Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.
eFigure1. Selection of analytic cohort.
The starting year (2011) corresponds to the first immune checkpoint inhibitor approved for melanoma in the US. Numbers shown next to the arrows are the exclusions at each step. *Or coverage until death for people who survived < 12 months. Stage I excluded because <1% of these patients received an ICI.
**eTable 1.** Healthcare Common Procedure Coding System (HCPCS) and International Classification of diseases-9th revision (ICD-9) codes for identifying immunotherapy, chemotherapy, and radiotherapy from Medicare claims

| A. Immunotherapy | Codes |
|------------------|-------|
| **Checkpoint inhibitors** | |
| Avelumab | C9491 |
| Atezolizumab | C9483 |
| Imlygic | C9472 |
| Ipilimumab | C9284, J9228 |
| Nivolumab | C9453, J9299 |
| Pembrolizumab | C9027, J9271 |
| Durvalumab | C9492 |
| **Cytokines** | |
| Denileukin | C1084, J9160 |
| IFN2A | J9213 |
| IFN2B | J9214 |
| IFNG2B | J9216 |
| IFNAIphacon | J9212 |
| IFN3 | J9215 |
| IL2 | 00.15 (ICD-9 procedure), J9015 |
| PegIFN2A | S0145 |
| PegIFN2B | S0146, S0148 |
| **Other/unspecified** | |
| BCG | C9416, J9031 |
| TVEC | C9472, J9325 |
| Unspecified | 99.28 (ICD-9 procedure), S2107, V58.12 (ICD-9 diagnostic) |

| B. Chemotherapy | Codes |
|-----------------|-------|
| Ado-trastuzumab emtansine | C9131, J9354 |
| Aflibercept | J0178, J9400, Q2046 |
| Alemtuzumab | C9110, J9010, S0087 |
| Arsenic | C9012, J9017 |
| Asparaginase | J9019, J9020 |
| Azacitidine | J9025, C9218 |
| Belinostat | J9032 |
| Bendamustine | J9033 |
| Bevacizumab | C9214, C9257, J9035, Q2024, S0116 |
| Bleomycin | C9417, J9040 |
| Blinatumomab | J9039 |
| Bortezomib | C9207, J9041, S0115 |
| Brentuximab | C9287, J9042 |
| Drug                  | J0 Codes               |
|-----------------------|------------------------|
| Busulfan              | C1178, J0594, J8510    |
| Cabazitaxel           | J9043                  |
| Capecitabine          | J8520, J8521           |
| Carboplatin           | J9045                  |
| Carfilzomib           | J9047                  |
| Carmustine            | C9437, J9050           |
| Cetuximab             | C9215, J9055           |
| Chlorambucil          | S0172                  |
| Cisplatin             | C9418, J9060, J9062    |
| Cladribine            | C9419, J9065           |
| Clofarabine           | J9027                  |
| Cyclophosphamide      | C9420, C9421, J8530, J9070, J9080, J9090, J9091, J9092, J9093, J9094, J9095, J9096, J9097 |
| Cytarabine            | C1166, C9422, J9098, J9100, J9110 |
| Dacarbazine           | C9423, J9130, J9140    |
| Dactinomycin          | J9120                  |
| Daunorubicin          | C9424, J9150, J9151    |
| Decitabine            | J0894                  |
| Docetaxel             | J9170, J9171           |
| Doxorubicin           | C9415, J9000, J9001, J9002, Q2048, Q2049, Q2050 |
| Epirubicin            | C1167, J9178, J9180    |
| Eribulin              | J9179                  |
| Etoposide             | C9414, C9425, J8560, J9181, J9182 |
| Everolimus            | J7527, J8561           |
| Fludarabine           | C9262, J8562, J9185    |
| Fluorouracil          | J9190                  |
| Gefitinib             | J8565                  |
| Gemcitabine           | J9201                  |
| Gemtuzumab            | C9004, J9300           |
| Hydroxyurea           | S0176                  |
| Idarubicin            | C9429, J9211           |
| Ifosfamide            | C9427, J9208           |
| Imatinib              | S0088                  |
| Irinotecan            | J9206                  |
| Ixabepilone           | J9207                  |
| Leucovorin            | J0640                  |
| Levroleucovorin       | J0641                  |
| Lomustine             | S0178                  |
| Mechlorethamine       | J9230                  |
| Melphalan             | J8600, J9245           |
| Methotrexate          | J8610, J9250, J9260    |
| Mitomycin             | C9432, J9280, J9290, J9291 |
| Mitoxantrone          | J9293                  |

