**Protocol**

**Background**

Programmed cell death 1 (PD-1) and its ligand (PD-L1) play an important role in tumour recurrence, metastasis and infiltration. Moreover, the use of their corresponding inhibitors has led to progress in the treatment of many cancer types. However, these inhibitors also cause various immune-related adverse events and their effectiveness was observed in select patients. Therefore, it is urgent to identify biomarkers that can predict a patient’s response to PD-1/PD-L1 inhibitors, thereby aiding in selecting appropriate patients.

**Objectives**

This study aimed to evaluate the diagnostic value of PD-L1 expression in clinical practice, particularly in patients with advanced malignancies treated with PD-1/PD-L1 inhibitors.

**Selection critiera**(Types of studies/Types of participants/Types of interventions/Types of outcomes)

Both the exclusion and inclusion criteria were predetermined. The inclusion criteria were as follows: (1) the PD-L1 status of the included patients (aged >18) were examined, either in the primary tumour or at the metastatic site, using immunohistochemistry (IHC) staining methods. The threshold for PD-L1 positivity or negativity was that the stained PD-L1 cells accounted for 1% of tumour cells or tumour and immune cells; (2) the primary outcome was overall survival and the study had available number of death or hazard ratios (HRs), which were evaluated based on the positivity or negativity of PD-L1 expression; (3) participants were treated with at least one globally approved PD-1/PD-L1 inhibitor (e.g., nivolumab, pembrolizumab, avelumab, atezolizumab or durvalumab), disregarding dosage and duration; (4) studies that were reported only an abstract but were later published in full form were included, while case reports, reviews and prior meta-analyses were excluded. Studies not matching the selection criteria were excluded. Other exclusion criteria included the following: (1) studies in which participants were treated with combination therapies consisting of PD-1 and PD-L1 inhibitors; (2) phase I and non-randomised phase II studies; (3) retrospective or prospective observational cohort studies.

**Search strategy**

Frame 1 Search strategies

#1 Pembrolizumab[Title/Abstract] OR Nivolumab[Title/Abstract] OR Cemiplimab[Title/Abstract] OR Camrelizumab[Title/Abstract] OR Sintilimab[Title/Abstract] OR Tislelizumab[Title/Abstract] OR Toripalimab[Title/Abstract] OR PD-1 inhibitor[MeSH Terms]

#2 Atezolizumab[Title/Abstract] OR Durvalumab[Title/Abstract] OR Avelumab[Title/Abstract] OR Sugemalimab[Title/Abstract] OR PD-L1 inhibitor [MeSH Terms]

#3"PD-1"[All Fields] OR "PD-L1"[All Fields]

#4 randomized, controlled trial [MeSH Terms] OR randomized controlled trial [Title/Abstract]

#5 （#1 OR #2）AND #3 AND #4

**Study selection**

Study selection was performed independently by two investigators and a consensus was reached for all eligible studies. The included trials represented unique studies. Moreover, when the same clinical trial appeared in multiple articles or cases overlapped between different publications, the most recent or most complete reporting study, or both, were included.

**Data extraction**

The primary endpoint was overall survival, with odds ratios (ORs) and their 95% CIs used as summary statistics for dichotomous data analysis in the two subgroups of patients assigned to the experimental treatment according to the PD-L1 expression status. Additionally, (HRs for death and their 95% CIs were extracted from each study for patients that were PD-L1 positive or PD-L1 negative.

**Data synthesis**

A two-tailed P value < 0.05 was considered statistically significant. Statistical heterogeneity was assessed using the Chi-square test across the different studies included in the meta-analysis and inconsistency was quantified using the I2 test. The assumption of homogeneity was considered invalid for I2 > 25% and P < 0.05. Furthermore, a fixed-effects meta-analysis was performed for the calculation of pooled ORs and HRs of death as no significant heterogeneities were observed in the conducted analyses. Heterogeneity in efficacy between PD-L1 positive and PD-L1 negative patients was assessed using the interaction test, with P indicated as the interaction. Subgroup analysis based on the intervention drug target, cancer histotype, drug strategies, type of PD-L1 immunohistochemical scoring method, median follow-up time and type of control group were conducted to explore the variation of the effect of PD-L1 expression on the efficacy of immunotherapy. All statistical analyses were performed using the Stata statistical software version 16.0 (Stata Corporation, College Station, Texas, USA) and Rev Man5.4 softwa