PRELIMINARY INSIGHTS INTO CAR-T THERAPY FOR MELANOMA: A SYSTEMATIC REVIEW

F HAKEM ZADEH[1,2*], H HASHIM [1,2*], E HMEDAT [3], U IYER [4]

1. University of Central Florida College of Medicine, Orlando, FL, USA
2. HCA Healthcare Florida North Florida Hospital, Internal Medicine Residency, Gainesville
3. University of Kufa, Faculty of Medicine, Najaf, Iraq
4. Florida Cancer Specialists & Research Institute, Gainesville, FL

* **First Co-authors**

Introduction

Melanoma is a highly aggressive skin cancer with limited response to chemotherapy. Immune checkpoint inhibitors (ICIs) have improved survival, but resistance remains [1]. Chimeric Antigen Receptor T-cell (CAR-T) therapy offers a targeted immunotherapy approach, though its use in solid tumors is still evolving [2].

Aim

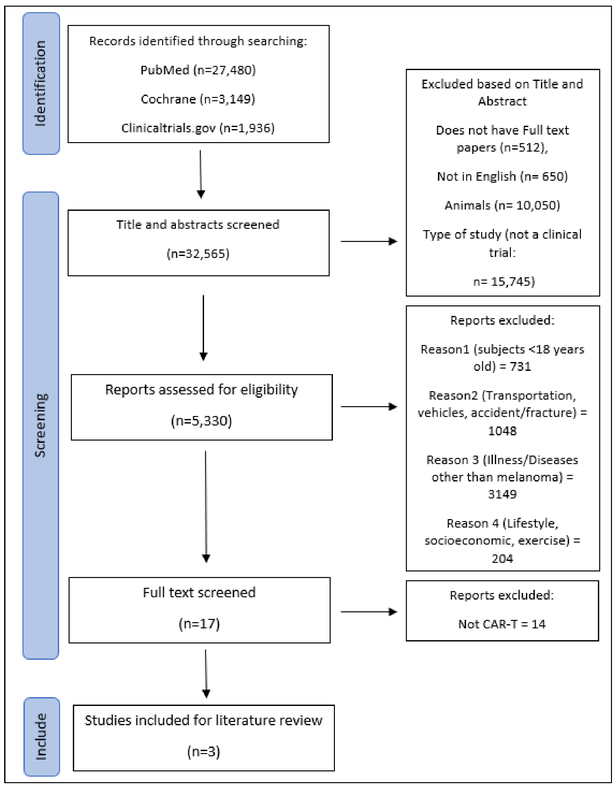
To systematically evaluate the safety and preliminary efficacy of CAR-T therapy in patients with advanced melanoma by analyzing early-phase clinical trials.

Objectives

Assess safety and early efficacy of CAR-T therapy in melanoma. Review clinical trials to identify trends and challenges.

Methods

Systematic review (2014–2024) following PRISMA guidelines [3]. Databases: PubMed, Cochrane, ClinicalTrials.gov., Inclusion: Prospective trials on CAR-T in melanoma. Final selection: 3 trials, 26 patients.



Results

Across three phase I/II trials (n=26), 24 patients (92%) had no grade ≥3 adverse events, with no dose-limiting toxicities or neurotoxicity. CRS occurred in 2 patients (7.7%). Stable disease was seen in 6 of 21 patients (28.6%), and disease progression in 8 of 21 (38.1%). A partial/complete response was reported in 5 of 14 patients (35.7%) in one study, possibly linked to BRAF/MEK inhibition.

Author, year of publication	Shah et al, 2023	Coupe et al, 2022	Gargett et al, 2024
Disease	Melanoma and Breast Carcinoma	Melanoma and Non-small cell lung cancer	Melanoma and other solid cancers with GD2
T-cell source	Autologous	Allogenic	Autologous
CAR-T type	Anti cMET CAR	iNKT cells	GD-2
CAR-T Generation	II	Not reported	III
Lymphodepletion with therapy	No	Not reported	Yes
Number of doses	6	6	Single
Number of infusions	6	6	Single
Study phase	I	I/II	I
Sample size	77	5 (still enrolling)	24
Cohort size	7	5	14
Safety evaluation period	16 weeks	Not reported	6 weeks
Dose limiting toxicities	0	0	0
Cytokine Release Syndrome	1/7 (14%)	0	1/14 (7%)
Neurotoxicity	0	0	0
Safety (no Grade ≥3 adverse event	7/7 (100%)	3/5 (60%), 2 have not completed the study	14/14 (100%)
Stable disease	4/7 (57%)	Not reported	2/14 (14%)
Disease progression	3/7 (42%)	Not reported	5/14 (35%)
Partial or complete response	0	Not reported	5/14 (35%), could be related to BRAF and MEK inhibition with CAR infusion

Summary

CAR-T therapy was well tolerated (92% no severe events), one trial showed a 35.7% response rate

Discussion

CAR-T therapy shows promising safety in advanced melanoma. Response variability may stem from CAR design, tumor microenvironment, and combination therapies. BRAF/MEK inhibitors may enhance CAR-T efficacy [5]. Larger trials are needed to optimize protocols and identify responsive patient subgroups.

References

1.Mahdiabadi S et al. Expert Rev Anticancer Ther. 2023;23(12):1281–1293.
2.Daei Sorkhabi A et al. Front Immunol. 2023;14:1113882.
3.Haddaway NR et al. Campbell Systematic Reviews. 2022;18:e1230.
4.Shah PD et al. Cancer Res Commun. 2023;3(5):821–829.
5.Gargett T et al. J Immunother Cancer. 2024;12(5):e008659.

The authors have no relevant financial relationships or conflicts of interest to disclose. The authors gratefully acknowledge Dr. Iyer for their guidance and HCA Healthcare for their support of this study.

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

SOHO2025