INPLASY PROTOCOL

To cite: Cai et al. A comparative study of the effectiveness and safety of combined procarbazine, lomustine, and vincristine as a therapeutic method for recurrent high-grade glioma: a protocol for systematic review and meta-analysis. Inplasy protocol 202080078. doi: 10.37766/inplasy2020.8.0078

Received: 18 August 2020

Published: 18 August 2020

Corresponding author:
Zhi-Gang Tan

158202099@csu.edu.cn

Author Affiliation:
Department of Neurosurgery, The Second Xiangya Hospital, Central South University, Changsha, Hunan, 410011, P. R. China.

Support: **Grant number: 2018SK21213**

Review Stage at time of this submission: **Formal screening of search results against eligibility criteria.**

Conflicts of interest:
The authors declare that they have no competing interests.

A comparative study of the effectiveness and safety of combined procarbazine, lomustine, and vincristine as a therapeutic method for recurrent high-grade glioma: a protocol for systematic review and meta-analysis

Cai, Y[1]; Jiang, YG[2]; Wang, M[3]; Jiang, ZH[4]; Tan, ZG.

Review question / Objective: **1. Types of participants The present study recruited adults (aged 18 years or older), the participants were treated previously for histologically confirmed grade III or IV glioma according to the criteria of the WHO during the initial diagnosis. 2. Types of interventions and comparisons The evaluations is inclusive of all variations of PCV chemotherapy in either arm, these evaluations have been carried out in terms of dosage, intensity, median number of cycles received, and duration of treatment. Additional salvage therapy encompasses corticosteroids, reirradiations with different dosages, and re-surgeries either with or without BCNU chemotherapy-containing wafers within the tumor cavity (as long as it is similar in both arms). Moreover, the control arm was eligible to receive any of the following: placebo; best supportive care; an active intervention with second-line chemotherapy, or re-challenge with TMZ; anti-angiogenics (medications to inhibit the formation of new blood vessels within tumors); novel therapy, such as electrical stimulation; or combined medications that could comprise of one or two of procarbazine, lomustine, or vincristine.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 August 2020 and was last updated on 18 August 2020 (registration number INPLASY202080078).

INTRODUCTION

Review question / Objective: **1. Types of participants The present study recruited adults (aged 18 years or older), the participants were treated previously for histologically confirmed grade III or IV glioma according to the criteria of the WHO**

during the initial diagnosis. 2. Types of interventions and comparisons The evaluations is inclusive of all variations of PCV chemotherapy in either arm, these evaluations have been carried out in terms of dosage, intensity, median number of cycles received, and duration of treatment. Additional salvage therapy encompasses corticosteroids, reirradiations with different dosages, and re-surgeries either with or without BCNU chemotherapy-containing wafers within the tumor cavity (as long as it is similar in both arms). Moreover, the control arm was eligible to receive any of the following: placebo; best supportive care; an active intervention with second-line chemotherapy, or re-challenge with TMZ; anti-angiogenics (medications to inhibit the formation of new blood vessels within tumors); novel therapy, such as electrical stimulation; or combined medications that could comprise of one or two of procarbazine, lomustine, or vincristine.

Condition being studied: Evidently, both empirical studies and clinical analysis have established that, combined procarbazine, lomustine, and vincristine has the capability to effectively treat the symptoms and improve the life standard of a patient. However, there has not been any systematic review aimed at evaluating the effectiveness and safety of combined procarbazine, lomustine, and vincristine for treating recurrent high-grade glioma. Consequently, the present study aims at conducting a systematic review to evaluate the effectiveness and safety of combined procarbazine, lomustine, and vincristine as a therapeutic means for treating recurrent high-grade glioma.

METHODS

Participant or population: The present study recruited adults (aged 18 years or older), the participants were treated previously for histologically confirmed grade III or IV glioma according to the criteria of the WHO during the initial diagnosis.

Intervention: Combined procarbazine, lomustine, and vincristine.

