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Data obtained through Sentinel are intended to complement other types of evidence such as preclinical studies, clinical trials, postmarket studies, and adverse event reports, all of which are used by FDA to inform regulatory decisions regarding medical product safety. The information contained in this report is provided as part of FDA's commitment to place knowledge acquired from Sentinel in the public domain as soon as possible. Any public health actions taken by FDA regarding products involved in Sentinel queries will continue to be communicated through existing channels.

FDA wants to emphasize that the fact that FDA has initiated a query involving a medical product and is reporting findings related to that query does not mean that FDA is suggesting health care practitioners should change their prescribing practices for the medical product or that patients taking the medical product should stop using it. Patients who have questions about the use of an identified medical product should contact their health care practitioners.

The following report contains a description of the request, request specifications, and results from the modular program run(s). If you are using a web page screen reader and are unable to access this document, please contact the Sentinel Operations Center for assistance at info@sentinelssystem.org.

Overview for Request cder_mpl1r_wp118

Request ID: cder_mpl1r_wp118_nsdv_v01

Request Description: In this request, we examined the number of checkpoint inhibitor users with a diagnosis of Guillain-Barré syndrome (GBS) or Bell's palsy after drug initiation in the Sentinel Distributed Database (SDD). We also examined the time to Guillain-Barré syndrome (GBS) or Bell's palsy diagnosis after checkpoint inhibitor initiation among users in the SDD.

Sentinel Modular Program Tool Used: Cohort Identification and Descriptive Analysis (CIDA) tool, version 5.4.4

Data Source: We used data from March 1, 2011 to June 30, 2018 from 17 Data Partners contributing to the SDD in this report. We distributed this request to Data Partners on September 25, 2018. Please see Appendix A for dates of available data for each Data Partner.

Study Design: We designed this request to identify incident and prevalent exposures to checkpoint inhibitors and outcomes of GBS or Bell's palsy. We reported results overall and stratified by year, sex, and age. We also calculated and reported summary statistics for follow-up time from checkpoint inhibitor initiation to the end of treatment episode and to the outcome of interest (GBS or Bell's palsy), when applicable.

Exposures of Interest: The administered checkpoint inhibitor exposures of interest in this request were: ipilimumab, atezolizumab, avelumab, durvalumab, nivolumab, and pembrolizumab. We also examined same-day administration of ipilimumab and nivolumab as a separate exposure of interest. We used National Drug Codes (NDCs) to define exposures of interest in this request. Please see Appendix B for a list of generic and brand drug names with Food and Drug Administration (FDA) approval dates used to define exposures of interest in this request. We defined checkpoint inhibitor administration using Healthcare Common Procedure Coding System (HCPCS) procedure codes and analyzed incident and prevalent administrations separately. See Appendix C for a list of HCPCS procedure codes used to define checkpoint inhibitor administration in this request.

Cohort Eligibility Criteria: We required members included in either the prevalent or incident cohorts to have no evidence of GBS or Bell's palsy in their enrollment history prior to their first qualifying (index) checkpoint inhibitor administration. We included all qualifying incident and prevalent exposures of interest in this report; cohort re-entry was allowed. The following age groups were included in both cohorts: <65 and 65+ years.

Incident Cohort: We required members included in the incident cohort to be continuously enrolled in health plans with medical and drug coverage for at least 6 months (183 days) prior to their index checkpoint inhibitor administration, during which gaps in coverage of up to 45 days were allowed. We excluded exposure episodes if there was evidence of any checkpoint inhibitor administration in the 183 days prior to the index exposure.

Prevalent Cohort: We required members included in the prevalent cohort to be enrolled in medical and drug coverage only on the index checkpoint inhibitor administration date.

Outcomes of Interest: The outcomes of interest in this request were the occurrence of GBS and Bell's palsy, in any care setting, among checkpoint inhibitor users. We defined these outcomes using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis codes. See Appendix D for a list of ICD-9-CM and ICD-10-CM diagnosis codes used to define GBS and Bell's palsy in this request.

Follow-Up Time: We implemented two distinct follow-up time approaches within this request.

Intent-to-Treat: Follow-up time began on the day of the index checkpoint inhibitor administration and continued for 12 weeks or until the first occurrence of any of the following: 1) disenrollment; 2) death; 3) the end date of the data provided by each Data Partner; or 4) the outcome of interest. This was the only follow-up time method we used for the same-day combination exposure of ipilimumab and nivolumab cohort.

