INPLASY PROTOCOL

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Corresponding author:
Meixia Zhang

coretina@gmail.com

Author Affiliation:
West China Hospital, Sichuan University, China

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None of the authors have any financial/conflicting interests to disclose.

Comparative efficacy and safety of anti-vascular endothelial growth factor monotherapies for neovascular age-related macular degeneration: a systematic review and network meta-analysis

Zhang, Y[1]; Cai, Z[2]; Liu, X[3]; Chang, T[4]; Li, X[5]; Tang, Y[6]; Zhang, B[7]; Zhang, M[8].

Review question / Objective: **To evaluate the efficacy and safety of anti-vascular endothelial growth factor monotherapies for neovascular age-related macular degeneration.**
Condition being studied: **Different anti-vascular endothelial growth factor monotherapy regimens are available for patients with neovascular age-related macular degeneration. However, the comparative effectiveness of different anti-vascular endothelial growth factor monotherapy regimens for neovascular age-related macular degeneration is still unknown.**
Information sources: **We will systematically search for eligible randomized controlled trials in PubMed, Embase, and the Cochrane Library.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 02 July 2020 and was last updated on 02 July 2020 (registration number INPLASY202070007).

INTRODUCTION

Review question / Objective: **To evaluate the efficacy and safety of anti-vascular endothelial growth factor monotherapies for neovascular age-related macular degeneration.**

Rationale: **The comparative efficacy and safety profiles of the anti-VEGF**

monotherapies with different therapeutic regimens have not been addressed in existing practice guidelines or systematic reviews due to a shortage of head-to-head trials and the limitation of the traditional pairwise meta-analysis.

Condition being studied: Different anti-vascular endothelial growth factor monotherapy regimens are available for patients with neovascular age-related macular degeneration. However, the comparative effectiveness of different anti-vascular endothelial growth factor monotherapy regimens for neovascular age-related macular degeneration is still unknown.

METHODS

Search strategy: We will systematically search for eligible randomized controlled trials in PubMed, Embase, and the Cochrane Library without search date and language restrictions. The search terms will include "macular degenerations", "age related maculopathy", "age related macular degeneration", "ranibizumab", "pegaptanib", "aflibercept","brolucizumab", "conbercept","angiogenesis inhibitors", "verteporfin".

Participant or population: Patients with neovascular age-related macular degeneration.

Intervention: Different anti-vascular endothelial growth factor monotherapy regimens in terms of frequency and dose.

Comparator: Ranibizumab.

Study designs to be included: Published randomized controlled trials.

Eligibility criteria: We included RCTs that compared two or more of the following treatment strategies (placebo and different anti-VEGF monotherapy regimens, including ranibizumab, pegaptanib, aflibercept, brolucizumab, conbercept with different therapeutic regimens) for patients with neovascular age-related macular degeneration.

Information sources: We will systematically search for eligible randomized controlled trials in PubMed, Embase, and the Cochrane Library.

Main outcome(s): 1. The mean change in best-corrected visual acuity (BCVA) from baseline; 2. The number of serious adverse events.

Additional outcome(s): 1.Mean change in central retinal thickness from baseline; 2.The proportion of patients who gained ≥15 letters in BCVA from baseline; 3.The proportion of patients who lost <15 letters in BCVA from baseline; 4.The mean number of injections.

Quality assessment / Risk of bias analysis: The risk of bias will be assessed using the Cochrane Collaboration's tool for randomized controlled trials.

Strategy of data synthesis: Fixed effect and random effects models will be used to pool the data, and R 3.5.0 software and Stata version 14.0 (College Station, TX) will be used to conduct the data synthesis.

Subgroup analysis: Subgroup analyses are planned based on selected participant characteristics.

Sensibility analysis: Not planed.

Language: No language restrictions.

Country(ies) involved: China.

Keywords: anti-vascular endothelial growth factor, neovascular age-related macular degeneration, network meta-analysis.

Contributions of each author:
Author 1 - Yun Zhang - Yun Zhang designed the study, screened studies and extracted data, interpreted the data, reviewed the results, prepared, wrote and reviewed the manuscript.
Author 2 - Zhaolun Cai - Zhaolun Cai designed the study, assessed the risk of

bias, performed the statistical analyses, interpreted the data, reviewed the results and manuscript.
Author 3 - Xueting Liu - Xueting Liu assessed the risk of bias.
Author 4 - Tiancong Chang - Tiancong Chang screened the studies and extracted data.
Author 5 - Xun Li - Xun Li participated the discussion and resolved the disagreements.
Author 6 - You Tang - You Tang screened the studies.
Author 7 - Bo Zhang - Bo Zhang reviewed the results and manuscript. He had full access to all the data in the study and take esponsibility for the integrity of the data and the accuracy of the data analysis.
Author 8 - Meixia Zhang - Bo Zhang reviewed the results and manuscript. He had full access to all the data in the study and take esponsibility for the integrity of the data and the accuracy of the data analysis.