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INPLASY

Tumour Infiltrating Lymphocytes in cutaneous Squamous Cell Carcinoma: A Protocol for Systematic Review

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202590114

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 27 September 2025 and was last updated on 27 September 2025.

INTRODUCTION

Review question / Objective The aim of this systematic review is to determine the characteristics (including but not limited to number, histological subtypes, associated cytokines, modulation by therapeutic agents) of Tumour Infiltrating Lymphocytes in cutaneous squamous cell carcinoma, as well as its influence on the treatment and prognosis.

Rationale Cutaneous Squamous Cell Carcinoma (cSCC), a non-melanoma skin cancer, is an invasive malignancy that arises from keratinocytes. Its rising global incidence and severe burden in immunosuppressed individuals put forth an urgent need to develop novel approaches for treating and preventing cSCC. Adoptive cell therapy with tumour-infiltrating lymphocytes (TILs) has demonstrated promising antitumour activity in patients with advanced solid organ tumours, including skin malignancies. In advanced melanoma, lifileucel has emerged as a viable treatment option in the post-immune checkpoint inhibitor setting. Taking a leaf out of melanoma research, TILs may also be of clinical relevance in cSCC. It is thus of clinical relevance to clarify the role of TILs in cSCC from existing literature. Doing so may define the role of TILs in cSCC as supported by histopathological evidence, help us assess the clinical translatability of TILs in cSCC treatment and prognosis and justify further characterisation of the dynamic skin immunological ecosystem to understand its contribution to skin malignancies.

Condition being studied Cutaneous squamous cell carcinoma is an invasive malignancy arising from keratinocytes.

METHODS

Search strategy Terms: ("tumour infiltrating lymphocytes"[All Fields] OR "lymphocytes, tumor infiltrating"[MeSH Terms] OR ("lymphocytes"[All Fields] AND "tumor infiltrating"[All Fields]) OR

"tumor-infiltrating lymphocytes"[All Fields] OR ("tumor"[All Fields] AND "infiltrating"[All Fields] AND "lymphocytes"[All Fields]) OR "tumor infiltrating lymphocytes"[All Fields]) AND ("cutaneous"[All Fields] OR "cutaneously"[All Fields] OR "cutanous"[All Fields]) AND ("neoplasms, squamous cell"[MeSH Terms] OR ("neoplasms"[All Fields] AND "squamous"[All Fields] AND "cell"[All Fields]) OR "squamous cell neoplasms"[All Fields] OR ("squamous"[All Fields] AND "cell"[All Fields] AND "cancer"[All Fields]) OR "squamous cell cancer"[All Fields] OR "carcinoma, squamous cell"[MeSH Terms] OR ("carcinoma"[All Fields] AND "squamous"[All Fields] AND "cell"[All Fields]) OR "squamous cell carcinoma"[All Fields])
Databases: Embase, Pubmed.

Participant or population Human cutaneous squamous cell carcinoma in which Tumour Infiltrating Lymphocytes were evaluated.

Intervention Nil.

Comparator Nil.

Study designs to be included Cohort studies, cross-sectional studies, case series, case reports.

Eligibility criteria
• Inclusion criteria: Human cutaneous squamous cell carcinoma in which Tumour Infiltrating Lymphocytes were evaluated
• Exclusion criteria
1. Non-human samples
2. Non-cutaneous squamous cell carcinoma
3. No tumour infiltrating lymphocytes described or evaluated.

Information sources Electronic databases PubMed, Embase.

Main outcome(s) Histological subtypes of TILs at different stages in cSCC.

Additional outcome(s)
Amount of TILs at different stages in cSCC
Cytokines associated with TILs at different stages in SCC
Modulation of TILs by therapeutic agents in SCC.

Data management This systematic review will be conducted in accordance with PRISMA guidelines. The screening process including manual removal of duplicates found will be done by 1 author (LLY). This is followed by title and full abstract screening performed independently by 2 authors (OCC and LLY) manually by applying the inclusion and exclusion criteria. All full text publications assessed are checked independently again by the 2 authors and any inconsistencies between the authors discussed and resolved. A standardized excel spreadsheet will be used to record and manage data extraction according to the outcomes desired.

Quality assessment / Risk of bias analysis The Newcastle-Ottawa and modified Newcastle-Ottawa score will be used to assess the quality of included studies. Publication bias will be addressed by performing a comprehensive search strategy that includes multiple databases to ensure that all relevant cases are captured. We will also assess for evidence of publication bias using funnel plots if a meta-analysis of sufficient size can be performed. Selective reporting bias will be evaluated by comparing the outcomes reported across included case reports and case series. To avoid duplication bias, we will carefully cross-reference all included studies to identify potential duplicate publications of the same case. Studies with overlapping patient descriptions will be flagged, and duplicate data will be excluded from analysis. Any suspected duplicates will be verified through patient demographics and clinical details.

Strategy of data synthesis Basic descriptive statistical analysis will be performed using GNU PSPP Software (Version 2.0.1). Where relevant, univariable logistic regression will be used to compare the outcomes between groups with different demographics and clinical features.

Subgroup analysis Nil.

Sensitivity analysis Nil.

Language restriction English.

Country(ies) involved Singapore.

Keywords Tumour Infiltrating Lymphocytes, cutaneous squamous cell carcinoma.

Dissemination plans Publish in a medical journal, present at medical conferences.

Contributions of each author
Author 1 - Li Yang Loo - Define inclusion and exclusion criteria, develop search strategy and locate studies, select studies, extract data, analyse and interpret results, disseminate findings.
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