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**ADMINISTRATIVE INFORMATION**

**Support** - None.  
**Review Stage at time of this submission** - Data analysis.  
**Conflicts of interest** - None declared.

**INPLASY registration number:** INPLASY202450069

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 May 2024 and was last updated on 14 May 2024.

**INTRODUCTION**

**Review question / Objective** Is metabolic tumor volume (MTV) derived from PET-scan before infusion associated with the prognosis of patients with Non-Hodgkin lymphoma (NHL) treated with chimeric antigen receptor T cell (CAR-T) therapy?

**Rationale** Non-Hodgkin lymphoma (NHL) is a heterogeneous group of lymphoid malignancies with varying clinical behaviors and responses to treatment. Chimeric antigen receptor (CAR) T cell therapy has emerged as a promising treatment modality for relapsed or refractory NHL, demonstrating remarkable efficacy in clinical trials. However, there is substantial variability in treatment outcomes among patients, and identifying prognostic factors is crucial for optimizing patient selection and therapeutic strategies.

One such potential prognostic factor is metabolic tumor volume (MTV), which quantifies the total volume of metabolically active tumor tissue. Previous studies in various cancer types have suggested that MTV is associated with treatment response and survival outcomes. However, the role of MTV in predicting the survival of patients with NHL treated with CAR T cell therapy remains unclear due to conflicting results from individual studies.

**Condition being studied** Non-Hodgkin lymphoma (NHL) represents a diverse group of lymphoid malignancies arising from B cells, T cells, or natural killer cells. Its incidence has been steadily rising over the past few decades, making it one of the most common hematologic malignancies globally. The exact etiology of NHL is multifactorial and not entirely understood, with factors such as immune dysfunction, viral infections (e.g., Epstein-Barr virus, human immunodeficiency virus), genetic

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predisposition, and environmental exposures implicated in its development.

## METHODS

**Search strategy** Terms derived from "metabolic tumor volume" AND "non-Hodgkin lymphoma" AND "Chimeric antigen receptor T cell" AND "survival" to search PubMed, Embase, and Web of Science.

**Participant or population** Patients with NHL treated with CAR T cell therapy.

**Intervention** MTV derived from PET-scan before CAR-T infusion.

**Comparator** A low baseline MTV group.

**Study designs to be included** Observational studies.

**Eligibility criteria** None.

**Information sources** PubMed, Embase, and Web of Science.

**Main outcome(s)** Progression-free survival and overall survival, compared between NHL patients with high versus low baseline MTV.

**Additional outcome(s)** None.

**Data management** Two independent authors will perform data extraction.

**Quality assessment / Risk of bias analysis** The Newcastle-Ottawa Scale.

**Strategy of data synthesis** A random-effects model will be used to combine the data, by incorporating heterogeneity.

**Subgroup analysis** Subgroup analysis according to categorized variables will be performed.

**Sensitivity analysis** Leave-one-out sensitivity analysis will be performed.

**Language restriction** Only publications in English will be considered.

**Country(ies) involved** China.

**Keywords** Metabolic tumor volume; chimeric antigen receptor T cell therapy; lymphoma; survival.

## Contributions of each author

Author 1 - Lin Liu.

Author 2 - Feng Jin.

Author 3 - Hua Fan.