

Table S1. Procedure codes for Immune Checkpoint Inhibitors (ICIs)

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|--|-------|--|
| ICI procedure codes | | |
| HCPCS | C9027 | Injection, pembrolizumab, 1 mg (deprecated 2015) |
| HCPCS | C9453 | Injection, nivolumab, 1 mg (deprecated 2015) |
| HCPCS | C9483 | Injection, atezolizumab, 10 mg (deprecated 2017) |
| HCPCS | C9491 | Injection, avelumab, 10 mg (deprecated 2017) |
| HCPCS | C9492 | Injection, durvalumab, 10 mg (deprecated 2018) |
| HCPCS | J9022 | Injection, atezolizumab, 10 mg |
| HCPCS | J9023 | Injection, avelumab, 10 mg |
| HCPCS | J9228 | Injection, ipilimumab, 1 mg |
| HCPCS | J9271 | Injection, pembrolizumab, 1 mg |
| HCPCS | J9299 | Injection, nivolumab, 1 mg |
| General chemotherapy administration procedure codes | | |
| CPT | 96401 | Chemotherapy administration, subcutaneous or intramuscular; non-hormonal anti-neoplastic |
| CPT | 96405 | Chemotherapy administration; intralesional, up to and including 7 lesions |
| CPT | 96409 | Chemotherapy administration; intravenous, push technique, single or initial substance/drug |
| CPT | 96411 | Chemotherapy administration; intravenous, push technique, each additional substance/drug (List separately in addition to code for primary procedure) |
| CPT | 96413 | Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug |

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|-------|-------|--|
| CPT | 96415 | Chemotherapy administration, intravenous infusion technique; each additional hour (List separately in addition to code for primary procedure) |
| CPT | 96416 | Chemotherapy administration, intravenous infusion technique; initiation of prolonged chemotherapy infusion (more than 8 hours), requiring use of a portable or implantable pump |
| CPT | 96417 | Chemotherapy administration, intravenous infusion technique; each additional sequential infusion (different substance/drug), up to 1 hour (List separately in addition to code for primary procedure) |
| HCPCS | G0498 | Chemotherapy administration, intravenous infusion technique; initiation of infusion in the office/clinic setting using office/clinic pump/supplies, with continuation of the infusion in the community setting (e.g., home, domiciliary, rest home or assisted living) using a portable pump provided by the office/clinic, includes follow up office/clinic visit at the conclusion of the infusion |
| HCPCS | Q0084 | Chemotherapy administration by infusion technique only, per visit |
| HCPCS | J9999 | Antineoplastic drugs, not otherwise classified |

Table S2. Patient Characteristics by First ICI treatment

| | Fist ICI treatment | | | | | | | | | | | | | | | | p-value |
|---|--------------------|-------|-----------|--------|------------|-------|------------|-------|------------|-------|-------------|-------|---------------|-------|-----------------|-------|---------|
| | Atezolizumab | | Avelumab | | Cemiplimab | | Durvalumab | | Ipilimumab | | Nivolumab | | Pembrolizumab | | Combo (nip+niv) | | |
| Total, n | 201 | | 29 | | 21 | | 56 | | 470 | | 1766 | | 2505 | | 468 | | |
| Age at ICI Initiation | | | | | | | | | | | | | | | | | <.0001 |
| 18-44 | 6 | 3.0% | 1 | 3.4% | 3 | 14.3% | 0 | 0.0% | 76 | 16.2% | 140 | 7.9% | 215 | 8.6% | 86 | 18.4% | |
| 45-54 | 17 | 8.5% | 0 | 0.0% | 1 | 4.8% | 1 | 1.8% | 95 | 20.2% | 236 | 13.4% | 321 | 12.8% | 80 | 17.1% | |
| 55-64 | 62 | 30.8% | 9 | 31.0% | 5 | 23.8% | 18 | 32.1% | 113 | 24.0% | 546 | 30.9% | 746 | 29.8% | 156 | 33.3% | |
| 65-74 | 77 | 38.3% | 11 | 37.9% | 4 | 19.0% | 25 | 44.6% | 127 | 27.0% | 548 | 31.0% | 771 | 30.8% | 116 | 24.8% | |
| >=75 | 39 | 19.4% | 9 | 31.0% | 8 | 38.1% | 12 | 21.4% | 59 | 12.6% | 296 | 16.8% | 452 | 18.0% | 30 | 6.4% | |
| Sex | | | | | | | | | | | | | | | | | <.0001 |
| F | 98 | 48.8% | 13 | 44.8% | 3 | 14.3% | 21 | 37.5% | 182 | 38.7% | 749 | 42.4% | 1086 | 43.4% | 189 | 40.4% | |
| M | 103 | 51.2% | 16 | 55.2% | 18 | 85.7% | 35 | 62.5% | 288 | 61.3% | 1017 | 57.6% | 1419 | 56.6% | 279 | 59.6% | |
| Hispanic | | | | | | | | | | | | | | | | | 0.0354 |
| Yes | 6 | 3.0% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 8 | 1.7% | 58 | 3.3% | 84 | 3.4% | 10 | 2.1% | |
| No | 184 | 91.5% | 29 | 100.0% | 20 | 95.2% | 53 | 94.6% | 454 | 96.6% | 1544 | 87.4% | 2316 | 92.5% | 435 | 92.9% | |
| Unknown | 11 | 5.5% | 0 | 0.0% | 1 | 4.8% | 3 | 5.4% | 8 | 1.7% | 164 | 9.3% | 105 | 4.2% | 14 | 3.0% | |
| Race | | | | | | | | | | | | | | | | | <.0001 |
| American Indian or Alaska Native | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 2 | 0.1% | 7 | 0.3% | 2 | 0.4% | |
| Asian | 3 | 1.5% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 2 | 0.4% | 23 | 1.3% | 40 | 1.6% | 4 | 0.9% | |
| Black or African American | 20 | 10.0% | 1 | 3.4% | 0 | 0.0% | 1 | 1.8% | 4 | 0.9% | 170 | 9.6% | 171 | 6.8% | 15 | 3.2% | |
| Native Hawaiian/Other Pacific Islander | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 1 | 0.1% | 5 | 0.2% | 0 | 0.0% | |
| Unknown | 10 | 5.0% | 0 | 0.0% | 2 | 9.5% | 1 | 1.8% | 9 | 1.9% | 84 | 4.8% | 120 | 4.8% | 17 | 3.6% | |
| White | 168 | 83.6% | 28 | 96.6% | 19 | 90.5% | 54 | 96.4% | 455 | 96.8% | 1486 | 84.1% | 2162 | 86.3% | 430 | 91.9% | |
| Charlson Comorbidity Index¹ | | | | | | | | | | | | | | | | | <.0001 |
| 0 | 51 | 25.4% | 9 | 31.0% | 9 | 42.9% | 12 | 21.4% | 263 | 56.0% | 646 | 36.6% | 903 | 36.0% | 210 | 44.9% | |
| 1 | 46 | 22.9% | 9 | 31.0% | 1 | 4.8% | 16 | 28.6% | 132 | 28.1% | 442 | 25.0% | 656 | 26.2% | 113 | 24.1% | |