Overview for Request cder_mpl1r_wp118, continued

As Treated: Follow-up time began on the day of the index checkpoint inhibitor administration. We added an extension of follow-up time, which varied by generic name, to the last administration date for the length of time described below:

- Ipilimumab, atezolizumab, avelumab, and pembrolizumab: three weeks (allowable gap and extension)
- Durvalumab and nivolumab: two weeks (allowable gap and extension)

If multiple administrations of the same generic drug occurred within the allowable gap then the two "episodes" were bridged. For example, two administrations of ipilimumab occurring three weeks apart would have a follow-up time of six weeks and two days. This accounts for a three week gap plus two one-day administrations and a three week extension. Two administrations of ipilimumab occurring five days apart would have a follow-up time of four weeks. This accounts for a five day gap plus two one-day administrations and a three week extension.

Follow-up time continued until the first occurrence of the following: 1) disenrollment; 2) death; 3) the end date of the data provided by each Data Partner; or 4) the outcome of interest.

Please refer to Appendices E and F for specifications of parameters used in the analyses for this request.

Limitations: Algorithms used to define exposures and outcomes are imperfect; thus, it is possible that there may be misclassification. Therefore, data should be interpreted with this limitation in mind.

Notes: Please contact the Sentinel Operations Center (info@sentinelssystem.org) for questions and to provide comments/suggestions for future enhancements to this document.

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Appendix B List of Generic and Brand Drug Names with Food and Drug Administration (FDA) Approval Dates Used to Define Exposures of Interest in this Request

Appendix C List of Healthcare Common Procedure Coding System (HCPCS) Procedure Codes Used to Define Exposures and Incidence Criteria in this Request

Appendix D List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) Diagnosis Codes Used to Define Outcomes in this Request

Appendix E Specifications Defining Parameters in this Request, Incident Cohort

Appendix F Specifications Defining Parameters in this Request, Prevalent Cohort

**Glossary of Terms for Analyses Using
Cohort Identification and Descriptive Analysis (CIDA) Tool***

Amount Supplied - number of units (pills, tablets, vials) dispensed. Net amount per NDC per dispensing.

Blackout Period - number of days at the beginning of a treatment episode that events are to be ignored. If an event occurs during the blackout period, the episode is excluded.

Care Setting - type of medical encounter or facility where the exposure, event, or condition code was recorded. Possible care settings include: Inpatient Hospital Stay (IP), Non-Acute Institutional Stay (IS), Emergency Department (ED), Ambulatory Visit (AV), and Other Ambulatory Visit (OA). For laboratory results, possible care settings include: Emergency Department (E), Home (H), Inpatient (I), Outpatient (O), or Unknown or Missing (U). The Care Setting, along with the Principal Diagnosis Indicator (PDX), forms the Care Setting/PDX parameter.

Ambulatory Visit (AV) - includes visits at outpatient clinics, same-day surgeries, urgent care visits, and other same-day ambulatory hospital encounters, but excludes emergency department encounters.

Emergency Department (ED) - includes ED encounters that become inpatient stays (in which case inpatient stays would be a separate encounter). Excludes urgent care visits.

Inpatient Hospital Stay (IP) - includes all inpatient stays, same-day hospital discharges, hospital transfers, and acute hospital care where the discharge is after the admission date.

Non-Acute Institutional Stay (IS) - includes hospice, skilled nursing facility (SNF), rehab center, nursing home, residential, overnight non-hospital dialysis and other non-hospital stays.

Other Ambulatory Visit (OA) - includes other non overnight AV encounters such as hospice visits, home health visits, skilled nursing facility visits, other non-hospital visits, as well as telemedicine, telephone and email consultations.

Charlson/Elixhauser Combined Comorbidity Score - calculated based on comorbidities observed during a requester-defined window around the exposure episode start date (e.g., in the 183 days prior to index).

Cohort Definition (drug/exposure) - indicates how the cohort will be defined: 01: Cohort includes only the first valid treatment episode during the query period; 02: Cohort includes all valid treatment episodes during the query period; 03: Cohort includes all valid treatment episodes during the query period until an event occurs.

Computed Start Marketing Date - represents the first observed dispensing date among all valid users within a GROUP (scenario) within each Data Partner site.

Days Supplied - number of days supplied for all dispensings in qualifying treatment episodes.

Eligible Members - number of members eligible for an incident treatment episode (defined by the drug/exposure and event washout periods) with drug and medical coverage during the query period.

Enrollment Gap - number of days allowed between two consecutive enrollment periods without breaking a "continuously enrolled" sequence.

Episodes - treatment episodes; length of episode is determined by days supplied in one dispensing or consecutive dispensings bridged by the episode gap.

