INPLASY PROTOCOL

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None declared.

Polymorphism of rs1799782 (c.580C>T) is associated with outcome of NSCLC patients treated with platinum-based chemotherapy: a system review and meta-analysis

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Review question / Objective: **It remains controversial whether rs1799782 (c.580C>T) is associated with the response rate or the survival rate of non-small cell lung cancer (NSCLC) or not. Thus, we performed this meta-analysis to identify the prognostic effect of it among NSCLC patients.**
Condition being studied: **Lung cancer has been one of the most common cancer, only second to breast cancer in the year of 2020. It accounts for about 11.4% of all cancer cases. The mortality of the cancer has decreased rapidly in recent years, partly because of new therapies and new drugs. During 2014 to 2018, the mortality of lung cancer has a pace of declining about 5% every year, compared with the previous declining rate of 2.4%. For non-small cell lung cancer, the survival rate has increased about 8% in a year, which gives great aspiration to clinicians. The mutation test helps clinicians to carry out personalized therapy, and the rs1799782 (c.580C>T) has widely been investigated for several decades. However, the predictive role of the variant to platinum-based chemotherapy was still undetermined, as the results were different and always controversy. For decades of years, this issue has been in debate among the scholars and experts in the field. As a result, this study was designed aiming to discuss the problem by pooling all the previous studies together. We also made subgroup analysis according to the study nature adopted in the included studies.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 September 2021 and was last updated on 17 September 2021 (registration number INPLASY202190052).

INTRODUCTION

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METHODS

Participant or population: A total of 3139 NSCLC patients were finally analyzed.

Intervention: Platinum-based chemotherapy.

Comparator: rs1799782-CC wilde type.

Study designs to be included: Prospective and retrospective.

Eligibility criteria: (1) published original articles obeying peer-reviewed rules; (2) articles were published in English; (3) articles reporting the relationship between response and XRCC1 rs1799782; (4) studies with follow-up period that was at least more than 1 years.

Information sources: Three databases, Embase, pubmed and the Cochrane Library were searched out to identify the articles concerning our topic.

Main outcome(s): A total of 13 articles with 15 studies including 3139 NSCLC patients were finally analyzed. The total HR between rs1799782-TT and overall survival (OS) was 0.63 (95%CI 0.43-0.91) for all the included studies. For the prospective subgroup, the HR was 0.79 (95%CI 0.60-1.04; I2=12%; P=0.34 for Cochrane Q test). For the retrospective subgroup, the HR was 0.35 (95% CI 0.14-0.84; P=0.11; I2=50%; P=0.11 for Cochrane Q test); Sensitivity analysis showed that all the pooled results were robust. The relationship between rs1799782 and short-term response in dominant model showed that OR was 0.73 with the corresponding 95% CI 0.61-0.89. The Egger's test showed P=0.93 and the Begg's test showed P=0.81. The relationship between rs1799782 and short-term response in recessive model showed that OR was 0.63 (95% CI 0.48-0.83).

Quality assessment / Risk of bias analysis: Newcastle-Ottawa Scale (NOS) was employed to assess the quality of the included studies. Funnel plots with trim-and-fill method, Egger's test and Begg's test were employed to detect the publication bias that may exist. Sensitivity analysis was employed to detect the origin of the heterogeneity. For the prospective subgroup, the HR was 0.79 (95%CI 0.60-1.04; I2=12%; P=0.34 for Cochrane Q test). For the retrospective subgroup, the HR was 0.35 (95% CI 0.14-0.84; P=0.11; I2=50%; P=0.11 for Cochrane Q test); Sensitivity analysis showed that all the pooled results were robust. The relationship between rs1799782 and short-term response in dominant model showed that OR was 0.73 with the corresponding 95% CI 0.61-0.89. The Egger's test showed P=0.93 and the Begg's test showedP=0.81.

Strategy of data synthesis: Forest plots were employed to show the combined results using random-effects models. Funnel plots with trim-and-fill method, Egger's test and Begg's test were employed to detect the publication bias that may exist. Sensitivity analysis was

employed to detect the origin of the heterogeneity.

Subgroup analysis: **Subgroup analysis. At the same time, subgroup analysis was made in order to make more clear the origin of the heterogeneity. At the same time, random effect model was also used to calculate the pooling HR (Figure 2).**

Sensitivity analysis: **Sensitivity analysis showed that the pooled result was robust, as the value shifted in a mild degree after the procedure of one left out in turn (Supplementary Figure 2).**

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

Keywords: **Non-small cell lung cancer (NSCLC); Platinum-based chemotherapy; Polymorphism; Survival; Meta-analysis.**

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