| | | | | | | | | | | | | | | | | | |
|--|-----|-------|----|-------|----|-------|----|-------|-----|-------|------|-------|------|-------|-----|-------|--------|
| 2 | 50 | 24.9% | 5 | 17.2% | 1 | 4.8% | 14 | 25.0% | 39 | 8.3% | 276 | 15.6% | 429 | 17.1% | 67 | 14.3% | |
| ≥3 | 54 | 26.9% | 6 | 20.7% | 10 | 47.6% | 14 | 25.0% | 36 | 7.7% | 402 | 22.8% | 517 | 20.6% | 78 | 16.7% | |
| Comorbidities¹ | | | | | | | | | | | | | | | | | |
| AIDS/HIV | 0 | 0.0% | 0 | 0.0% | 1 | 4.8% | 0 | 0.0% | 3 | 0.6% | 18 | 1.0% | 9 | 0.4% | 2 | 0.4% | 0.0275 |
| Cerebrovascular disease | 21 | 10.4% | 5 | 17.2% | 3 | 14.3% | 8 | 14.3% | 37 | 7.9% | 170 | 9.6% | 296 | 11.8% | 45 | 9.6% | 0.0911 |
| Congestive heart failure | 10 | 5.0% | 0 | 0.0% | 0 | 0.0% | 1 | 1.8% | 3 | 0.6% | 62 | 3.5% | 21 | 0.8% | 68 | 14.5% | 0.0069 |
| Chronic pulmonary disease | 70 | 34.8% | 6 | 20.7% | 4 | 19.0% | 36 | 64.3% | 59 | 12.6% | 543 | 30.7% | 685 | 27.3% | 85 | 18.2% | <.0001 |
| Dementia | 0 | 0.0% | 0 | 0.0% | 1 | 4.8% | 0 | 0.0% | 0 | 0.0% | 10 | 0.6% | 20 | 0.8% | 0 | 0.0% | 0.0246 |
| Diabetes without chronic complication | 25 | 12.4% | 5 | 17.2% | 3 | 14.3% | 8 | 14.3% | 45 | 9.6% | 148 | 8.4% | 261 | 10.4% | 42 | 9.0% | 0.1528 |
| Diabetes with chronic complication | 19 | 9.5% | 2 | 6.9% | 4 | 19.0% | 3 | 5.4% | 11 | 2.3% | 6 | 0.3% | 137 | 5.5% | 24 | 5.1% | 0.0015 |
| Diabetes secondary to drug use | 7 | 3.5% | 0 | 0.0% | 1 | 4.8% | 0 | 0.0% | 1 | 0.2% | 21 | 1.2% | 28 | 1.1% | 4 | 0.9% | 0.0149 |
| Any diabetes ² | 47 | 23.4% | 7 | 24.1% | 7 | 33.3% | 11 | 19.6% | 56 | 11.9% | 255 | 14.4% | 402 | 16.0% | 67 | 14.3% | 0.001 |
| Hemiplegia/paraplegia | 5 | 2.5% | 0 | 0.0% | 0 | 0.0% | 2 | 3.6% | 2 | 0.4% | 34 | 1.9% | 62 | 2.5% | 9 | 1.9% | 0.1671 |
| Metastatic solid tumor | 183 | 91.0% | 25 | 86.2% | 16 | 76.2% | 43 | 76.8% | 432 | 91.9% | 1444 | 81.8% | 2168 | 86.5% | 427 | 91.2% | <.0001 |
| Myocardial infarction | 6 | 3.0% | 1 | 3.4% | 0 | 0.0% | 1 | 1.8% | 3 | 0.6% | 57 | 3.2% | 69 | 2.8% | 9 | 1.9% | 0.1135 |
| Mild liver disease | 56 | 27.9% | 6 | 20.7% | 2 | 9.5% | 7 | 12.5% | 83 | 17.7% | 378 | 21.4% | 528 | 21.1% | 110 | 23.5% | 0.0405 |
| Peptic ulcer disease | 4 | 2.0% | 2 | 6.9% | 0 | 0.0% | 2 | 3.6% | 5 | 1.1% | 52 | 2.9% | 72 | 2.9% | 6 | 1.3% | 0.0889 |
| Peripheral vascular disease | 31 | 15.4% | 2 | 6.9% | 2 | 9.5% | 10 | 17.9% | 28 | 6.0% | 250 | 14.2% | 339 | 13.5% | 38 | 8.1% | <.0001 |
| Renal disease | 36 | 17.9% | 4 | 13.8% | 7 | 33.3% | 4 | 7.1% | 13 | 2.8% | 228 | 12.9% | 270 | 10.8% | 55 | 11.8% | <.0001 |
| Rheumatic disease | 7 | 3.5% | 0 | 0.0% | 0 | 0.0% | 3 | 5.4% | 5 | 1.1% | 40 | 2.3% | 75 | 3.0% | 12 | 2.6% | 0.166 |
| Moderate/severe liver disease | 2 | 1.0% | 1 | 3.4% | 1 | 4.8% | 0 | 0.0% | 4 | 0.9% | 63 | 3.6% | 72 | 2.9% | 6 | 1.3% | 0.0075 |
| Hypertension | 108 | 53.7% | 16 | 55.2% | 10 | 47.6% | 33 | 58.9% | 144 | 30.6% | 870 | 49.3% | 1161 | 46.3% | 184 | 39.3% | <.0001 |
| Primary Cancer Site³ | | | | | | | | | | | | | | | | | |
| Esophageal | 3 | 1.5% | 0 | 0.0% | 0 | 0.0% | 4 | 7.1% | 0 | 0.0% | 18 | 1.0% | 74 | 3.0% | 1 | 0.2% | <.0001 |
| Gastric | 3 | 1.5% | 1 | 3.4% | 0 | 0.0% | 2 | 3.6% | 6 | 1.3% | 20 | 1.1% | 95 | 3.8% | 3 | 0.6% | <.0001 |

