Minimal Toxicity from Systemic Therapy Given Concurrently with Stereotactic Radiosurgery for Brain Metastases

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Introduction

Chemotherapy is typically not given concurrently with whole brain radiation therapy (WBRT) for treatment of metastatic disease due to increased risk of myelosuppression and neurotoxicity. The goal of this study is to evaluate the prevalence, outcomes, and toxicities of concurrent delivery of systemic therapy with stereotactic radiosurgery (SRS) for treatment of brain metastases.

Methods

- Retrospective review of 195 patients treated with SRS without WBRT for brain metastases, 2009-2014.
- Outcomes: administration of concurrent systemic therapy, grade of myelosuppression, development of neurological symptoms/toxicity, and overall survival.
- Concurrent systemic therapy: therapy started with or prior to SRS and continued through SRS treatment.
- Grade of myelosuppression: defined by laboratory values within 1 month of SRS, per CTCAE v4.
- Grade of neurotoxicity, defined by RTOG acute radiation morbidity scoring criteria, and dexamethasone use evaluated over 3 months following SRS. Radiation necrosis defined by radiographic (MRI) suspicion or pathologic confirmation, along with corresponding neurologic symptoms (no time limit).

Results

Table 1: Patient demographics

Characteristic		Number	Percent
Total number of patients		195	
Total number of treatments		292	
Sex	Male	96	49.2
	Female	99	50.8
Age	Median: 61 years (range 27-85)		
Histology	Breast	27	13.8
	Lung (NSCLC)	79	40.5
	Melanoma	36	18.5
	Renal	18	9.2
	Other	35	17.9
Performance status (ECOG)	0	45	23.1
	1	115	59.0
	2	28	14.4
	3	7	3.6
Extracranial disease status	Controlled	69	35.8
	Not controlled	124	64.2

Table 2: Treatment data

SRS with concurrent systemic therapy		Number	Percent
Total number SRS treatments		292	
Number SRS treatments delivered with systemic therapy		115	39.4
Of SRS treatments delivered with systemic therapy (n=115):			
Myelosuppressive systemic therapy		58	50.4
Non-myelosuppressive systemic therapy		57	49.6
Timing of systemic therapy with SRS:	Same week	79	68.7
	Not same week	22	19.1
	Unknown	14	12.2

SRS treatment data	Mean	SD	Median	Min	Max
Total SRS treatments per patient	1.5	0.8	1	1	6
Number lesions per treatment	2.5	2.0	2	1	11

Systemic therapy data	Number	Percent
Single agent systemic therapy	70	60.9
Multiple agent systemic therapy	45	39.2
Myelosuppressive		
Platinum	24	20.9
Taxane	18	15.7
Pemetrexed	14	12.2
5-FU / capecitabine	7	6.1
Gemcitabine	6	5.2
Non-myelosuppressive		
Ipilimumab or anti-PD1/PDL1 (immune therapy)	20	17.4
Trastuzumab (targeted therapy)	15	13.0
EGFR tyrosine kinase inhibitor (targeted therapy)	7	6.1

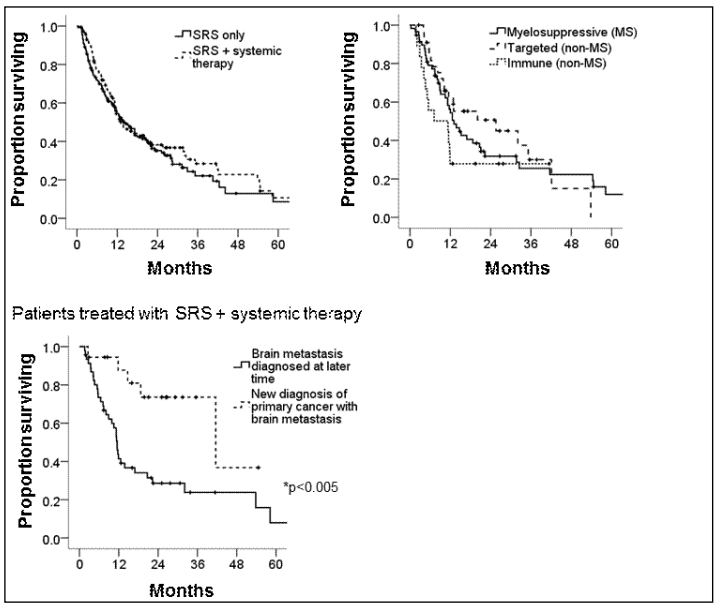
Table 3: Myelosuppression with SRS and systemic therapy

