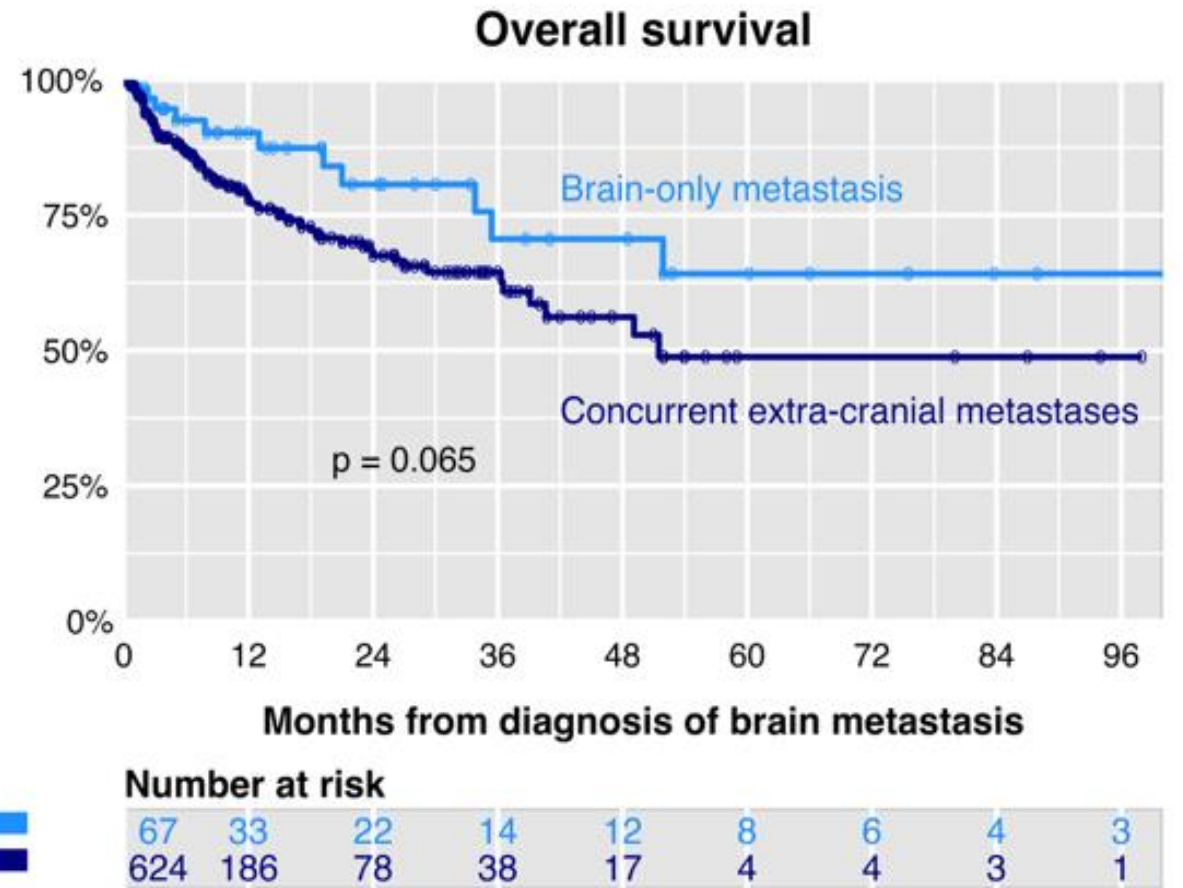
- Single BrM (OR 3.41 [1.62-7.19], p=0.001)
- HER2+ (OR 3.3 [1.32-9.65], p=0.03)
- TNBC (OR 4.09 [1.42-11.74], p=0.009)

### PREDICTORS OF OS

Table 3: Clinical and pathological factors associated with overall survival				
	Univariable		Multivariable	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Metastases				
Extracranial metastases (ECM)	Ref		Ref	
Brain-only without subsequent ECM/LMD	0.35 (0.13, 0.95)	0.01	0.26 (0.09, 0.74)	0.002
Brain-only +/- subsequent ECM/LMD	0.56 (0.29, 1.04)	0.04	0.45 (0.22-0.86)	0.008
Age at initial breast cancer diagnosis	1.29 (1.11, 1.50)	0.001	1.03 (1.01, 1.05)	0.0004
Age at MBC diagnosi	1.30 (1.12, 1.51)	0.0005		
Time from BC to brain metastases (mths)	1 (0.99, 1.004)	0.9		
Breast cancer subtype				
HR+HER2-	Ref		Ref	
HER2+	0.55 (0.35, 0.89)	0.0004	0.58 (0.35, 0.97)	0.0002
Triple negative	1.49 (0.96, 2.31)		1.75 (1.1, 2.78)	
Karnofsky Performance Scale (KPS)				
Less than 60	Ref		NA	NA <sup>c</sup>
60 or higher	0.40 (0.24, 0.66)	0.001		
No. of brain metastases (BrM)				
>1 metastases	Ref			
Single	0.58 (0.32, 1.03)	0.04		
Surgery for BrM	0.36 (0.21, 0.67)	0.0001	NA	NA
Whole brain radiotherapy	2.99 (1.76, 5.09)	<0.0001	NA	NA
Stereotactic radiosurgery	0.35 (0.23, 0.54)	<0.0001	NA	NA

Patients who presented with brain-only MBC had

- Longer OS (HR 0.45, [0.22-0.86], p=0.008)
- Trend toward longer bsPFS (HR 0.67 [0.44-1.03], p=0.05)



## CONCLUSION

Brain-only MBC had a longer bsPFS and OS than those with ECM. Patients with HER2+ and TNBC were more likely to have brain-only disease compared to HR+/HER2- MBC.