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|--|-----|-------|----|-------|----|-------|----|-------|-----|-------|-----|-------|-----|-------|-----|-------|--------|
| Colon | 4 | 2.0% | 0 | 0.0% | 0 | 0.0% | 2 | 3.6% | 4 | 0.9% | 47 | 2.7% | 155 | 6.2% | 11 | 2.4% | <.0001 |
| Liver | 11 | 5.5% | 1 | 3.4% | 0 | 0.0% | 0 | 0.0% | 6 | 1.3% | 152 | 8.6% | 150 | 6.0% | 16 | 3.4% | <.0001 |
| Hodgkin's | 0 | 0.0% | 1 | 3.4% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 36 | 2.0% | 13 | 0.5% | 1 | 0.2% | <.0001 |
| Melanoma | 5 | 2.5% | 8 | 27.6% | 6 | 28.6% | 1 | 1.8% | 462 | 98.3% | 445 | 25.2% | 650 | 25.9% | 282 | 60.3% | <.0001 |
| Lung | 101 | 50.2% | 10 | 34.5% | 0 | 0.0% | 53 | 94.6% | 21 | 4.5% | 736 | 41.7% | 963 | 38.4% | 84 | 17.9% | <.0001 |
| Renal Cell Carcinoma | 21 | 10.4% | 1 | 3.4% | 0 | 0.0% | 0 | 0.0% | 2 | 0.4% | 248 | 14.0% | 89 | 3.6% | 106 | 22.6% | <.0001 |
| Bladder Markel Cell Carcinoma | 65 | 32.3% | 0 | 0.0% | 0 | 0.0% | 2 | 3.6% | 1 | 0.2% | 74 | 4.2% | 189 | 7.5% | 8 | 1.7% | <.0001 |
| Head and Neck | 10 | 5.0% | 6 | 20.7% | 0 | 0.0% | 0 | 0.0% | 1 | 0.2% | 7 | 0.4% | 15 | 0.6% | 1 | 0.2% | <.0001 |
| Breast | 10 | 5.0% | 6 | 20.7% | 5 | 23.8% | 1 | 1.8% | 9 | 1.9% | 146 | 8.3% | 219 | 8.7% | 14 | 3.0% | <.0001 |
| Cervix | 31 | 15.4% | 2 | 6.9% | 0 | 0.0% | 0 | 0.0% | 11 | 2.3% | 59 | 3.3% | 141 | 5.6% | 10 | 2.1% | <.0001 |
| Primary mediastinal (thymic) large B-cell lymphoma | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 2 | 0.4% | 10 | 0.6% | 39 | 1.6% | 3 | 0.6% | 0.0187 |
| Other | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 1 | 0.2% | 1 | 0.1% | 0 | 0.0% | 0 | 0.0% | 0.6074 |
| Prior Cancer Treatment | 9 | 4.5% | 2 | 6.9% | 12 | 57.1% | 0 | 0.0% | 6 | 1.3% | 117 | 6.6% | 291 | 11.6% | 14 | 3.0% | <.0001 |
| Radiation(Y/N) | 63 | 31.3% | 15 | 51.7% | 6 | 28.6% | 45 | 80.4% | 108 | 23.0% | 626 | 35.4% | 887 | 35.4% | 123 | 26.3% | <.0001 |
| Chemotherapy (Y/N) | 59 | 29.4% | 4 | 13.8% | 0 | 0.0% | 26 | 46.4% | 26 | 5.5% | 575 | 32.6% | 496 | 19.8% | 38 | 8.1% | <.0001 |
| Alkylating Agent | 45 | 22.4% | 4 | 13.8% | 0 | 0.0% | 26 | 46.4% | 16 | 3.4% | 495 | 28.0% | 407 | 16.2% | 34 | 7.3% | <.0001 |
| Antimetabolite | 23 | 11.4% | 1 | 3.4% | 0 | 0.0% | 3 | 5.4% | 3 | 0.6% | 305 | 17.3% | 235 | 9.4% | 9 | 1.9% | <.0001 |
| Antimitotic Agent | 19 | 9.5% | 2 | 6.9% | 0 | 0.0% | 16 | 28.6% | 5 | 1.1% | 213 | 12.1% | 4 | 0.2% | 194 | 41.5% | <.0001 |
| Antitumor Antibiotic | 18 | 9.0% | 0 | 0.0% | 0 | 0.0% | 1 | 1.8% | 3 | 0.6% | 84 | 4.8% | 92 | 3.7% | 3 | 0.6% | <.0001 |
| Enzyme Inhibitor | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 8 | 1.7% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 0.0173 |
| Plant Alkaloid | 15 | 7.5% | 2 | 6.9% | 0 | 0.0% | 10 | 17.9% | 0 | 0.0% | 75 | 4.2% | 36 | 1.4% | 28 | 6.0% | <.0001 |
| Proteasome Inhibitor Topoisomerase I Inhibitor | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 4 | 0.9% | 0 | 0.0% | 6 | 0.2% | 0 | 0.0% | 0.8914 |
| Chemotherapy - non specific | 4 | 2.0% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 1 | 0.2% | 25 | 1.4% | 34 | 1.4% | 8 | 1.7% | 0.3982 |
| | 1 | 0.5% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 6 | 1.3% | 6 | 0.3% | 24 | 1.0% | 1 | 0.2% | 0.159 |