Episode Gap - number of days allowed between two (or more) consecutive exposures (dispensings/procedures) to be considered the same treatment episode.

Event Deduplication - specifies how events are counted by the Modular Program (MP) algorithm: 0: Counts all occurrences of a health outcome of interest (HOI) during an exposure episode; 1: de-duplicates occurrences of the same HOI code and code type on the same day; 2: de-duplicates occurrences of the same HOI group on the same day (e.g., de-duplicates at the group level).

Exposure Episode Length - number of days after exposure initiation that is considered "exposed time."

Exposure Extension Period - number of days post treatment period in which the outcomes/events are counted for a treatment episode. Extensions are added after any episode gaps have been bridged.

Lookback Period - number of days wherein a member is required to have evidence of pre-existing condition (diagnosis/procedure/drug dispensing).

Maximum Episode Duration - truncates exposure episodes after a requester-specified number of exposed days. Applied after any gaps are bridged and extension days added to the length of the exposure episode.

Member-Years - sum of all days of enrollment with medical and drug coverage in the query period preceded by an exposure washout period all divided by 365.25.

Minimum Days Supplied - specifies a minimum number of days in length of the days supplied for the episode to be considered.

Minimum Episode Duration - specifies a minimum number of days in length of the episode for it to be considered. Applied after any gaps are bridged and extension days added to the length of the exposure episode.

Monitoring Period - used to define time periods of interest for both sequential analysis and simple cohort characterization requests.

Principal Diagnosis (PDX) - diagnosis or condition established to be chiefly responsible for admission of the patient to the hospital. 'P' = principal diagnosis, 'S' = secondary diagnosis, 'X' = unspecified diagnosis, '.' = blank. Along with the Care Setting values, forms the Caresetting/PDX parameter.

Query Period - period in which the modular program looks for exposures and outcomes of interest.

Switch Evaluation Step Value - value used to differentiate evaluation step. Each switch pattern can support up to 2 evaluation steps (0 = switch pattern evaluation start; 1 = first evaluation; 2 = second evaluation).

Switch Gap Inclusion Indicator - indicator for whether gaps in treatment episodes that are included in a switch episode will be counted as part of the switch episode duration.

Switch Pattern Cohort Inclusion Date - indicates which date to use for inclusion into the switch pattern cohort of interest as well as optionally as the index date of the treatment episode initiating the switch pattern. Valid options are the product approval date, product marketing date, other requester defined date, or computed start marketing date.

Switch Pattern Cohort Inclusion Strategy - indicates how the switch pattern cohort inclusion date will be used: 01: used only as a switch cohort entry date. First treatment episode dispensing date is used as index for computing time to first switch; 02: used as switch cohort entry date and as initial switch step index date for computing time to first switch.

Treatment Episode Truncation Indicator - indicates whether the exposure episode will be truncated at the occurrence of a requester-specified code.

Washout Period (drug/exposure) - number of days a user is required to have no evidence of prior exposure (drug dispensing/procedure) and continuous drug and medical coverage prior to an incident treatment episode.

Washout Period (event/outcome) - number of days a user is required to have no evidence of a prior event (procedure/diagnosis) and continuous drug and medical coverage prior to an incident treatment episode.

Years at Risk - number of days supplied plus any episode gaps and exposure extension periods all divided by 365.25.

*All terms listed above may not be used in this report

Table 1a. Summary of Guillain-Barré Syndrome (GBS) Diagnosis following Incident Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, Overall

Drug	Number of New Users	Number of Episodes	Years at Risk	New Episodes with Outcome	New Episodes with Outcome per 1,000 Years at Risk	Eligible Members ¹	Eligible Member-Years ¹	New Users per 10,000 Eligible Members
As Treated								
Ipilimumab	8,043	8,254	****	****	5.90	137,930,140	363,835,032.5	0.58
Atezolizumab	1,290	1,293	154.7	0	0.00	137,930,140	363,835,032.5	0.09
Avelumab	30	30	2.5	0	0.00	137,930,140	363,835,032.5	0.00
Durvalumab	85	85	7.2	0	0.00	137,930,140	363,835,032.5	0.01
Nivolumab	26,960	27,175	****	****	0.30	137,930,140	363,835,032.5	1.95
Pembrolizumab	10,450	10,555	****	****	1.19	137,930,140	363,835,032.5	0.76
Intent-to-Treat								
Ipilimumab	8,043	8,254	1,711.8	12	7.01	137,930,140	363,835,032.5	0.58
Atezolizumab	1,290	1,293	216.0	0	0.00	137,930,140	363,835,032.5	0.09
Avelumab	30	30	4.5	0	0.00	137,930,140	363,835,032.5	0.00
Durvalumab	85	85	11.0	0	0.00	137,930,140	363,835,032.5	0.01
Nivolumab	26,960	27,175	****	****	1.87	137,930,140	363,835,032.5	1.95
Pembrolizumab	10,450	10,555	****	****	1.50	137,930,140	363,835,032.5	0.76
Same-Day Ipilimumab and Nivolumab	1,438	1,440	****	****	10.88	137,930,140	363,835,032.5	0.10

¹Eligible members and member-years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period.