Toxicity	Grade	All concurrent treatments No. (%)	Myelosuppressive (MS) No. (%)	Targeted (non-MS) No. (%)	Immune (non-MS) No. (%)	p-val	Same week No. (%)	Not same week No. (%)	p-val
Leukopenia	0-2	66 (93.0)	37 (88.1)	14 (100)	14 (100)	0.243	49 (94.2)	15 (88.2)	0.596
	3-4	5 (7.0)	5 (11.9)	0 (0)	0 (0)		3 (5.8)	2 (11.8)	
Lymphopenia	0-2	59 (86.8)	34 (82.9)	13 (92.9)	11 (91.7)	0.289	44 (89.8)	14 (82.4)	0.773
	3-4	9 (13.2)	7 (17.1)	1 (7.1)	1 (8.3)		5 (10.2)	3 (17.6)	
Neutropenia	0-2	65 (95.6)	38 (92.7)	14 (100)	12 (100)	0.215	47 (95.9)	16 (94.1)	0.867
	3-4	3 (4.4)	3 (7.3)	0 (0)	0 (0)		2 (4.1)	1 (5.9)	
Anemia	0-2	66 (93.0)	38 (90.5)	13 (92.9)	14 (100)	0.097	50 (96.2)	14 (82.4)	0.025
	3-4	5 (7.0)	4 (9.5)	1 (7.1)	0 (0)		2 (3.8)	3 (17.6)	
Thrombocytopenia	0-2	67 (94.4)	38 (90.5)	14 (100)	14 (100)	0.059	51 (98.1)	14 (82.4)	0.232
	3-4	4 (5.6)	4 (9.5)	0 (0)	0 (0)		1 (1.9)	3 (17.6)	

Table 4: Neurotoxicity with SRS and systemic therapy

Toxicity		All concurrent treatments No. (%)	Myelosuppressive (MS) No. (%)	Targeted (non-MS) No. (%)	Immune (non-MS) No. (%)	p-val	Same week No. (%)	Not same week No. (%)	p-val
CNS acute RTOG morbidity grade	0	47 (42.0)	22 (38.6)	17 (53.1)	5 (25.0)	0.012	31 (39.7)	9 (40.9)	0.888
	1	29 (25.9)	15 (26.3)	10 (31.3)	4 (20.0)		21 (26.9)	7 (31.8)	
	2	33 (29.5)	19 (33.3)	5 (15.6)	9 (45.0)		24 (30.8)	6 (27.3)	
	3	3 (2.7)	1 (1.8)	0 (0)	2 (10.0)		2 (2.6)	0 (0)	
	4	0 (0)	0 (0)	0 (0)	0 (0)		0 (0)	0 (0)	
Dexamethasone following SRS	Yes	36 (32.1)	20 (35.1)	5 (15.6)	11 (55.0)	0.017	26 (33.3)	6 (27.3)	0.172
	No	76 (67.9)	37 (64.9)	27 (84.4)	9 (45.0)		52 (66.7)	16 (72.7)	
Radiation necrosis	Yes	4 (3.5)	1 (1.8)	3 (8.8)	0 (0)	0.294	3 (3.8)	0 (0)	0.317
	No	110 (96.5)	56 (98.2)	31 (91.2)	20 (100)		76 (96.2)	21 (100)	

Figure 1: Overall survival from time of SRS



Conclusions

- Systemic therapy can be safely given with SRS for brain metastases, for patients with intra- and extracranial disease.
- Myelosuppression is overall low with concurrent therapy; no difference between systemic therapy types or timing with SRS.
- While neurotoxicity is overall low, targeted therapies may lead to lower toxicity and steroid use, and immune therapies may result in higher toxicity requiring increased steroid use.
- Concurrent therapy may improve survival in patients with new presentations of primary with metastatic disease who can receive systemic therapy and SRS immediately.