Other irAEs developed within 1 year of ICI initiation⁴

| | | | | | | | | | | | | | | | | | |
|--------------------------------|------------|-------|-----------|-------|----------|-------|-----------|-------|------------|-------|------------|-------|-------------|-------|------------|-------|--------|
| Hematologic | 109 | 54.2% | 13 | 44.8% | 5 | 23.8% | 19 | 33.9% | 177 | 37.7% | 758 | 42.9% | 1140 | 45.5% | 172 | 36.8% | <.0001 |
| Pulmonary (pneumonitis) | 55 | 27.4% | 9 | 31.0% | 1 | 4.8% | 28 | 50.0% | 79 | 16.8% | 436 | 24.7% | 629 | 25.1% | 110 | 23.5% | <.0001 |
| Endocrine | 88 | 43.8% | 11 | 37.9% | 7 | 33.3% | 19 | 33.9% | 228 | 48.5% | 770 | 43.6% | 1103 | 44.0% | 252 | 53.8% | 0.0011 |
| Renal (acute kidney injury) | 56 | 27.9% | 6 | 20.7% | 0 | 0.0% | 9 | 16.1% | 107 | 22.8% | 360 | 20.4% | 553 | 22.1% | 127 | 27.1% | 0.0036 |
| Neurological | 68 | 33.8% | 10 | 34.5% | 4 | 19.0% | 13 | 23.2% | 87 | 18.5% | 409 | 23.2% | 739 | 29.5% | 103 | 22.0% | <.0001 |
| Hepatic | 44 | 21.9% | 6 | 20.7% | 2 | 9.5% | 11 | 19.6% | 95 | 20.2% | 286 | 16.2% | 510 | 20.4% | 137 | 29.3% | <.0001 |
| Gastrointestinal | 44 | 21.9% | 8 | 27.6% | 2 | 9.5% | 5 | 8.9% | 144 | 30.6% | 384 | 21.7% | 553 | 22.1% | 131 | 28.0% | <.0001 |
| Skin(vitiligo) | 3 | 1.5% | 0 | 0.0% | 0 | 0.0% | 1 | 1.8% | 78 | 16.6% | 102 | 5.8% | 180 | 7.2% | 55 | 11.8% | <.0001 |

