Retrospective Determination of Prognostic Factors in BRAF-V600E Melanoma Brain Metastases

Lily Erickson, Sahana Ramaswamy, Sherise Ferguson, James Long, Hussein Tawbi, Merve Hasanov, Alicia Bea Davies, Elizabeth Sirmans, Chantal Saberian, Eliza L. Posada, Jared Malke, Lauren Haydu, Caroline Chung

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

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Introduction

BRAF-mutant melanoma brain metastases (MBM) have poor prognosis with overall survival (OS) for these patients averaging 4 months from BM diagnosis[1]. Despite this poor prognosis, the disease is historically understudied and there is little evidence arguing for a standardized treatment plan across the field.

Purpose

This study aims to retrospectively identify clinical and treatment-related variables that may predict differences in overall survival for patients with BRAF-mutant MBM that could help inform a data-driven standard of care.

Methods

Inclusion criteria (100 patients):

- BRAF-mutant cutaneous melanoma
- No other concurrent cancer diagnosis
- Diagnosed with BM from 1/1/2009-12/31/2018
- Received initial BM treatment at MDACC

Data was collected using institutional databases and manual chart review (see Table 1 for descriptive statistics). Data was cleaned and validated in Microsoft Power BI (PBI). Preliminary analysis was conducted using PBI, and further analysis was completed using Python package *kaplanmeier*.

n		100
AGE, mean (SD)		56.5 (14.2)
GENDER, n (%)	**FEMALE**	46 (46.0)
	MALE	54 (54.0)
Developed LMD, n (%)	**N**	73 (73.0)
	Y	27 (27.0)
MBM_Categorical_LDH, n (%)	**Elevated**	39 (39.0)
	Not Elevated	61 (61.0)
Breakthrough Case, n (%)	**N**	57 (57.0)
	Y	43 (43.0)
initial - immuno, n (%)	**N**	69 (69.0)
	Y	31 (31.0)
initial - targetted, n (%)	**N**	53 (53.0)
	Y	47 (47.0)
initial - local, n (%)	**N**	51 (51.0)
	Y	49 (49.0)

Table 1. Patient demographics and treatment summary.

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Results

- 97 different treatment sequences represented in 100 patients (Fig. 1)
- Gender not associated with differences in OS (Log rank, p=0.91051)[2]
- Initial treatment with immunotherapy (IT) did not demonstrate survival advantage to initial targeted therapy (TT) (Log rank, p=0.57813)[3]
- Breakthrough BM (develop despite ongoing systemic therapy at time of diagnosis) did not show OS difference compared to non-breakthrough cases (Fig. 2a)
- Non-breakthrough cases were associated with a survival advantage compared to breakthrough cases for those who received initial TT or IT (Fig. 2b)

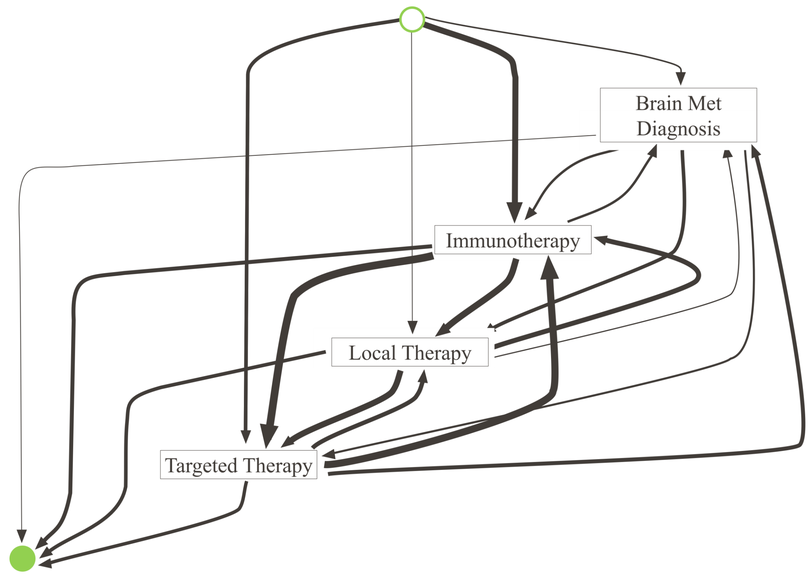

Fig. 1. Treatment flow diagram demonstrating sequence of various treatments and diagnosis. The open circle represents primary melanoma diagnosis. The closed circle represents death or end of study period. The weight of each line is proportionate to the number of patients represented.