****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

Table 1b. Summary of Bell's Palsy Diagnosis following Incident Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, Overall

Drug	Number of New Users	Number of Episodes	Years at Risk	New Episodes with Outcome	New Episodes with Outcome per 1,000 Years at Risk	Eligible Members ¹	Eligible Member-Years ¹	New Users per 10,000 Eligible Members
As Treated								
Ipilimumab	7,958	8,164	1,004.1	21	20.91	137,763,972	362,594,228.5	0.58
Atezolizumab	1,280	1,283	153.8	0	0.00	137,763,972	362,594,228.5	0.09
Avelumab	28	28	2.3	0	0.00	137,763,972	362,594,228.5	0.00
Durvalumab	84	84	7.2	0	0.00	137,763,972	362,594,228.5	0.01
Nivolumab	26,726	26,938	3,333.8	25	7.50	137,763,972	362,594,228.5	1.94
Pembrolizumab	10,292	10,394	1,654.2	13	7.86	137,763,972	362,594,228.5	0.75
Intent-to-Treat								
Ipilimumab	7,958	8,164	1,690.7	31	18.34	137,763,972	362,594,228.5	0.58
Atezolizumab	1,280	1,283	214.6	0	0.00	137,763,972	362,594,228.5	0.09
Avelumab	28	28	4.2	0	0.00	137,763,972	362,594,228.5	0.00
Durvalumab	84	84	10.8	0	0.00	137,763,972	362,594,228.5	0.01
Nivolumab	26,726	26,938	5,294.7	42	7.93	137,763,972	362,594,228.5	1.94
Pembrolizumab	10,292	10,394	1,962.3	16	8.15	137,763,972	362,594,228.5	0.75
Same-Day Ipilimumab and Nivolumab	1,422	1,424	****	****	36.76	137,763,972	362,594,228.5	0.10

¹Eligible members and member-years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period.

****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

Table 1c. Summary of Guillain-Barré Syndrome (GBS) Diagnosis following Prevalent Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, Overall

Drug	Number of Users	Number of Episodes	Years at Risk	Episodes with Outcome	Episodes with Outcome per 1,000 Years at Risk	Eligible Members ¹	Eligible Member-Years ¹	New Users per 10,000 Eligible Members
As Treated								
Ipilimumab	10,001	15,542	*****	*****	4.77	158,748,006	418,761,197.2	0.63
Atezolizumab	1,471	2,277	271.5	0	0.00	158,748,006	418,761,197.2	0.09
Avelumab	37	48	3.9	0	0.00	158,748,006	418,761,197.2	0.00
Durvalumab	90	123	9.7	0	0.00	158,748,006	418,761,197.2	0.01
Nivolumab	31,917	82,692	*****	*****	0.95	158,748,006	418,761,197.2	2.01
Pembrolizumab	12,816	26,361	*****	*****	1.01	158,748,006	418,761,197.2	0.81
Intent-to-Treat								
Ipilimumab	10,001	11,074	2,292.8	14	6.11	158,748,006	418,758,889.9	0.63
Atezolizumab	1,471	1,493	250.4	0	0.00	158,748,006	418,760,945.0	0.09
Avelumab	37	39	5.5	0	0.00	158,748,006	418,761,191.8	0.00
Durvalumab	90	90	11.5	0	0.00	158,748,006	418,761,185.9	0.01
Nivolumab	31,917	33,230	6,543.0	15	2.29	158,748,006	418,754,584.7	2.01
Pembrolizumab	12,816	13,446	*****	*****	1.95	158,748,006	418,758,625.1	0.81
Same-Day Ipilimumab and Nivolumab	2,159	2,204	*****	*****	7.06	158,748,006	418,760,769.1	0.14

¹Eligible members and member-years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

Table 1d. Summary of Bell's Palsy Diagnosis following Prevalent Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, Overall