1. Comorbidities and Charlson Comorbidity Index (CCI) were calculated based on diagnoses before or on the day of ICI initiation. ICD 9 and 10 codes used to calculate the CCI were from Quan et al. (2005). Primary cancer diagnoses were not included in the calculation of the index but metastatic/secondary cancers were included. Hierarchy coding was applied to prevent duplicated accounting. For instance, if a person had diagnoses of both a mild and a severe form of the disease (e.g. mild and moderate/severe liver disease, diabetes with and without chronic complications), the patient was only scored on the more severe disease in the CCI.
2. Any diabetes included patients who had any of the following diagnoses, diabetes without chronic complication, diabetes with chronic complication, or diabetes secondary to drug use, prior to or on the day of ICI initiation.
3. Primary can sites are based on diagnoses of primary cancers (excluding secondary diagnoses) before ICI initiation or 30 days after. Site variables are not mutually exclusive and patients may have multiple cancer sites.
4. Other irAEs included hematologic [anemia, thrombocytopenia, leukopenia], pneumonitis, endocrine [hypothyroidism, hyperthyroidism, hypophysitis/PGA, Hyper/hypoparathyroidism, diabetes type I, dysfunctional uterine bleeding/infertility], renal [acute kidney injury/AKI], neurological [encephalitis/myelitis/encephalomyelitis, neuritis, meningitis], hepatic [hepatitis], gastrointestinal (GI) [colitis, pancreatitis, mucositis] and skin [vitiligo].

Table S3 Patient Characteristics by Primary Cancer Site

| | Primary Cancer Site ¹ | | | | | | | | | | | | | |
|---|----------------------------------|-------|-------------|-------|------------|-------|------------|-------|-------------|-------|-----------|-------|------------|-------|
| | Lung | | Melanoma | | RCC | | Urothelial | | Head & Neck | | MCC | | Liver | |
| Total, n | 1968 | | 1861 | | 467 | | 339 | | 410 | | 35 | | 336 | |
| Age at ICI Initiation | | | | | | | | | | | | | | |
| 18-44 | 74 | 3.8% | 286 | 15.4% | 20 | 4.3% | 6 | 1.8% | 24 | 5.9% | 0 | 0.0% | 23 | 6.8% |
| 45-54 | 188 | 9.6% | 301 | 16.2% | 64 | 13.7% | 32 | 9.4% | 61 | 14.9% | 1 | 2.9% | 42 | 12.5% |
| 55-64 | 662 | 33.6% | 470 | 25.3% | 139 | 29.8% | 83 | 24.5% | 138 | 33.7% | 2 | 5.7% | 118 | 35.1% |
| 65-74 | 686 | 34.9% | 513 | 27.6% | 158 | 33.8% | 115 | 33.9% | 117 | 28.5% | 16 | 45.7% | 107 | 31.8% |
| >=75 | 358 | 18.2% | 291 | 15.6% | 86 | 18.4% | 103 | 30.4% | 70 | 17.1% | 16 | 45.7% | 46 | 13.7% |
| Sex | | | | | | | | | | | | | | |
| F | 957 | 48.6% | 707 | 38.0% | 151 | 32.3% | 99 | 29.2% | 97 | 23.7% | 10 | 28.6% | 123 | 36.6% |
| M | 1011 | 51.4% | 1154 | 62.0% | 316 | 67.7% | 240 | 70.8% | 313 | 76.3% | 25 | 71.4% | 213 | 63.4% |
| Hispanic | | | | | | | | | | | | | | |
| Yes | 48 | 2.4% | 39 | 2.1% | 22 | 4.7% | 13 | 3.8% | 15 | 3.7% | 2 | 5.7% | 17 | 5.1% |
| No | 1782 | 90.5% | 1761 | 94.6% | 425 | 91.0% | 310 | 91.4% | 365 | 89.0% | 31 | 88.6% | 295 | 87.8% |
| Unknown | 138 | 7.0% | 61 | 3.3% | 20 | 4.3% | 16 | 4.7% | 30 | 7.3% | 2 | 5.7% | 24 | 7.1% |
| Race | | | | | | | | | | | | | | |
| American Indian or Alaska Native | 3 | 0.2% | 2 | 0.1% | 2 | 0.4% | 1 | 0.3% | 2 | 0.5% | 0 | 0.0% | 11 | 3.3% |
| Asian | 29 | 1.5% | 7 | 0.4% | 5 | 1.1% | 21 | 6.2% | 8 | 2.0% | 0 | 0.0% | 44 | 13.1% |
| Black or African American | 233 | 11.8% | 10 | 0.5% | 36 | 7.7% | 0 | 0.0% | 27 | 6.6% | 0 | 0.0% | 0 | 0.0% |
| Hawaiian/Other Pacific Islander | 3 | 0.2% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% |
| Unknown | 67 | 3.4% | 51 | 2.7% | 26 | 5.6% | 21 | 6.2% | 22 | 5.4% | 4 | 11.4% | 19 | 5.7% |
| White | 1633 | 83.0% | 1791 | 96.2% | 398 | 85.2% | 296 | 87.3% | 351 | 85.6% | 31 | 88.6% | 262 | 78.0% |
| Charlson Comorbidity Index² | | | | | | | | | | | | | | |
| 0 | 564 | 28.7% | 979 | 52.6% | 120 | 25.7% | 85 | 25.1% | 142 | 34.6% | 4 | 11.4% | 22 | 6.5% |
| 1 | 568 | 28.9% | 465 | 25.0% | 84 | 18.0% | 60 | 17.7% | 116 | 28.3% | 13 | 37.1% | 101 | 30.1% |