Comparator: placebo; best supportive care; an active intervention with second-line chemotherapy, or re-challenge with TMZ.

Study designs to be included: Double-blind, randomized, and parallel-group.

Eligibility criteria: 1. Types of studies Each study included was double-blind, randomized, and parallel-group, the studies were all aimed at evaluating combined procarbazine, lomustine, and vincristine as a treatment method for current high-grade glioma. Numerous other studies were excluded, such as, observational studies, non-randomized control studies, and case reports. 2. Types of participants The present study recruited adults (aged 18 years or older), the participants were treated previously for histologically confirmed grade III or IV glioma according to the criteria of the WHO during the initial diagnosis. 3. Types of interventions and comparisons The evaluations is inclusive of all variations of PCV chemotherapy in either arm, these evaluations have been carried out in terms of dosage, intensity, median number of cycles received, and duration of treatment. Additional salvage therapy encompasses corticosteroids, reirradiations with different dosages, and re-surgeries either with or without BCNU chemotherapy-containing wafers within the tumor cavity (as long as it is similar in both arms). Moreover, the control arm was eligible to receive any of the following: placebo; best supportive care; an active intervention with second-line chemotherapy, or re-challenge with TMZ; anti-angiogenics (medications to inhibit the formation of new blood vessels within tumors); novel therapy, such as electrical stimulation.

Information sources: Electronic databases such as, PubMed, MEDLINE, EMBASE, Cochrane Library Central Register of Controlled Trials, WanFang, and China National Knowledge Infrastructure (CNKI) were utilized to search for studies that were related to the utilization of combined

procarbazine, lomustine, and vincristine for treating recurrent high-grade glioma. Each of the databases listed above will be searched from inception to the present, without any restrictions on the language and publication time.

Main outcome(s): The definition of the overall survival is time from randomization to death from any cause.

Additional outcome(s): i) The definition of progression-free survival (PFS) is the time from randomization to progression of disease. ii) Either the European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life Questionnaire or Brain Cancer Module scale, or both the questionnaire and scale are used to measure quality of life. iii) Participants who were experiencing chemotherapy toxicity were grouped. During the grading of toxicity, the process conformed with the Common Terminology Criteria for Adverse Events.

Quality assessment / Risk of bias analysis: In accordance with the criteria outlined in the Cochrane Collaboration's tool, two authors conduct an independent evaluation of the quality of the studies included. . In the event of any disagreement, a discussion or the consultation of a third scholar will be used to resolve the disagreement.. The risk bias of each study included was assessed with the use of the following domains: selection bias, detection bias, reporting bias, performance bias, attrition bias, and other source of bias. Each potential source of bias will be graded according to three levels: "High risk", "Low risk", and "Unclear risk".

Strategy of data synthesis: Standard Chi-squared statistic and I2 test will be used to detect the statistical heterogeneity across all included studies[5], where minor heterogeneity is implied by I2 < 50% or P-value > 0.1, and the data will be pooled with the use of the fixed-effects model[6]. Meanwhile, considerable heterogeneity is implied by I2 > 50% or P-value < 0.1, and the data is pooled with the use of the random-effects model.

Subgroup analysis: Subgroup analysis will be handled according to the different drugs.

Sensibility analysis: The stability and robustness of the process to find studies will be tested through a sensitivity analysis, this will be achieved by excluding studies identified with high-risk of bias or those containing unclear methodological data.

Country(ies) involved: China.

Keywords: procarbazine, lomustine, vincristine, glioma, efficacy, safety.

Contributions of each author:
Author 1 - Yang Cai - Data curation, formal analysis, methodology, software, investigation, visualization, and writing.
Author 2 - Yu-Gang Jiang - Data curation.
Author 3 - Ming Wang - Data curation, formal analysis, and resources.
Author 4 - Zhuo-Hang Jiang - formal analysis and software.
Author 5 - Zhi-Gang Tan - software, supervision, investigation, resources, and writing.