# Risk of Immune Checkpoint Inhibitor (ICI) Discontinuation in Older Adults with Melanoma

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## INTRODUCTION

- Immune checkpoint inhibitors (ICIs) have become a standard treatment for melanoma, significantly improving outcomes for patients.
- However, the data on the risk factors associated with the ICI discontinuation in older adults is limited, as these patients are often excluded from ICI clinical trials due to the increased risk of immune-related adverse events.

## OBJECTIVE

This study aims to assess the risk factors for ICI discontinuation among older adults with melanoma.

## METHODS

**Dataset:** Surveillance, Epidemiology, and End Results (SEER)-Medicare database (1999-2019)

**Inclusion criteria**

- Patients diagnosed with melanoma (1999-2017)
- Treated with immune checkpoint inhibitors (2011-2019)
- Had continuous Medicare coverage up to 2 years after treatment or until death
- Chemo-naïve: 12 months before ICI initiation

**Exclusion criteria**

- Missing date of diagnosis or diagnosed at death, or having HMO coverage
- Diagnosed with AID after ICI initiation

**Index date:** First ICI treatment date

**Exposure**

- ICIs were identified using the Healthcare Common Procedure Coding System (HCPCS) codes.
- Pre-existing AID status was determined using ICD-9/10 diagnosis codes and included neurological, dermatological, hematological, endocrinological, musculoskeletal, vascular, gastrointestinal, etc.

**Outcome**

- **ICI discontinuation** was defined as a ≥ 120-day gap between claims for initial ICI and/or initiation of new cancer therapy.
- Fine and Gray's competing risk model was used to determine the ICI discontinuation risk by pre-existing AID status. The model was adjusted for age, sex, marital status, region, education, income, year of ICI initiation, Charlson Comorbidity Index (CCI) score, and type of ICI therapy (combination vs monotherapy).

## RESULTS

- Of the 3,220 patients, 71.3% were male, 64% were older than 75 years, 98% were white and, 35.6% had pre-existing AID. (Table 1).
- Patients on combination ICI therapy were **8.9 times** more likely to discontinue ICI than patients on ICI monotherapy. (Table 2 and Figure 1).
- Risk of ICI discontinuation was lower in the patients who initiated ICI in the later years; **46% lower** for those who initiated ICI therapy in 2015-16 and **74% lower** for those who initiated ICI therapy in 2017-19, when compared to those who started ICI therapy in 2011-14 (Table 2 and Figure 2).
- Age, Pre-existing AID status, and CCI score did not affect the ICI discontinuation rates among melanoma patients (Table 2).

**TABLE 1. PATIENT CHARACTERISTICS BY AID STATUS**

| Characteristic | Autoimmune disease (n=1145) | No Autoimmune Disease (n=2075) | p-value |
|---|---|---|---|
| **Age Group at first ICI treatment (years)** | | | <0.001 |
| **66-70** | 109 (9.5%) | 319 (15.4%) | |
| **71-75** | 247 (21.6%) | 480 (23.1%) | |
| **76-80** | 295 (25.8%) | 523 (25.2%) | |
| **≥80** | 494 (43.1%) | 753 (36.3%) | |
| **Sex** | | | 0.0019 |
| **Male** | 778 (67.9%) | 1,517 (73.1%) | |
| **Female** | 367 (32.1%) | 558 (26.9%) | |
| **Year of ICI** | | | <0.001 |
| **2011-2014** | 201 (17.6%) | 558 (26.9%) | |
| **2015-2016** | 348 (30.4%) | 534 (25.7%) | |
| **2017-2019** | 596 (52.1%) | 983 (47.4%) | |
| **Charlson Comorbidity Index** | | | <0.001 |
| **0** | 285 (24.9%) | 853 (41.1%) | |
| **1-2** | 493 (43.1%) | 835 (40.2%) | |
| **≥3** | 367 (32.1%) | 387 (18.7%) | |
| **ICI Therapy** | | | 0.6851 |
| **Monotherapy** | 242 (21.1%) | 426 (20.5%) | |
| **Combination** | 903 (78.9%) | 1,649 (79.5%) | |

