





# The combined use of steroids and immune checkpoint inhibitors in brain metastasis patients: a systematic review and meta-analysis

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#### Introduction

Immune checkpoint inhibitors (ICI) have been a breakthrough for cancer patients, including those with brain metastases (BMs). Steroids have been an integral component of symptom management in BM patients. However, little is known about the interaction between ICI and steroids. The aim of this study was to perform a systematic literature review and meta-analysis on the association between steroid use and overall survival (OS) in BM patients receiving ICI.

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### Results

After screening 1145 abstracts, fifteen studies were included. Fourteen studies reported sufficient data for meta-analysis, comprising 1102 BM patients of which 354 (32.1%) had received steroids. In the steroid group, median OS ranged from 2.9 - 10.2 months across studies. In the non-steroid group, median OS ranged from 4.9 - 25.1 months. Pooling results demonstrated significantly worse OS (HR 1.77, 95% CI 1.14-2.74, p = 0.01) and systemic progression free survival (PFS) (HR 2.00, 95% CI 1.37-2.91, p = 0.01) in the steroid group. Stratified analysis showed a consistent effect across the melanoma (HR 1.67, 95% CI 1.49-1.87), although not in non-small cell lung cancer (HR 2.26, 95% CI 1.49-3.43) subgroup. No significant association was seen between steroid use and intracranial PFS (HR 1.15, 95% CI 0.31-4.24).

#### Methodology

A systematic literature search was performed in several research databases on 2 July 2019. Pooled effect estimates were calculated using random-effects models; analysis was performed across all included studies and stratified by tumor type.

## Conclusion

Administration of steroids was associated with significantly worse OS in BM patients receiving ICI. Further research on dose, timing and duration of steroids is needed to elucidate the cause of this association and optimize outcomes in BM patients receiving ICI.

			Rando	om effects	s mode	l forest plo	for ove	rall sur	vival
Study	Sample siz	ze	На	zard Rat	io	HR	9	5%-CI	Weight
Arbour (2018)	154			+:		2.67	[0.73;	9.74]	5.0%
Banks (2019)	12			-		1.18	[0.15;	9.44]	2.6%
Carron (2020)	50					0.35	[0.18;	0.68]	9.2%
Chasset (2015)	23				_	1.75	[0.51;	5.98]	5.4%
Galli (2019)	36			++-		1.50	[0.85;	2.64]	10.0%
Hendriks (2019a)	14				_	1.89	[0.62;	5.78]	6.0%
Hendriks (2019b)	255			- + <del></del>	_	2.37	[0.83;	6.74]	6.4%
Jones (2015)	12		-			0.86	[0.22;	3.31]	4.8%
Kotecha (2019)	150					2.46	[1.44;	4.20]	10.3%
Margolin (2012)	72					1.89	[1.08;	3.30]	10.1%
Minniti (2019)	80					1.74	[0.93;	3.27]	9.5%
Parakh (2017)	66			- <u>i</u>		2.06	[0.44;	9.56]	4.0%
Queirolo (2014)	146					1.69	[1.29;	2.22]	12.2%
Zhang (2020)	32				-	25.29	[6.21; 1	02.97]	4.5%
Random effects n				-		1.76	[1.09;	2.82]	100.0%
Heterogeneity: $I^2 = 6$	68%, <i>p</i> < 0.01						•		
		0.01	0.1	1	10	100			
		Favo	ors stero	ids Fav	ors no	steroids			

HR         95%-CI         Weight           2.55         [0.91; 7.14]         14.0%           1.75         [0.62; 4.98]         13.6%           1.06         [0.35; 3.23]         11.9%           2.78         [0.93; 8.27]         12.5%           2.08         [1.19; 3.62]         48.0%           5         5         5         5
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s no steroids
del forest plot for intracranial PFS
HR 95%-CI Weight
0.35 [0.17; 0.72] 25.9%
- 1.58 [0.91; 2.75] 28.3%
1.97 [0.94; 4.15] 25.6%
1.72 [0.56; 5.27] 20.2%
1.15 [0.31; 4.24] 100.0%

Favors steroids Favors no steroids