| | | | | | | | | | | | | | | |
|---------------------------------------|------|-------|------|-------|-----|-------|-----|-------|-----|-------|----|--------|-----|-------|
| 2 | 384 | 19.5% | 222 | 11.9% | 85 | 18.2% | 70 | 20.6% | 63 | 15.4% | 12 | 34.3% | 51 | 15.2% |
| ≥3 | 452 | 23.0% | 195 | 10.5% | 178 | 38.1% | 124 | 36.6% | 89 | 21.7% | 6 | 17.1% | 162 | 48.2% |
| Comorbidities² | | | | | | | | | | | | | | |
| AIDS/HIV | 13 | 0.7% | 10 | 0.5% | 3 | 0.6% | 1 | 0.3% | 3 | 0.7% | 1 | 2.9% | 4 | 1.2% |
| Cerebrovascular disease | 266 | 13.5% | 175 | 9.4% | 36 | 7.7% | 33 | 9.7% | 59 | 14.4% | 8 | 22.9% | 37 | 11.0% |
| Congestive heart failure | 78 | 4.0% | 29 | 1.6% | 25 | 5.4% | 18 | 5.3% | 13 | 3.2% | 35 | 100.0% | 14 | 4.2% |
| Chronic pulmonary disease | 910 | 46.2% | 256 | 13.8% | 94 | 20.1% | 84 | 24.8% | 110 | 26.8% | 6 | 17.1% | 89 | 26.5% |
| Dementia | 12 | 0.6% | 6 | 0.3% | 3 | 0.6% | 3 | 0.9% | 4 | 1.0% | 36 | 102.9% | 2 | 0.6% |
| Diabetes without chronic complication | 207 | 10.5% | 157 | 8.4% | 47 | 10.1% | 35 | 10.3% | 51 | 12.4% | 7 | 20.0% | 45 | 13.4% |
| Diabetes with chronic complication | 113 | 5.7% | 55 | 3.0% | 58 | 12.4% | 39 | 11.5% | 19 | 4.6% | 2 | 5.7% | 31 | 9.2% |
| Diabetes secondary to drug use | 27 | 2.5% | 12 | 0.6% | 6 | 1.3% | 6 | 1.8% | 3 | 0.7% | 1 | 2.9% | 6 | 1.8% |
| Any diabetes ³ | 324 | 16.5% | 215 | 11.6% | 105 | 22.5% | 74 | 21.8% | 70 | 17.1% | 10 | 28.6% | 76 | 22.6% |
| Hemiplegia/paraplegia | 49 | 2.5% | 20 | 1.1% | 15 | 3.2% | 9 | 2.7% | 14 | 3.4% | 0 | 0.0% | 3 | 0.9% |
| Metastatic solid tumor | 1682 | 85.5% | 1697 | 91.2% | 428 | 91.6% | 307 | 90.6% | 377 | 92.0% | 26 | 74.3% | 267 | 12.0% |
| Myocardial infarction | 67 | 3.4% | 35 | 1.9% | 16 | 3.4% | 18 | 5.3% | 11 | 2.7% | 1 | 2.9% | 12 | 3.6% |
| Mild liver disease | 397 | 20.2% | 358 | 19.2% | 136 | 29.1% | 73 | 21.5% | 78 | 19.0% | 5 | 14.3% | 183 | 54.5% |
| Peptic ulcer disease | 53 | 2.7% | 21 | 1.1% | 14 | 3.0% | 8 | 2.4% | 11 | 2.7% | 1 | 2.9% | 19 | 5.7% |
| Peripheral vascular disease | 337 | 17.1% | 156 | 8.4% | 71 | 15.2% | 59 | 17.4% | 75 | 18.3% | 3 | 8.6% | 52 | 15.5% |
| Renal disease | 187 | 9.5% | 94 | 5.1% | 191 | 40.9% | 131 | 38.6% | 42 | 10.2% | 9 | 25.7% | 35 | 10.4% |
| Rheumatic disease | 59 | 3.0% | 47 | 2.5% | 12 | 2.6% | 9 | 2.7% | 9 | 2.2% | 4 | 11.4% | 11 | 3.3% |
| Moderate/severe liver disease | 20 | 1.0% | 13 | 0.7% | 5 | 1.1% | 9 | 2.7% | 5 | 1.2% | 0 | 0.0% | 102 | 30.4% |
| Hypertension | 985 | 50.1% | 669 | 35.9% | 318 | 68.1% | 208 | 61.4% | 200 | 48.8% | 22 | 62.9% | 193 | 57.4% |
| Prior Cancer Treatment | | | | | | | | | | | | | | |
| Radiation(Y/N) | 906 | 46.0% | 346 | 18.6% | 139 | 29.8% | 97 | 28.6% | 248 | 60.5% | 16 | 45.7% | 104 | 31.0% |
| Chemotherapy (Y/N) | 601 | 30.5% | 57 | 3.1% | 55 | 11.8% | 114 | 33.6% | 152 | 37.1% | 3 | 8.6% | 112 | 33.3% |

