Pre-Existing Autoimmune Disease and Immune-Related Adverse Events (irAE) with Checkpoint Inhibitors in Metastatic Melanoma

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BACKGROUND

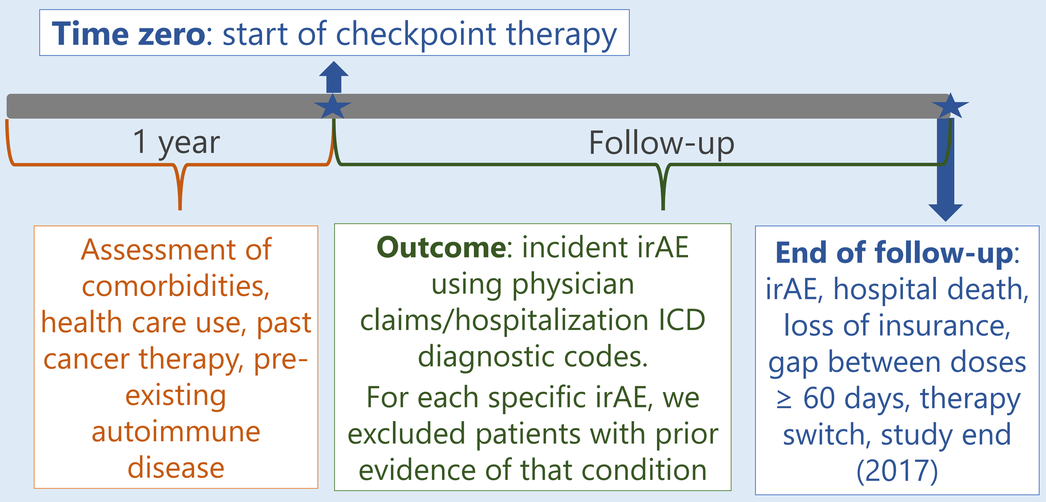
- Real-world safety data on metastatic melanoma patients with **pre-existing autoimmune disease is** limited.
- Typically, these patients are not represented in clinical trials.

OBJECTIVE

To study **immune-related adverse events (irAE)** with checkpoint inhibitors in metastatic melanoma, with and without pre-existing autoimmune disease.

METHODS

We used MarketScan® Databases (US health administrative data) to perform a **retrospective cohort study** of adults with metastatic melanoma initiating therapy with ipilimumab (IPI), pembrolizumab (PEM), nivolumab (NIV), or NIV/IPI over 2012-2017 (required health/drug plan coverage for 1 year before time zero).



Analyses:

- irAEs incidence rates with 95% confidence intervals (CI), stratified by pre-existing autoimmune disease, sex, and checkpoint inhibitor.
- Hazard ratios (HR) with 95% CI, adjusted for age, sex, calendar year, comorbidities, past health care use, past/current cancer therapy, and pre-existing autoimmune disease (Cox regression model).

RESULTS

- 2315 patients initiating IPI (62%), PEM (17%), NIV/IPI (12%), NIV (9%).
- Median follow-up: 273 days (interquartile range 129-537).
- Median age 60 years old, 62% male.
- Pre-existing autoimmune disease in 28% of patients, mostly hypothyroidism, interstitial lung disease, and myositis.

RESULTS

Crude irAE incidence rates* per 100 person-year (p-y) with 95% CI.

Group of patient	Nº events	Rate per 100 p-y	95% CI
Entire cohort	30	5.0	3.5-7.2
Presence of pre-existing autoimmunity	13	7.3	4.2-12.6
Absence of pre-existing autoimmunity	17	4.1	2.5-6.6
Male	20	5.4	3.5-8.3
Female	10	4.5	2.4-8.3
Users of ipilimumab	14	5.9	3.5-9.9
Users of nivolumab/ipilimumab	7	8.5	4.1-17.9
Users of pembrolizumab	9	4.9	2.6-9.5

*Users of nivolumab monotherapy did not develop any irAE.

Multivariable Analyses of irAE Risk

Four drug exposure categories: IPI, PEM, NIV, and NIV/IPI

- Presence **vs** absence of pre-existing autoimmune disease: HR 2.17 (95% CI 1.01-4.66)
- IPI **vs** NIV/IPI: HR 0.19 (95% CI 0.04-0.86)
- PEM **vs** NIV/IPI: HR 0.53 (95% CI 0.18-1.51)

Three drug exposure categories: anti-PD-1 agents (PEM or NIV), anti-CTLA-4 agent (IPI), and NIV/IPI

- Presence **vs** absence of pre-existing autoimmune disease: HR 2.03 (95% CI 0.94-4.35)
- IPI **vs** NIV/IPI: HR 0.19 (95% CI 0.04-0.86)
- Anti-PD-1 **vs** NIV/IPI: HR 0.34 (95% CI 0.12-0.96)

SUMMARY

- Metastatic melanoma patients with **pre-existing autoimmune disease** are more likely to develop irAE.
- Overall, metastatic melanoma patients on **combo checkpoint inhibitors (NIV/IPI)** have higher risk of irAE.

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Competing Interests: MH has received unrestricted research funding from Roche and BMS for work related to immune related adverse events from immune checkpoint inhibitors. RJ was an investigator on checkmate 067, the phase III trial evaluation of the combination of ipilimumab and nivolumab. The remaining authors have no competing interests to declare.