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| Medication                        | Code(s)  |
|----------------------------------|----------|
| Nelarabine                       | J9261    |
| Obinutuzumab                     | J9301    |
| Ofatumumab                       | J9302    |
| Omacetaxine                      | J9262    |
| Oxaliplatin                      | C9205, J9263 |
| Paclitaxel                       | C9431, J9264, J9265, J9267, C9127 |
| Panitumumab                      | C9235, J9303 |
| Pegasparagase                    | J9266    |
| Pemetrexed                       | C9213, J9305 |
| Pentostatin                      | J9268    |
| Pertuzumab                       | J9306    |
| Plicamycin                       | J9270    |
| Pralatrexate                     | J9307    |
| Procarbazine                     | S0182    |
| Ramucirumab                      | J9308    |
| Rituximab                        | J9310    |
| Romidepsin                       | C9265, J9315 |
| Sipuleucel                       | Q2043    |
| Streptozocin                     | J9320    |
| Temozolomide                     | C1086, J8700, J9328 |
| Temsirolimus                     | J9330    |
| Teniposide                       | Q2017    |
| Thiotepa                         | C9433, J9340 |
| Topotecan                        | J8705, J9350, J9351 |
| Trastuzumab                      | J9355    |
| Valrubicin                       | J9357    |
| Vinblastine                      | J9360    |
| Vincristine                      | J9370, J9371, J9375, J9380 |
| Vinorelbine                      | C9440, J9390 |

**C. Radiotherapy**

**ICD-9 codes**

- Diagnostic: V58.0, V67.1
- Procedure: 92.21-92.29

**HCPCS Codes**

- 77261-77299, 77300-77399, 77401-77499, 77520, 77523, 76370, 76950, 77750-77799, C1325, C1348, C1350, C1700-C1712, C1715-C1720, C1728, C1790-C1806, C2616, C2632, C2633, C9714, C9715, G0174, G0178, G0179, G0261, G0256, G0273, G0274, G0338-G0340

a. Medicare claims files (MEDPAR, Carrier claims (NCH), OUTPT, and DME) searched beginning 90 days prior to diagnosis of first primary melanoma
b. HCPCS unless otherwise specified
**eTable 2.** International Classification of diseases-9th revision (ICD-9) codes for identifying immune-related adverse events (AEs)\(^a\)

| Designation: Chronic or transient\(^b\) | ICD-9 Codes |
|----------------------------------------|-------------|
| **I. Autoimmune-related AEs**          |             |
| Systemic/Connective tissue             | Chronic     |
| Ankylosing spondylitis                 | Chronic     | 720.0 |
| Dermatomyositis/polymyositis           | Chronic     | 710.3, 710.4 |
| Felty's syndrome                       | Chronic     | 714.1 |
| Systemic lupus erythematosus           | Chronic     | 710.0 |
| Polymyalgia rheumatica                 | Chronic     | 725 |
| Reactive arthritis                     | Chronic     | 99.3 |
| Rheumatoid arthritis                   | Chronic     | 714.0, 714.2 |
| Sarcoidosis                            | Chronic     | 135 |
| Sjogren’s syndrome                     | Chronic     | 710.2 |
| Systemic sclerosis/scleroderma         | Chronic     | 710.1 |
| Cardiovascular                         | Chronic     |     |
| Giant cell arteritis                   | Chronic     | 446.5 |
| Polyarteritis nodosa and allied conditions (systemic vasculitis) | Chronic | 446, 447.6 |
| Endocrine                              | Chronic     |     |
| Primary adrenal insufficiency          | Chronic     | 255.4 |
| Chronic thyroiditis/Hashimoto thyroiditis | Chronic     | 245.2 |
| Primary biliary cirrhosis              | Chronic     | 571.6 |
| Autoimmune hepatitis                   | Chronic     | 571.42 |
| Skin                                   | Chronic     |     |
| Alopecia areata                        | Chronic     | 704.01 |
| Dermatitis herpetiformis and other bullous dermatoses | Chronic | 694\(^c\) |
| Discoid lupus                          | Chronic     | 695.4 |
| Localized scleroderma and other hypertrophic and atrophic conditions of skin | Chronic | 701.0, 701.2, 701.3 |
| Psoriasis and similar disorders        | Chronic     | 696\(^c\) |
| Gastrointestinal                       | Chronic     |     |
| Celiac disease                         | Chronic     | 579.0 |
| Regional enteritis/Crohn’s disease     | Chronic     | 555\(^c\) |
| Pernicious anemia                      | Chronic     | 281.0 |
### Ulcerative Colitis
- **Category:** Chronic
- **Code:** 556c