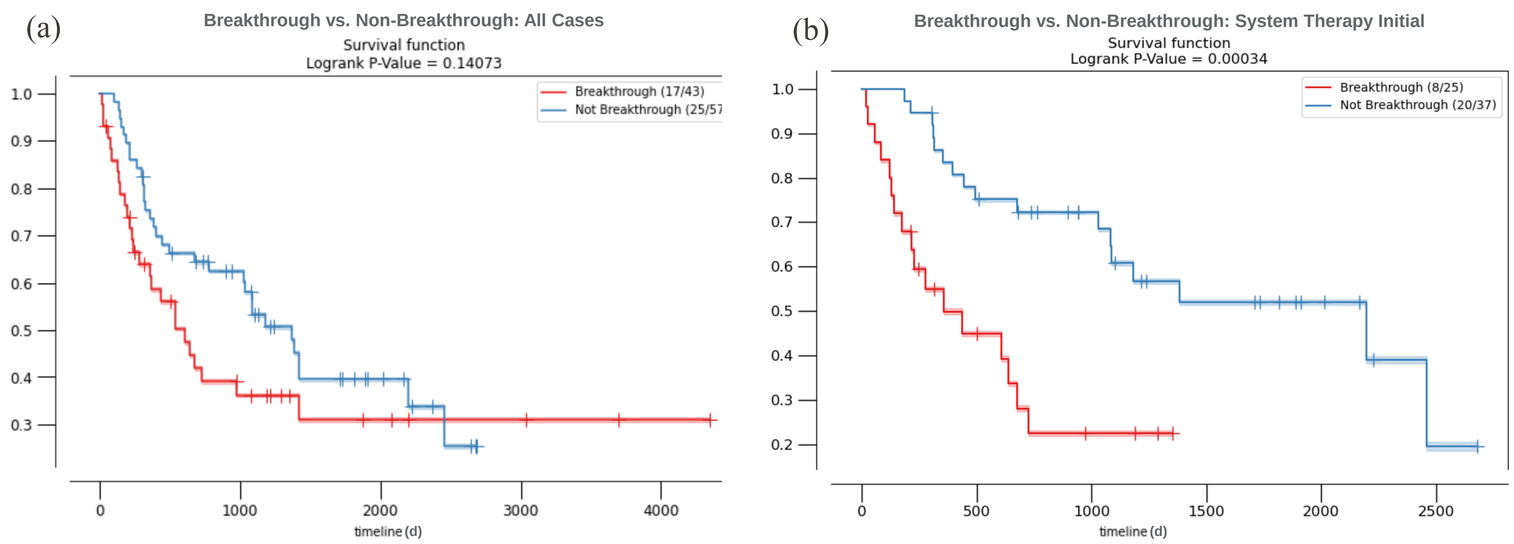

Fig. 2. (a) Kaplan Meier curve showing OS comparison for all breakthrough vs. non-breakthrough cases. (b) Kaplan Meier curve showing OS comparison for breakthrough vs. non-breakthrough cases where patient received initial BM therapy of immunotherapy or targeted therapy.

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Conclusions

- Highly variable treatment strategies complicate our analysis of treatment response
- BRAF-MBM does not follow anticipated patterns from extracranial disease
- Initial systemic therapy may improve survival in the context of non-breakthrough MBM

Future Directions

- Elucidate mechanisms behind treatment-related survival differences
- Understand patterns for progression, other outcome metrics

Acknowledgements

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