INPLASY PROTOCOL

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Review Stage at time of this submission: Piloting of the study selection process.

Combined chemotherapy in new diagnosed primary central nervous system lymphoma: a systematic review and network meta-analysis

Li, Y[1]; Zhao, Z[2]; Liu, Y[3].

Review question / Objective: The aim of this network meta-analysis of case-control studies and cohort studies is to evaluate the efficacy of combined chemotherapy for newly diagnosed primary central nervous system lymphoma.

Condition being studied: Primary central nervous system (CNS) lymphoma (PCNSL) is a diffuse large B-cell lymphoma (DLBCL) solely confined to the CNS compartment. It is a rare malignancy with an incidence of 0.5/100000, accounting for approximately 4% of all primary brain tumors. Since the neurologic toxic effects seen using chemotherapy combined with radiotherapy and unsatisfied results using radiotherapy alone, numerous phase I and phase II studies over two decades established combined therapies for PCNSL. Intravenous high-dose methotrexate (HD-MTX) is considered a central component of all PCNSL chemotherapy protocols. It is commonly used in combination with other drugs such as vincristine, procarbazine, cytarabine, rituximab, and temozolomide. The quality of those combined therapies response has been shown to improve overall survival and progression-free survival. However, as new combined chemotherapies are continuously being developed, selecting a specific combination of drugs became an ever-increasing challenge.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 September 2020 and was last updated on 23 September 2020 (registration number INPLASY202090084).

INTRODUCTION

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METHODS

Search strategy: In this network meta-analysis, we search for relevant RCTs, case-control studies and cohort studies in PubMed, Embase, and the Cochrane Library. We use the medical subject heading "primary central nervous system lymphoma", "Methotrexate", "Rituximab", "Cytarabine", "Thiotepa", "Temozolomide", "Teniposide", "fotemustine", "Etoposide", "Cyclophosphamide", "Carboplatin", "Idarubicin", "Busulfan", "Carmustine", "Vincristine", and "Procarbazine" combined with free text words for searching. We also hand-search references from prior systematic reviews.

Participant or population: Adults with newly diagnosed primary central nervous system lymphoma.

Intervention: Combined chemotherapy for newly diagnosed primary central nervous system lymphoma is the main intervention.

Comparator: Combined chemotherapy regimen which is different from intervention for newly diagnosed primary central nervous system lymphoma is set as reference comparator.

Study designs to be included: Randomized clinical trials, case-control studies and cohort studies.

Eligibility criteria: We select patient population involved newly diagnosed primary central nervous system lymphoma patients without previous history of systematic lymphoma. Randomized clinical trials and retrospective analyses comparing two or more combined chemotherapies for PCNSL are included. Abstracts are allowed to be included if they reported sufficient data to extraction. Studies are excluded if design was considered unclear. No prior treatment is allowed except for brief corticosteroid exposure. Other treatments as radiotherapy and autonomic stem cell transplantation (ASCT) are allowed if they were evenly distributed on trial arms, but trials comparing only radiation/ASCT use are not considered in this meta-analysis.

Information sources: All information is searched from PubMed, Embase, and the Cochrane Library.

Main outcome(s): Overall response rate (ORR), overall survival (OS), and progression-free survival (PFS).

Quality assessment / Risk of bias analysis: We will assess the methodologic quality and bias of the included studies using the Newcastle–Ottawa scale (NOS) for observational studies. RCT studies were assessed for quality and risk of bias considering recommendations from The Cochrane Collaboration group. If information for bias assessment was not reported, correspondent author will contact and ask to provide study details. If no contact could be established, evaluated item will be ranked unclear.

Strategy of data synthesis: We perform our analysis using the linear regression model

within the Baysesian framework. The network plot will be drawn using R software V.4.0.2. Nodes will be used to represent different interventions and edges to represent the head-to-head comparisons between interventions. The size of nodes is proportional to the number of studies evaluating a test, and thickness of the lines between the nodes is proportional to the number of direct comparisons between test.

Subgroup analysis: None.

Sensibility analysis: None.

Language: We placed no restriction on language, as long as the abstract was available in English.

Country(ies) involved: China.

Keywords: Primary central nervous system lymphoma; Combined chemotherapy; Network Meta-Analysis; Systematic review.

Contributions of each author:
Author 1 - Yanming Li independently extracted the basic characteristics of studies that meet the inclusion criteria and evaluate the risk of bias of included studies. Additionally, Yanming Li will draft the manuscript and perform the statistical analysis.
Author 2 - Zhigang Zhao independently extracted the basic characteristics of studies that meet the inclusion criteria and evaluate the risk of bias of included studies.
Author 3 - Yuanbo Liu will test the data extraction sheet before formally extracting the data. If information for bias assessment was not reported, correspondent author will contact and ask to provide study details.