### Hematologic
- **Autoimmune hemolytic anemia**
- **Category:** Chronic
- **Code:** 283.0

- **Immune thrombocytopenic purpura**
- **Category:** Chronic
- **Code:** 287.31

### Nervous System
- **Multiple sclerosis**
- **Category:** Chronic
- **Code:** 340

- **Guillain-Barre syndrome**
- **Category:** Chronic
- **Code:** 357.0

- **Myasthenia gravis**
- **Category:** Chronic
- **Code:** 358.0

### Miscellaneous
- **Asthma**
- **Category:** Chronic
- **Code:** 493c

- **Autoimmune disease, not otherwise specified**
- **Category:** Chronic
- **Code:** 279.4

### II. Other immune-related AEs

#### Cardiovascular
- **Myocarditis (includes acute, subacute)**
- **Category:** Transient
- **Code:** 422.0, 422.9, 429.0

- **Pericarditis**
- **Category:** Transient
- **Code:** 420c

#### Endocrine
- **Cushing's syndrome**
- **Category:** Chronic
- **Code:** 255.0

- **Thyrotoxicosis with or without goiter (hyperthyroidism)**
- **Category:** Chronic
- **Code:** 242c

- **Hypopituitarism**
- **Category:** Chronic
- **Code:** 253.2, 253.7

- **Hypothyroidism**
- **Category:** Chronic
- **Code:** 244c

- **Thyroiditis (acute thyroiditis, subacute thyroiditis, iatrogenic thyroiditis, thyroiditis unspecified)**
- **Category:** Chronic
- **Code:** 245.1, 245.4, 245.9

- **Other disorders of the pituitary gland (includes hypophysitis)**
- **Category:** Chronic
- **Code:** 253.8

#### Eye
- **Ocular myositis**
- **Category:** Transient
- **Code:** 376.1

- **Optic neuritis**
- **Category:** Transient
- **Code:** 377.3

- **Uveitis and Iritis**
- **Category:** Transient
- **Code:** 364.0, 360.11

#### Gastrointestinal
- **Gastroenteritis and colitis excluding ulcerative colitis**
- **Category:** Transient
- **Code:** 009.0, 009.1, 558

- **Diarrhea**
- **Category:** Transient
- **Code:** 787.9

- **Pancreatitis**
- **Category:** Transient
- **Code:** 577.0, 577.1

- **Stomatitis and mucositis (includes ulcerative, aphthous)**
- **Category:** Transient
- **Code:** 528.0, 528.2

- **Hepatitis (chronic hepatitis unspecified, chronic persistent hepatitis)**
- **Category:** Chronic
- **Code:** 573.3, 571.40

- **Myalgia and myositis, not otherwise specified**
- **Category:** Transient
- **Code:** 729.1
| Condition                                      | Status     | ICD Codes |
|-----------------------------------------------|------------|-----------|
| Pneumonitis                                   | Transient  | 516.32, 516.33 |
| Vitiligo                                      | Chronic    | 709.01    |
| Septicemia, sepsis, septic shock              | Transient  | 785.52, 995.9 |

a. For each outcome, we identified the first claim [Claim types: MEDPAR, Carrier claims (NCH), OUTPT, and DME] at or before 1st primary melanoma diagnosis as well as the first claim after first primary melanoma diagnosis.
b. Immune-related AEs were designated as "chronic" or "transient". For chronic diseases, it is assumed that an individual can only have one incident diagnosis per lifetime. For transient diseases, it is assumed that an individual can have multiple independent events in the lifetime.
c. Includes all codes beyond the decimal point.
d. Although not typically considered among immune-related AEs, we included this as rare events have been reported after immune checkpoint inhibitors (Reference 20 in the main text).
e. Although not typically considered among immune-related AEs, we included this as rare events have been reported after immune checkpoint inhibitors (References 2,3 in the main text).
### eTable 3. Hazard ratios for selected immune-related adverse events (AEs) after ipilimumab only and after any immune checkpoint inhibitor (ICI) - among patients diagnosed with stages III-IV melanoma, by time since first ICI, and by baseline history of autoimmune disease*  