| | | | | | | | | | | | | | | | |
|--|-----|-------|-----|-------|-----|-------|-----|-------|-----|-------|----|-------|------|-------|--|
| Alkylating Agent | 561 | 28.5% | 37 | 2.0% | 34 | 7.3% | 86 | 25.4% | 138 | 33.7% | 2 | 5.7% | 60 | 17.9% | |
| Antimetabolite | 289 | 14.7% | 16 | 0.9% | 31 | 6.6% | 78 | 23.0% | 46 | 11.2% | 1 | 2.9% | 43 | 12.8% | |
| Antimitotic Agent | 260 | 13.2% | 15 | 0.8% | 15 | 3.2% | 19 | 5.6% | 55 | 13.4% | 1 | 2.9% | 25 | 7.4% | |
| Antitumor Antibiotic | 20 | 1.0% | 8 | 0.4% | 20 | 4.3% | 43 | 12.7% | 12 | 2.9% | 0 | 0.0% | 54 | 16.1% | |
| Enzyme Inhibitor | 3 | 0.2% | 0 | 0.0% | 5 | 1.1% | 1 | 0.3% | 0 | 0.0% | 0 | 0.0% | 1 | 0.3% | |
| Plant Alkaloid | 114 | 5.8% | 3 | 0.2% | 7 | 1.5% | 9 | 2.7% | 8 | 2.0% | 1 | 2.9% | 9 | 2.7% | |
| Proteasome Inhibitor | 0 | 0.0% | 0 | 0.0% | 1 | 0.2% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 1 | 0.3% | |
| Topoisomerase I Inhibitor | 15 | 0.8% | 1 | 0.1% | 2 | 0.4% | 1 | 0.3% | 1 | 0.2% | 0 | 0.0% | 14 | 4.2% | |
| Chemotherapy - non specific | 6 | 0.3% | 12 | 0.6% | 1 | 0.2% | 2 | 0.6% | 0 | 0.0% | 0 | 0.0% | 1 | 0.3% | |
| First ICI treatment | | | | | | | | | | | | | | | |
| Atezolizumab | 101 | 5.1% | 5 | 0.3% | 21 | 4.5% | 65 | 19.2% | 10 | 2.4% | 0 | 0.0% | 11 | 3.3% | |
| Avelumab | 10 | 0.5% | 8 | 0.4% | 1 | 0.2% | 0 | 0.0% | 6 | 1.5% | 11 | 31.4% | 1 | 0.3% | |
| Cemiplimab | 0 | 0.0% | 6 | 0.3% | 0 | 0.0% | 0 | 0.0% | 5 | 1.2% | 0 | 0.0% | 0 | 0.0% | |
| Durvalumab | 53 | 2.7% | 1 | 0.1% | 0 | 0.0% | 2 | 0.6% | 1 | 0.2% | 0 | 0.0% | 0 | 0.0% | |
| Ipilimumab | 21 | 1.1% | 462 | 24.8% | 2 | 0.4% | 1 | 0.3% | 9 | 2.2% | 1 | 2.9% | 6 | 1.8% | |
| Nivolumab | 736 | 37.4% | 445 | 23.9% | 248 | 53.1% | 74 | 21.8% | 146 | 35.6% | 7 | 20.0% | 152 | 45.2% | |
| Combo (niv+ipi) | 84 | 4.3% | 282 | 15.2% | 106 | 22.7% | 8 | 2.4% | 14 | 3.4% | 1 | 2.9% | 16 | 4.8% | |
| Pembrolizumab | 963 | 48.9% | 650 | 34.9% | 89 | 19.1% | 189 | 55.8% | 219 | 53.4% | 15 | 42.9% | 150 | 44.6% | |
| Other irAEs developed within 1 year of ICI initiation[†] | | | | | | | | | | 0.0% | | | 0.0% | | |
| Hematologic | 886 | 45.0% | 569 | 30.6% | 220 | 47.1% | 198 | 58.4% | 180 | 43.9% | 18 | 51.4% | 191 | 56.8% | |
| Pulmonary (pneumonitis) | 741 | 37.7% | 294 | 15.8% | 110 | 23.6% | 62 | 18.3% | 118 | 28.8% | 5 | 14.3% | 62 | 18.5% | |
| Endocrine | 899 | 45.7% | 835 | 44.9% | 263 | 56.3% | 133 | 39.2% | 204 | 49.8% | 19 | 54.3% | 130 | 38.7% | |
| Renal (acute kidney injury) | 381 | 19.4% | 316 | 17.0% | 198 | 42.4% | 162 | 47.8% | 80 | 19.5% | 5 | 14.3% | 90 | 26.8% | |
| Neurological | 552 | 28.0% | 339 | 18.2% | 107 | 22.9% | 109 | 32.2% | 125 | 30.5% | 10 | 28.6% | 77 | 22.9% | |
| Hepatic | 295 | 15.0% | 424 | 22.8% | 105 | 22.5% | 66 | 19.5% | 60 | 14.6% | 7 | 20.0% | 121 | 36.0% | |
| Gastrointestinal | 395 | 20.1% | 421 | 22.6% | 134 | 28.7% | 72 | 21.2% | 150 | 36.6% | 9 | 25.7% | 78 | 23.2% | |

