

# INPLASY PROTOCOL

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None declared.

## Efficacy and safety of RCHOP-X (X:Nalidomide, Bortezomib, Ibrutinib or Etoposide) in the treatment of diffuse large B-cell lymphoma—a systematic review and meta-analysis

Jiang, X<sup>1</sup>; Yu, L<sup>2</sup>; Wang, X<sup>3</sup>; Zhang, H<sup>4</sup>; Ding, K<sup>5</sup>.

**Review question / Objective:** The aim of this study was to systematically evaluate the efficacy and safety of RCHOP plus some new drugs (lenalidomide, bortezomib, ibrutinib, etoposide) in patients with diffuse large B-cell lymphoma (DLBCL).

**Condition being studied:** In this meta-analysis, we aimed to evaluate the relative efficacy in terms of the treatment of CHOP, R-CHOP and R-CHOP-X. For every study, hazard ratios (HR) and relative 95% confidence intervals (CIs) of the OS, EFS and PFS were set out in selected studies. The first-line setup of the entire cohort was reported respectively.

**Information sources:** We conducted systematic searches in PUBMED, EMBASE, and WEB OF SCIENCE to identify all relevant studies which published from 1990 to Mar 2021.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 December 2021 and was last updated on 23 December 2021 (registration number INPLASY2021120105).

### INTRODUCTION

**Review question / Objective:** The aim of this study was to systematically evaluate the efficacy and safety of RCHOP plus some new drugs (lenalidomide, bortezomib, ibrutinib, etoposide) in patients

with diffuse large B-cell lymphoma (DLBCL).

**Condition being studied:** In this meta-analysis, we aimed to evaluate the relative efficacy in terms of the treatment of CHOP, R-CHOP and R-CHOP-X. For every study,

hazard ratios (HR) and relative 95% confidence intervals (CIs) of the OS, EFS and PFS were set out in selected studies. The first-line setup of the entire cohort was reported respectively.

## METHODS

**Participant or population:** Patients with diffuse large B-cell lymphoma.

**Intervention:** Patients with diffuse large B were treated with R-CHOP and R-CHOPX (X:Nalidomide, Bortezomib, Ibrutinib or Etoposide) regimens respectively.

**Comparator:** For every study, hazard ratios (HR) and relative 95% confidence intervals (CIs) of the OS, EFS and PFS were set out in selected studies.

**Study designs to be included:** Randomized controlled studies and retrospective studies were searched in the electronic database, and the hazard ratios (HR) and its 95% corresponding interval (95% CI) were used to evaluate the overall survival (OS) and progression-free survival (PFS).

**Eligibility criteria:** Our meta-analysis included phase III or phase II clinical trials and retrospective studies. The titles and abstracts of the retrieved articles were independently screened (). We included the studies which provided the HR and relative 95% CIs of the OS, EFS and PFS of CHOP, R-CHOP and R-CHOP-X. The studies without valuable data on therapies of CHOP, R-CHOP and R-CHOP-X for analysis were excluded.

**Information sources:** We conducted systematic searches in PUBMED, EMBASE, and WEB OF SCIENCE to identify all relevant studies which published from 1990 to Mar 2021.

**Main outcome(s):** A total of 617 articles were identified, of which 13 studies compared the treat effects of CHOP and R-CHOP on DLBCL and 8 studies compared the treat effects of R-CHOP and R-CHOP-X on DLBCL. R-CHOP were associated with an improved PFS and OS compared to

CHOP. with a reduction of more than 50% of progression (HR by REM: 0.4940; 95% CI: 0.4221-0.5795) and mortality (HR by REM: 0.4677; 95% CI: 0.3487-0.6273). In the retrospective studies, R-CHOP-X were associated with an improved PFS and OS compared to R- CHOP, and reduced more than 50% of progression (HR by REM: 0.4683; 95% CI: 0.3345-0.6550) and mortality (HR by REM: 0.4788; 95% CI: 0.3680-0.6229). However, the results of clinical studies show that R-CHOP-X chemotherapy regimens demonstrated advantages in specific DLBCL patients, and did not significantly reduce the risk of progression (HR by REM: 0.9222; 95% CI: 0.7568-1.1237) and mortality (HR by REM: 0.9181; 95% CI: 0.7839-1.0754).

### Quality assessment / Risk of bias analysis:

In order to minimize the deviation and improve the reliability, the three researchers independently extracted the data and resolved the differences between them through discussion. In addition to the data about HRs of PFS and OS with relative 95% CI and number of patients achieving lymphoma response for each arm, the following data were also extracted: first author, country's publication date, publication year. Engauge Digitizer version 5.0 (<https://sourceforge.net/projects/digitizer/>) was used to extract information from graphics. After extracting the data, the researchers examine the differences in the data to minimize the possibility of errors. Two researchers () assessed the risk of bias and focused on nine areas, including randomization, assignment concealment, confusion (design/analysis), accidental exposure, the same experimental conditions, compliance with the protocol, the blindness of the researcher, lack of outcome data and evaluation of chaotic variables.

**Strategy of data synthesis:** All statistical analyses were performed in R version 4.0.3 (R Statistical Computing Foundation, Vienna, Austria; <http://www.R-project.org>). We Extracted the HRS of PFS, OS and EFS with relative 95% confidence interval (CIs) for each study.

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**Subgroup analysis:** In this meta-analysis, we aimed to evaluate the relative efficacy in terms of the treatment of CHOP, R-CHOP and R-CHOP-X. Patients were divided into CHOP regimen, RCHOP regimen and RCHOPX regimen to compare the efficacy of each regimen.

**Sensitivity analysis:** Sensitivity analysis was conducted to assess the impact of individual studies on the overall effect estimate.

**Country(ies) involved:** China.

**Keywords:** Diffuse large B-cell lymphoma, R-CHOP, meta-analysis.

**Contributions of each author:**

Author 1 - Xinlu Jiang.

Author 2 - Lu Yu.

Author 3 - Xiaoyan Wang.

Author 4 - Huanhuan Zhang.

Author 5 - Kaiyang Ding.