|                          | After ipilimumab – all patients | After any ICI – restricted to stages III-IV melanoma | By time since first ICI claim – all patients | By baseline history of autoimmune disease – all patients |
|--------------------------|---------------------------------|-----------------------------------------------------|---------------------------------------------|-----------------------------------------------------|
|                          | HR (95% CI)b                    | HR (95% CI)b                                       | HR (95% CI)b c                             | HR (95% CI)b e                                      | P het^d                               |
| I. Autoimmune-related AEs|                                 |                                                    |                                             |                                                    |                                      |
| Endocrine                | 2.7 (1.7-4.3)                   | 1.8 (1.0-3.2)                                      | 3.2 (2.0-5.2)                              | 1.4 (0.7-2.9)                                      | 0.02                                 |
| Primary adrenal insufficiency | 9.1 (4.4-18.6)                 | 6.7 (2.9-15.6)                                    | 9.2 (4.3-19.7)                             | 8.1 (3.5-19.1)                                     | 0.75                                 |
| Gastrointestinal         | 3.7 (1.7-8.0)                   | 2.7 (1.0-7.1)                                      | 5.7 (2.7-12.0)                             | N.E.                                               | <0.001                               |
| Ulcerative colitis       | 8.8 (2.9-26.5)                  | 5.2 (1.3-21.7)                                    | 15.8 (5.3-47.1)                            | N.E.                                               | <0.001                               |
| II. Other immune-related AEs | 2.2 (1.8-2.9)                   | 1.9 (1.4-2.6)                                      | 3.0 (2.3-3.8)                              | 0.7 (0.4-1.1)                                      | <0.001                               |
| Endocrine                | 3.3 (2.0-5.2)                   | 3.2 (1.8-5.6)                                      | 4.9 (3.1-7.7)                              | 1.1 (0.5-2.3)                                      | <0.001                               |
| Hypopituitarism          | 20.4 (5.6-74.3)                 | 14.9 (3.4-66.1)                                   | 24.8 (6.4-95.6)                            | 12.5 (2.6-61.1)                                    | 0.31                                 |
| Hypothyroidism           | 3.8 (2.4-6.1)                   | 3.8 (2.2-6.8)                                      | 5.5 (3.5-8.7)                              | 1.5 (0.8-3.1)                                      | <0.001                               |
| Gastrointestinal         | 3.2 (2.3-4.3)                   | 2.5 (1.7-3.7)                                      | 5.1 (3.7-7.0)                              | 0.6 (0.3-1.2)                                      | <0.001                               |
| Diarrhea                 | 3.8 (2.7-5.2)                   | 3.4 (2.2-5.2)                                      | 5.9 (4.2-8.3)                              | 0.7 (0.3-1.4)                                      | <0.001                               |
| Myalgia and myositis, nos | 1.1 (0.6-2.3)                   | 1.4 (0.6-3.1)                                      | 2.2 (1.1-4.3)                              | N.E.                                               | 0.02                                 |
| Septicemia, sepsis       | 2.2 (1.4-3.4)                   | 1.9 (1.2-3.1)                                      | 3.3 (2.1-5.1)                              | 0.9 (0.5-1.7)                                      | <0.001                               |

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Abbreviations: ICI, immune checkpoint inhibitor; AE, adverse event; HR, hazard ratio; CI, confidence interval; N.E., not estimated; NOS, not otherwise specified

a. Study population restricted to white patients diagnosed with AJCC stage II-IV (or unknown stage) cutaneous melanoma during 2011-2015 as identified in SEER-Medicare linked database. Selected outcomes include those with at least 11 events after ICIs from the full analysis presented in Table 2.

b. Hazard ratios (HRs) and 95% Confidence intervals (CIs) estimated from multivariable Cox Proportional hazards regression with person-years as the time scale and stratified by calendar year of melanoma diagnosis. All models adjusted for age at melanoma diagnosis (66-69, 70-74, 75-79,80-84), sex, stage at melanoma diagnosis, NCI comorbidity index, (0, >0-1 - <1.69, 1.69+; cutpoints derived from individuals with non-zero values), and time-dependent variables for history of autoimmune and non-autoimmune disease; chemotherapy, radiotherapy, and other types of immunotherapy. Models of transient outcomes further adjusted for baseline history of that disease. HRs suppressed if N < 5.

