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

Charissa Jessurun, BS[1,2]; Alexander Hulsbergen, BS[2,3]; Anouk de Wit, MD[4]; Ishaan Tewarie, BS[2]; Rania Mekary, PhD, M.Sc[5]; Marike Broekman, MD, PhD, LLM[3,4,6]

[1] Faculty of Medicine, University of Amsterdam/Academic Medical Center Amsterdam; Amsterdam, The Netherlands. [2] Computational Neuroscience Outcomes Center (CNOC), Department of Neurosurgery, Brigham and Women's Hospital, Harvard Medical School; Boston, United States. [3]Department of Neurosurgery, Haaglanden Medical Center,, The Hague, The Netherlands; Department of Neurosurgery, Leiden University Medical Center,, Leiden, The Netherlands. [4] Department of Psychiatry, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands. [5] Department of Pharmaceutical Business and Administrative Sciences, School of Pharmacy, Massachusetts College of Pharmacy and Health Sciences; Boston, United States. [6] Department of Neurology, Massachusetts General Hospital, Harvard Medical School; Boston, United States.

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.

Objective

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.

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).

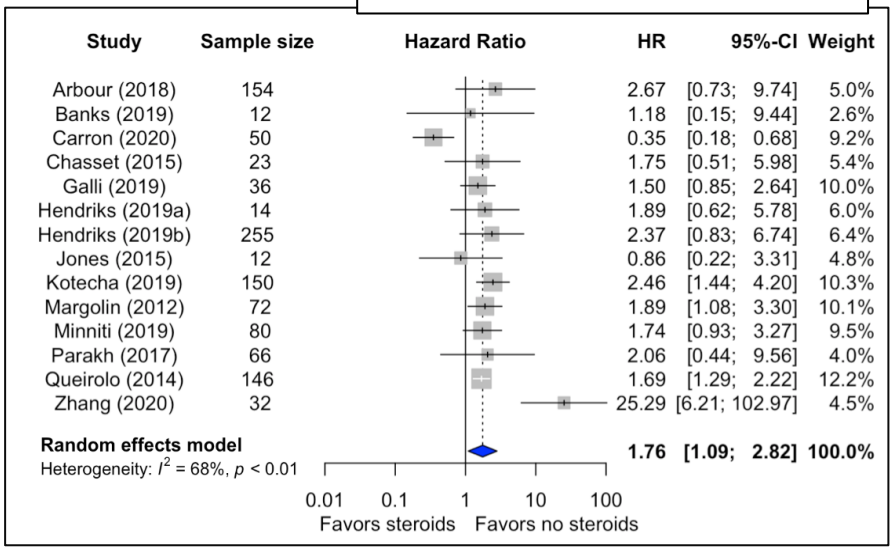
Methodology

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.

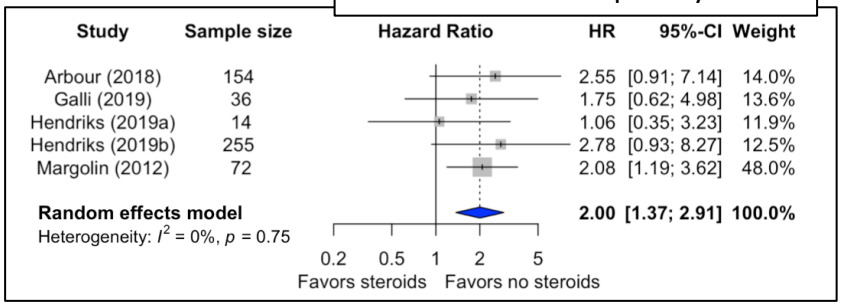
Conclusion

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.

Random effects model forest plot for overall survival



Random effects model forest plot for systemic PFS



Random effects model forest plot for intracranial PFS