Immune-Related and Cutaneous Adverse Events Associated with Relatlimab Mono/Combo Regimens Versus Other Immune Checkpoint Inhibitors in Advanced, Non-Resectable Cutaneous Melanoma: Systematic Review and Meta-Analysis

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Introduction

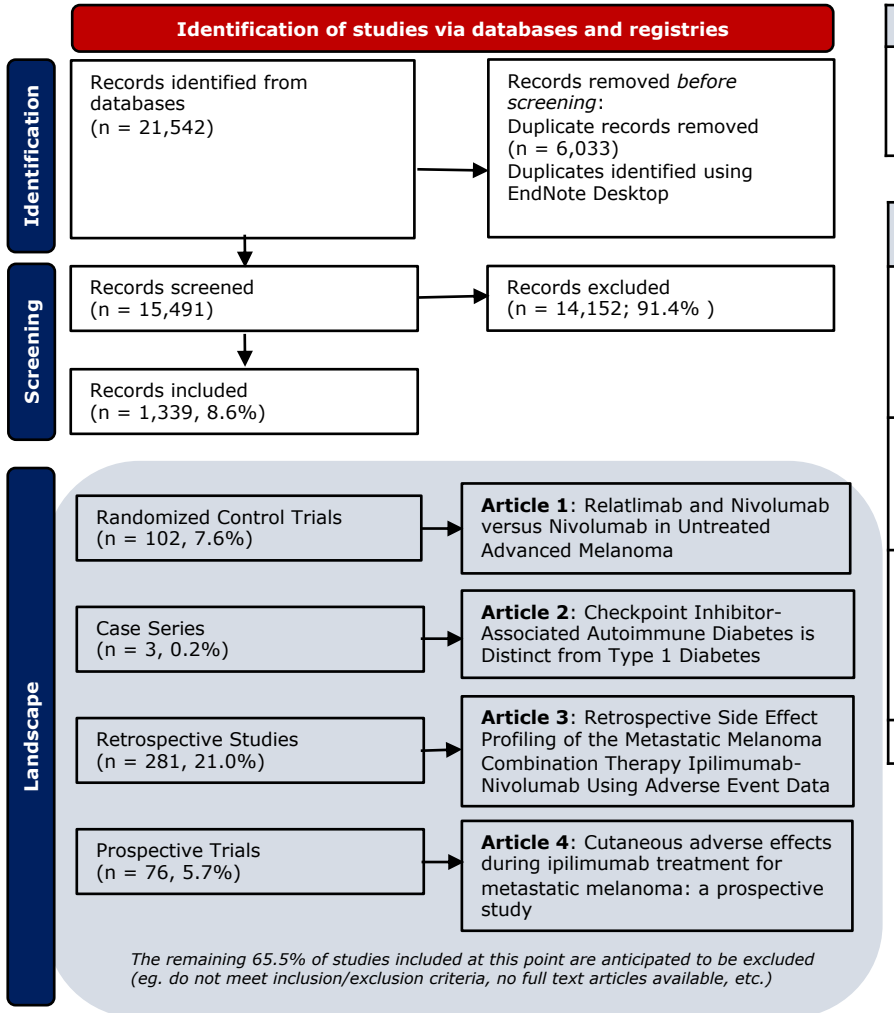
The introduction of relatlimab, a LAG-3 inhibitor, alongside nivolumab for advanced melanoma marks a significant advance. Comparable efficacy to existing therapies has positioned relatlimab and nivolumab combination as a first-line treatment per NCCN guidelines since 2022. Yet, there is still a significant knowledge gap concerning the safety profile of relatlimab, whether used alone or in combination.

Objective: Assess the safety of relatlimab as monotherapy or in combination with nivolumab for advanced, non-resectable cutaneous melanoma, compared to other immune checkpoint inhibitors (ICIs)

Methods

Category	Details
Reviewers	• Four independent reviewers evaluated publications in parts. Disagreements resolved by discussion or adjudication by a fifth reviewer
Databases	• Ovid MEDLINE, Elseviewer Embase, Cochrane Central Register of Controlled Trials, Elseviewer Scopus, Global Index Medicus, and ClinicalTrials.gov • Searched from January 2010 – April 2023
Eligible Studies	• RCTs, retrospective studies, prospective trials, case series (>100 persons). • We will be looking at Phase I-III studies.
Data to Extract	• Title, author, study methods, participants, interventions, cAEs (cutaneous adverse events), irAEs (immune-related adverse events)
Data Analysis	• Random-effect meta-analyses of binomial data • Estimate frequency and risk of cAE and irAE in relatlimab vs. other ICI regimens • Freeman-Tukey double arcsine transformation for accuracy and variance stabilization
Heterogeneity Assessment	• I^2 statistic • Subgroup analyses for I^2>75%
Risk of Bias Assessment	• Cochrane Collaboration Risk of Bias Assessment Tool for randomized trials • Newcastle-Ottawa Scale for nonrandomized studies

Landscape of Study In Progress



Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
• Patients ≥18 years • Advanced, non-resectable, cutaneous, acral melanoma • PD-1, CTLA-4 and LAG-3 inhibitor	• Age<18 yrs • Uveal, mucosal, bronchial melanoma • Patients with resected melanoma • Pre-existing autoimmune disease

Exemplary Study Results

Study	Treatment Arm	Adverse Events (A.Es) > 6%	A.Es Grade>3
Article 1	RELAT + NIVO	Pruritis 23.4%, Fatigue 23.1%, Rash 15.5%	Fatigue 1.1%, Rash 0.8%, Arthralgia 0.8%
	NIVO	Pruritis 15.9%, Fatigue 12.8%, Rash 12.0%, Arthralgia 7.2%	Pruritis 0.6%, Fatigue 0.3%,
Article 2	PEM, NIVO, NIVO+IPI, PEM+IPI	CIADM 1.9%; Acute pancreatitis 20%; Pancreatic exocrine failure 30%; Thyroiditis 30%; Hypophysitis 20%; Colitis 10%; Hepatitis 30%; Arthritis 10%	Not reported
Article 3	IPI	Diarrhea 14.3%, Colitis 11%, Rash 6.5%	Not reported
	IPI + NIVO	Diarrhea 9.9%, Colitis 9.5%, Pyrexia 7%	
	NIVO	Reported <6%	
Article 4	IPI	Rash and Folliculitis 7.2%	SJS 2.4%

Conclusions

Preliminary findings of our systematic review highlight the diverse literature on the safety profiles of established ICIs for melanoma treatment. This underscores the need for comparative safety data on relatlimab.

References

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