c. HRs by time since first receipt of ICI include the variables described in b and a time-dependent variable for ICI classified as none, <6 months since first claim and 6+ months since first claim.

d. P-value for heterogeneity by time since first ICI based on likelihood ratio test comparing models b and c.

e. HRs by baseline history of autoimmune disease estimated from model described in b with the addition of a main effect for baseline history of autoimmune disease and interaction term between ICI and baseline history of autoimmune disease.

f. P-value for heterogeneity by baseline history of autoimmune disease based on likelihood ratio test comparing model b (with additional parameter for baseline history of autoimmune disease and model e.
**eTable 4.** Cumulative incidence of selected immune-related adverse events (AEs) by time (years) accounting for competing risk of death.

| Event                  | After ICI<sup>a</sup> | No ICI/Prior to ICI<sup>b</sup> |
|------------------------|------------------------|---------------------------------|
|                        | Cumulative incidence (95% CI) | Cumulative incidence (95% CI) |
|                        | 6 months | 1 year | 2 years | 6 months | 1 year | 2 years |
| A. Total study population |          |        |         |          |        |         |
| Autoimmune-related AEs | 13.7 (9.7-18.3) | 18.5 (13.7-23.8) | 20.9 (15.6-26.8) | 4.5 (3.8-5.3) | 7.0 (6.1-8.1) | 11.0 (9.7-12.4) |
| Primary adrenal insufficiency | 4.5 (2.8-7.0) | 8.0 (5.4-11.3) | 10.5 (7.3-14.5) | 0.4 (0.2-0.6) | 0.6 (0.4-0.9) | 1.1 (0.8-1.5) |
| Ulcerative colitis | 3.7 (2.1-6.0) | 3.7 (2.1-6.0) | 4.3 (2.5-7.0) | 0.2 (0.1-0.4) | 0.3 (0.2-0.6) | 0.6 (0.4-1.0) |
| Other immune-related AEs | 46.8 (40.7-52.7) | 52.0 (45.7-57.9) | 55.0 (48.3-61.1) | 24.3 (23.0-25.6) | 32.7 (31.2-34.2) | 43.1 (41.4-44.9) |
| Diarrhea | 23.3 (19.1-27.8) | 25.2 (20.8-29.9) | 27.1 (22.3-32.1) | 3.4 (2.9-4.0) | 5.9 (5.2-6.7) | 10.4 (9.3-11.5) |
| Hypothyroidism | 16.6 (12.3-21.5) | 21.0 (16.1-26.3) | 23.2 (17.8-29.0) | 3.1 (2.5-3.8) | 5.2 (4.4-6.1) | 9.0 (7.8-10.3) |
| Hypopituitarism | 2.5 (1.2-4.5) | 4.0 (2.2-6.5) | 4.5 (2.5-7.3) | 0.1 (0.1-0.3) | 0.2 (0.1-0.4) | 0.3 (0.1-0.5) |
| Septicemia, sepsis | 12.1 (9.0-15.6) | 14.1 (10.8-17.9) | 17.3 (13.3-21.8) | 2.8 (2.3-3.3) | 4.3 (3.7-5.0) | 7.0 (6.1-7.9) |

