

INPLASY PROTOCOL

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None declared.

The Evolving Landscape of Leptomeningeal Cancer from Solid Tumors: A Systematic Review of Clinical Trials

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Review question / Objective: Among adult patients with leptomeningeal carcinomatosis from solid tumors (population) treated with chemotherapy, targeted therapy, or immunotherapy (intervention and comparator) what are the differences in overall survival (OS) and progression-free survival (PFS) and treatment response based on clinical trial outcomes?

Eligibility criteria: Included articles reported 1) human subjects ≥ 18 years 2) diagnosis of leptomeningeal carcinomatosis from solid tumors confirmed by imaging or cerebrospinal fluid (CSF) cytology and clinical or neurological symptoms 3) clinical trials 4) with either PFS or MOS outcomes listed. Book chapters, case reports, review articles, observational studies, ed-itorials, and publications of leptomeningeal cancer from hematological tumors and studies consisting solely of pediatric patients were excluded from the analysis.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 December 2022 and was last updated on 29 December 2022 (registration number INPLASY2022120112).

INTRODUCTION

Review question / Objective: Among adult patients with leptomeningeal carcinomatosis from solid tumors

(population) treated with chemotherapy, targeted therapy, or immunotherapy (intervention and comparator) what are the differences in overall survival (OS) and progression-free survival (PFS) and

treatment response based on clinical trial outcomes?

Condition being studied: Leptomeningeal Cancer from Solid Tumors.

METHODS

Search strategy: The systematic review of the literature was conducted adhering to the Preferred Reporting Items for Reviews and Meta-Analysis (PRISMA) guidelines and recommendations. PubMed, Medline, and Scopus were queried without restrictions on publication language. The search terms “Leptomeningeal Carcinomatosis” OR “Carcinomatous Meningitis” OR “Leptomeningeal Metastasis” OR “Neoplastic Meningitis” AND “Clinical Trial” were used to search these databases from inception to November 2022- additional publications were identified from the reference list of selected papers. Clinicaltrials.gov was searched for ongoing clinical trials.

Participant or population: Adult patients with leptomeningeal carcinomatosis from solid tumors.

Intervention: Chemotherapy.

Comparator: Targeted therapy, immunotherapy, radiotherapy.

Study designs to be included: Clinical Trials.

Eligibility criteria: Included articles reported 1) human subjects ≥ 18 years 2) diagnosis of leptomeningeal carcinomatosis from solid tumors confirmed by imaging or cerebrospinal fluid (CSF) cytology and clinical or neurological symptoms 3) clinical trials 4) with either PFS or MOS outcomes listed. Book chapters, case reports, review articles, observational studies, editorials, and publications of leptomeningeal cancer from hematological tumors and studies consisting solely of pediatric patients were excluded from the analysis.

Information sources: Electronic databases (PubMed, Medline, Scopus).

Main outcome(s): Overall Survival, Progression Free Survival, Treatment Response.

Quality assessment / Risk of bias analysis: The quality of non-randomized controlled trials was assessed using the Newcastle-Ottawa scale (total score: 5 = low quality; 6–7 = intermediate quality; 8–9 = high quality). Randomized controlled trials (RCTs) were evaluated using the Jadad scale (0 = very poor quality, 5 = rigorous quality). The risk of bias was evaluated by adhering to the Cochrane risk-of-bias tool for randomized trials (RoB2) for randomized clinical trials. RoB2 is an outcome-focused, domain-based tool that evaluates the risk of bias in outcomes in individually randomized, parallel-group trials, randomized crossover trials, and cluster RCTs. RoB2 has five risk of bias domains covering different aspects of trial design, conduct, and reporting. Those include 1) Bias arising from the randomization process 2) Bias due to deviations from intended interventions 3) Bias due to missing outcome data 4) bias in the measurement of the outcome 5) bias in the selection of the reported results. The Risk of Bias in Non-Randomized Studies of Interventions (ROBINS-I) will be applied to analyze non-randomized comparative studies included. The ROBINS-I is a domain-based evaluation tool that has seven risk-of-bias domains 1) Bias due to confounding 2) Bias in the selection of participants 3) Bias in the classification of interventions 4) Bias due to deviations from intended interventions 5) Bias due to missing data 6) Bias in measurement of outcomes 7) Bias in the selection of the reported result. Two researchers (L.M.H and M.A.B) will independently evaluate the risk of bias for each of the studies. After completion, the tables will be compared, and all disagreements will be resolved by discussion or adjudicated by a third observer if a consensus is not reached.

Strategy of data synthesis: Non-quantitative study.

Subgroup analysis: None.

Sensitivity analysis: Non-quantitative study.

Language restriction: English.

Country(ies) involved: United States.

Keywords: Leptomeningeal cancer, carcinomatous meningitis, neoplastic meningitis, clinical trial.

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