# INPLASY PROTOCOL

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**Conflicts of interest:**
**None declared.**

# Bone metastasis status as a predictor of prognosis and treatment response in patients with non-small cell lung cancer treated with immune checkpoint inhibitors: A Meta-Analysis

Qiao, YQ[1]; Hui, P[2]; Nan, YD[3].

**Review question / Objective:** **The influence of bone metastasis status on the prediction of prognosis and treatment response in patients with non-small cell lung cancer treated with immune checkpoint inhibitors is debatable. This meta-analysis was performed to explore the issue according to a larger sample capacity.**
**Condition being studied:** **Lung cancer has become the most common malignant tumor and the leading cause of cancer death in the world. Immune checkpoint inhibitors(ICIs) have emerged as powerful therapeutic strategy in different settings. It is imperative to identify new effective prognostic biomarkers to predict long-term survival or the treatment response of non-small cell lung cancer(NSCLC) patients. Recently, some clinical factors such as performance status and metastatic sites (liver or brain), have been identified as potential predictors for immunotherapy efficacy. Herein, we focus on the bone, another common site of metastasis in NSCLC. This is because bone marrow plays active functions in regulating immune system and trafficking of immune cells, and it is an immune regulatory organ potentially influencing response to immunotherapy. The aim of the present study is to assess whether prognosis and efficacy of ICIs was influenced by presence of bone metastasis in NSCLC.**

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 03 August 2022 and was last updated on 03 August 2022 (registration number INPLASY202280013).

## INTRODUCTION

**Review question / Objective:** **The influence of bone metastasis status on the prediction of prognosis and treatment response in patients with non-small cell lung cancer treated with immune checkpoint inhibitors is debatable. This meta-analysis was performed to explore the issue according to a larger sample capacity.**

**Condition being studied:** Lung cancer has become the most common malignant tumor and the leading cause of cancer death in the world. Immune checkpoint inhibitors(ICIs) have emerged as powerful therapeutic strategy in different settings. It is imperative to identify new effective prognostic biomarkers to predict long-term survival or the treatment response of non-small cell lung cancer(NSCLC) patients. Recently, some clinical factors such as performance status and metastatic sites (liver or brain), have been identified as potential predictors for immunotherapy efficacy. Herein, we focus on the bone, another common site of metastasis in NSCLC. This is because bone marrow plays active functions in regulating immune system and trafficking of immune cells, and it is an immune regulatory organ potentially influencing response to immunotherapy. The aim of the present study is to assess whether prognosis and efficacy of ICIs was influenced by presence of bone metastasis in NSCLC.

## METHODS

**Search strategy:** We performed a literature search through the following databases: Pubmed, Cochrane Library, Web of Science and Embase databases for studies published before August 2022. The strategy of keyword Search terms was as follows: non-small cell lung cancer; immune checkpoint inhibitors; nivolumab; pembrolizumab; durvalumab; ipilimumab; tremelimumab; sintilimab; atezolizumab; camrelizumab; bone metastasis; metastasis; objective response rate; prognosis.

**Participant or population:** Non-small cell lung cancer patients treated with immune checkpoint inhibitors.

**Intervention:** Non-small cell lung cancer patients with bone metastases.

**Comparator:** Non-small cell lung cancer patients without bone metastases.

**Study designs to be included:** Studies include cohort studies, case-control studies, retrospective and prospective studies.

**Eligibility criteria:** (1)All patients were diagnosed with non-small cell lung cancer based on cytology or histology; (2) All patients received treatments that included immune checkpoint inhibitors; (3) All articles reported prognostic survival outcomes or efficacy evaluation index associated with bone metastasis status, such as overall survival(OS), progression free survival(PFS), objective response rate(ORR) or disease control rate(DCR), and provided hazard ratios (HRs) /odds ratios (ORs) with 95% CI for these metrics or included sufficient data to calculate.

**Information sources:** Pubmed, Cochrane Library, Web of Science and EMBASE databases.

**Main outcome(s):** The HR and 95%CI were extracted to assess the correlation between bone metastasis status and the OS or PFS. The OR and 95%CI were extracted to assess the correlation between bone metastasis status and the ORR or DCR.

**Data management:** Two reviewers independently assessed and incorporated the following items from each study: first author's name, year of publication, country, study design, sample size, follow-up time, treatment method, HR/OR and 95%CI.

**Quality assessment / Risk of bias analysis:** The Newcastle-Ottawa Scale (NOS) was used to evaluate the quality of the included studies.

**Strategy of data synthesis:** The HR or OR and 95% CI from the multivariate or univariate analysis were retrieved directly from the included studies or calculated. Subsequently, the statistical heterogeneity of pooled results was assessed using the Cochran's Q test and I2 statistical methods. Our results were reckoned to have been unaffected by heterogeneity if I20.10. In this scenario, a fixed-effects model was utilized to obtain the pooled estimates; otherwise, a random-effects model was used.

**Subgroup analysis:** We conducted the subgroup analysis by treatment line and combination or monotherapy.

**Sensitivity analysis:** A sensitivity analysis was performed by sequentially excluding each study to assess the impact of each included study on the final pooled results.

**Language restriction:** English.

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

**Keywords:** non-small cell lung cancer; bone metastasis; immune checkpoint inhibitors; prognosis.

**Contributions of each author:**

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