B. Restricted to patients diagnosed with AJCC Stages III-IV melanoma

| Event                  | After ICI<sup>a</sup> | No ICI/Prior to ICI<sup>b</sup> |
|------------------------|------------------------|---------------------------------|
|                        | Cumulative incidence (95% CI) | Cumulative incidence (95% CI) |
|                        | 6 months | 1 year | 2 years | 6 months | 1 year | 2 years |
| Autoimmune-related AEs | 11.0 (6.9-16.3) | 17.7 (12.1-24.1) | 20.9 (14.6-28.0) | 5.5 (4.2-7.2) | 7.7 (6.0-9.7) | 12.4 (10.0-15.2) |
| Primary adrenal insufficiency | 2.8 (1.3-5.3) | 7.0 (4.2-10.7) | 9.6 (6.0-14.1) | 0.5 (0.2-1.1) | 0.6 (0.3-1.3) | 1.4 (0.7-2.4) |
| Ulcerative colitis | 2.9 (1.4-5.5) | 2.9 (1.4-5.5) | 3.7 (1.8-6.9) | 0.1 (0.0-0.4) | 0.3 (0.1-0.8) | 0.6 (0.2-1.3) |
| Other immune-related AEs | 46.0 (38.8-52.9) | 51.3 (43.8-58.3) | 54.4 (46.5-61.5) | 27.3 (24.8-29.9) | 34.7 (31.9-37.5) | 45.5 (42.2-48.8) |
| Diarrhea | 23.7 (18.7-29.0) | 25.8 (20.6-31.3) | 27.2 (21.7-32.9) | 4.5 (3.4-5.8) | 6.8 (5.4-8.4) | 11.6 (9.5-13.9) |
| Hypothyroidism | 16.6 (11.6-22.5) | 20.5 (14.9-26.8) | 23.4 (17.2-30.3) | 3.9 (2.7-5.3) | 6.0 (4.4-7.8) | 10.5 (8.1-13.2) |
| Hypopituitarism | 2.6 (1.2-5.1) | 4.1 (2.1-7.2) | 4.1 (2.1-7.2) | 0.4 (0.1-0.9) | 0.6 (0.2-1.2) | 0.7 (0.3-1.4) |
| Septicemia, sepsis | 12.5 (9.0-16.7) | 14.8 (10.8-19.3) | 16.9 (12.4-21.9) | 5.4 (4.2-6.8) | 7.5 (6.0-9.1) | 9.8 (8.0-11.9) |

**Abbreviations:** ICI, immune checkpoint inhibitor; adverse events, AEs; CI, confidence interval

<sup>a</sup> Cumulative incidence after ICI captures person-time beginning at date of first ICI claim and continues until earliest of the event of interest or end of follow-up as defined in the text.

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b. Cumulative incidence in the "no ICI/prior to ICI" group captures person-time from date of melanoma diagnosis until first ICI claim (for those who received an ICI), event of interest, or end of follow-up as defined in the text. Cumulative incidence in the absence of ICI is provided for perspective but it should be noted that the curves have different time scales and are not adjusted for differences between the populations and should therefore be interpreted cautiously.
eFigure 2. Cumulative incidence of selected autoimmune- and other- immune-related adverse events (AEs) among patients diagnosed with stages III-IV cutaneous melanoma, accounting for competing risk of death, by receipt of immune checkpoint inhibitors (ICIs).a

A. Autoimmune-related AEs

B. Primary adrenal insufficiency

C. Ulcerative colitis

D. CI of other irAEs

E. Diarrhea

F. Sepsis/septicemia

G. Hypopituitarism

H. Hypothyroidism

No. at risk
ICI 189 90 44 22
No/prior ICI 947 558 374 282

No. at risk
ICI 300 153 82 41
No/prior ICI 1329 815 554 424

No. at risk
ICI 297 151 86 48
No/prior ICI 1320 813 554 425

No. at risk
ICI 281 111 60 36
No/prior ICI 1336 792 528 397

No. at risk
ICI 285 142 82 46
No/prior ICI 1335 794 537 410

No. at risk
ICI 300 152 84 25
No/prior ICI 1334 818 557 429

No. at risk
ICI 197 83 46 25
No/prior ICI 932 559 364 274

No. at risk
ICI 197 83 46 25
No/prior ICI 932 559 364 274

a. See eTable 2 for definition of autoimmune- (panels A-C) and other- (panels D-H) immune-related AEs. Below each figure, “Number at risk” specifies the number of people at-risk at the start of each time interval. Small numbers suppressed for privacy. Cumulative incidence in the absence of immune checkpoint inhibitors (ICl) is provided for perspective but it should be noted that the curves have different time scales and are not adjusted for differences between the populations and should therefore be interpreted cautiously. See Supplement eTable 4 for point estimates and 95% confidence bounds. Individuals with a previous claim (at/prior to melanoma diagnosis) were excluded from analyses of autoimmune immune-related AEs (overall), primary adrenal insufficiency, ulcerative colitis, hypothyroidism, and hypopituitarism, as described in online eTable 2. For all outcomes, the number at risk at the start of an interval excludes people who had the event earlier in follow-up or died or ended follow-up prior to the start of the interval.