**TABLE 2. RELATIVE RISK OF ICI DISCONTINUATION**

| Characteristic | | Hazard Ratios | 95% Confidence Limits | |
|---|---|---|---|---|
| **Age Group at first ICI treatment (years)** | 71-75 vs 66-70 | 0.81 | 0.62 | 1.07 |
| | 76-80 vs 66-70 | 0.83 | 0.62 | 1.12 |
| | ≥80 vs 66-70 | 0.89 | 0.67 | 1.18 |
| **Charlson Comorbidity Index** | Score 1-2 vs Score 0 | 0.97 | 0.79 | 1.19 |
| | Score ≥3 vs Score 0 | 0.78 | 0.59 | 1.03 |
| **ICI Therapy** | Combination vs Monotherapy | **8.86** | **7.12** | **11.02** |
| **Year of ICI Treatment** | 2015-2016 vs 2011--2014 | **0.54** | **0.44** | **0.67** |
| | 2017-2019 vs 2011- 2014 | **0.26** | **0.21** | **0.34** |
| **Autoimmune Disease** | Yes vs No | 1.19 | 0.97 | 1.45 |

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**FIG. 1: CUMULATIVE RISK OF ICI DISCONTINUATION IN PATIENTS WITH ICI COMBINATION AND MONOTHERAPY**

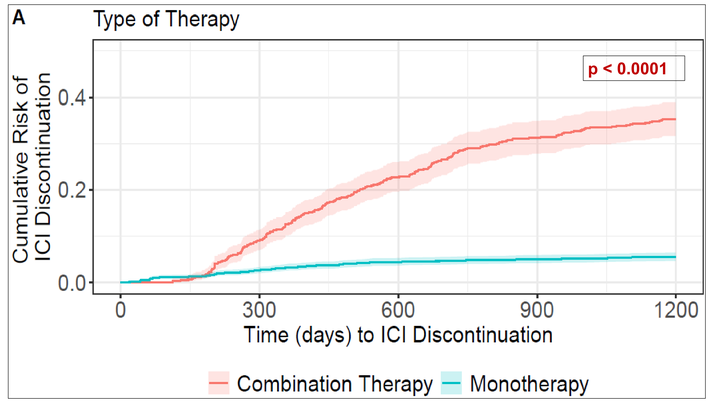
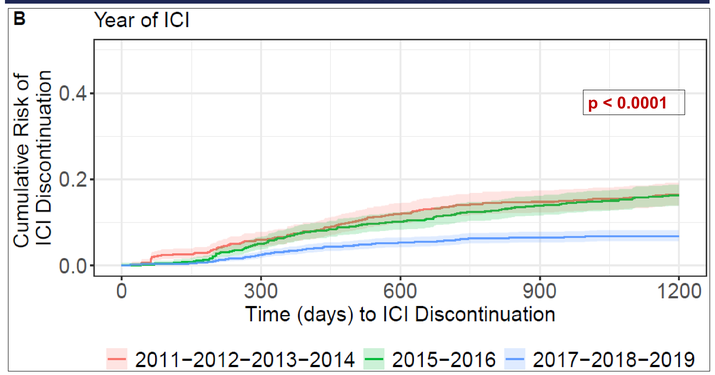



**FIG. 2: CUMULATIVE RISK OF ICI DISCONTINUATION BY YEAR OF ICI INITIATION**




## CONCLUSIONS

- Key factors associated with the risk of ICI discontinuation included the type of ICI therapy (Monotherapy vs. Combination) and the year of ICI therapy initiation.
- Patients receiving combination therapy had higher discontinuation rates and discontinued treatment earlier.
- The risk of ICI discontinuation was significantly lower in the patients initiating therapy in later years (2015–2019), suggesting improved treatment delivery, adverse event management, and greater physician knowledge.
- Age, Pre-existing AID status, and comorbidity had no significant impact on ICI discontinuation.

**Next Steps**

- We plan to differentiate adverse event–related ICI discontinuation from planned ICI treatment completion in future analyses.

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