| | | | | | | | | | | | | | | |
|----------------|----|------|-----|-------|----|------|---|------|----|------|---|------|----|------|
| Skin(vitiligo) | 65 | 3.3% | 295 | 15.9% | 21 | 4.5% | 8 | 2.4% | 25 | 6.1% | 2 | 5.7% | 13 | 3.9% |
|----------------|----|------|-----|-------|----|------|---|------|----|------|---|------|----|------|

1. Primary can sites are based on diagnoses of primary cancers (excluding secondary diagnoses) before ICI initiation or 30 days after. Site variables are not mutually exclusive and patients may have multiple cancer sites and could not be compared.
2. Comorbidities and Charlson Cormobidity Index (CCI) were calculated based on diagnoses before or on the day of ICI initiation. ICD 9 and 10 codes used to calculate the CCI were from Quan et al. (2005). Primary cancer diagnoses were not included in the calculation of the index but metastatic/secondary cancers were included. Hierarchy coding was applied to prevent duplicated accounting. For instance, if a person had diagnoses of both a mild and a severe form of the disease (e.g. mild and moderate/severe liver disease, diabetes with and without chronic complications), the patient was only scored on the more severe disease in the CCI.
3. Any diabetes included patients who had any of the following diagnoses, diabetes without chronic complicaiton, diabetes with chronic complication, or diabetes secondary to drug use, prior to or on the day of ICI initiation.
4. Other irAEs included hematologic [anemia, thrombocytopenia, leukopenia], pneumonitis, endocrine [hypothyroidism, hyperthyroidism, hypophysitis/PGA, Hyper/hypo-parathyroidism, diabetes type I, dysfunctional uterine bleeding/infertility], renal [acute kidney injury/AKI], neurological [encephalitis/myelitis/encephalomyelitis, neuritis, meningitis], hepatic [hepatitis], gastrointestinal (GI) [colitis, pancreatitis, mucositis] and skin [vitiligo].

Table S4. Estimated Rate per Person-Year

| | <i>n</i> | CAEs within One Year | | Follow-up time (in years) | | Total Person-Year | Rate per Person-Year | 95% CI | |
|-------------------------|----------|----------------------|-------|---------------------------|---------------|-------------------|----------------------|--------|-------|
| | | Yes | % | Median | IQR | | | | |
| Any CAE | 5518 | 691 | 12.5% | 0.647 | (0.252-1) | 3394.4 | 0.203 | 0.19 | 0.22 |
| Arrhythmia | 5518 | 511 | 9.3% | 0.647 | (0.252-1) | 3394.4 | 0.150 | 0.14 | 0.16 |
| Acute MI | 5518 | 94 | 1.7% | 0.647 | (0.252-1) | 3394.4 | 0.028 | 0.02 | 0.03 |
| Myocarditis | 5518 | 116 | 2.1% | 0.647 | (0.252-1) | 3394.4 | 0.034 | 0.03 | 0.04 |
| Pericarditis | 5518 | 68 | 1.2% | 0.647 | (0.252-1) | 3394.4 | 0.020 | 0.02 | 0.03 |
| Cardiomyopathy | 5518 | 47 | 0.9% | 0.647 | (0.252-1) | 3394.4 | 0.014 | 0.01 | 0.02 |
| | N | Overall Death | | Follow-up time (in years) | | Total Person-Year | Rate Per Person-Year | 95% CI | |
| | | Yes | % | Median | IQR | | | | |
| All | 5518 | 2070 | 37.5% | 0.647 | (0.252-1.441) | 5786.2 | 0.358 | 0.343 | 0.373 |
| CAE within 1 Year (Yes) | 691 | 380 | 55.0% | 0.682 | (0.301-1.230) | 679.6 | 0.331 | 0.316 | 0.347 |
| CAE within 1 Year (No) | 4827 | 1690 | 35.0% | 0.636 | (0.249-1.477) | 5106.7 | 0.559 | 0.506 | 0.618 |