Drug	Number of Users	Number of Episodes	Years at Risk	Episodes with Outcome	Episodes with Outcome per 1,000 Years at Risk	Eligible Members ¹	Eligible Member-Years ¹	New Users per 10,000 Eligible Members
As Treated								
Ipilimumab	9,903	15,372	1,657.2	31	18.71	158,623,545	417,484,831.5	0.62
Atezolizumab	1,462	2,260	269.8	0	0.00	158,623,545	417,484,831.5	0.09
Avelumab	35	45	3.6	0	0.00	158,623,545	417,484,831.5	0.00
Durvalumab	89	122	9.6	0	0.00	158,623,545	417,484,831.5	0.01
Nivolumab	31,667	82,049	8,373.1	53	6.33	158,623,545	417,484,831.5	2.00
Pembrolizumab	12,638	25,950	3,913.5	29	7.41	158,623,545	417,484,831.5	0.80
Intent-to-Treat								
Ipilimumab	9,903	10,953	2,264.3	42	18.55	158,623,545	417,482,552.9	0.62
Atezolizumab	1,462	1,483	249.0	0	0.00	158,623,545	417,484,580.8	0.09
Avelumab	35	37	5.1	0	0.00	158,623,545	417,484,826.5	0.00
Durvalumab	89	89	11.4	0	0.00	158,623,545	417,484,820.4	0.01
Nivolumab	31,667	32,972	6,488.4	50	7.71	158,623,545	417,478,274.8	2.00
Pembrolizumab	12,638	13,247	2,520.1	29	11.51	158,623,545	417,482,301.1	0.80
Same-Day Ipilimumab and Nivolumab	2,132	2,176	418.6	11	26.28	158,623,545	417,484,409.9	0.13

¹Eligible members and member-years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period.

Table 2a. Summary of Guillain-Barré Syndrome (GBS) Diagnosis following Incident Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Year

Year	New Users per 10,000 Eligible Members ¹	New Episodes with Outcome per 1,000 Years at Risk
As Treated		
Ipilimumab		
2011	0.07	0.00
2012	0.19	6.66
2013	0.19	0.00
2014	0.24	4.53
2015	0.20	11.10
2016	0.19	12.38
2017	0.15	0.00
2018	0.05	0.00
Atezolizumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.00	-
2016	0.10	0.00
2017	0.09	0.00
2018	0.09	0.00
Avelumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.00	-
2016	0.00	-
2017	0.00	0.00
2018	0.01	0.00



Table 2a. Summary of Guillain-Barré Syndrome (GBS) Diagnosis following Incident Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Year

Year	New Users per 10,000 Eligible Members ¹	New Episodes with Outcome per 1,000 Years at Risk
As Treated		
Durvalumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.00	-
2016	0.00	-
2017	0.01	0.00
2018	0.03	0.00
Nivolumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.70	1.64
2016	2.31	0.00
2017	0.95	0.00
2018	0.36	0.00
Pembrolizumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	0.00
2015	0.24	3.37
2016	0.63	1.35
2017	0.79	0.00
2018	0.35	0.00

Table 2a. Summary of Guillain-Barré Syndrome (GBS) Diagnosis following Incident Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Year

Year	New Users per 10,000 Eligible Members ¹	New Episodes with Outcome per 1,000 Years at Risk
Intent-to-Treat		
Ipilimumab		
2011	0.07	0.00
2012	0.19	4.02
2013	0.19	7.14
2014	0.24	2.77
2015	0.20	13.21
2016	0.19	14.05
2017	0.15	0.00
2018	0.05	0.00
Atezolizumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.00	-
2016	0.10	0.00
2017	0.09	0.00
2018	0.09	0.00
Avelumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.00	-
2016	0.00	-
2017	0.00	0.00
2018	0.01	0.00



Table 2a. Summary of Guillain-Barré Syndrome (GBS) Diagnosis following Incident Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Year

Year	New Users per 10,000 Eligible Members ¹	New Episodes with Outcome per 1,000 Years at Risk
Intent-to-Treat		
Durvalumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.00	-
2016	0.00	-
2017	0.01	0.00
2018	0.03	0.00
Nivolumab		
2011	0.00	-
2012	0.00	0.00
2013	0.00	-
2014	0.00	-
2015	0.70	0.95
2016	2.31	2.65
2017	0.95	0.00
2018	0.36	0.00
Pembrolizumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	0.00
2015	0.24	2.67
2016	0.63	2.29
2017	0.79	0.00
2018	0.35	0.00

Table 2a. Summary of Guillain-Barré Syndrome (GBS) Diagnosis following Incident Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Year

Year	New Users per 10,000 Eligible Members ¹	New Episodes with Outcome per 1,000 Years at Risk
Intent-to-Treat		
Same-Day Ipilimumab & Nivolumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.02	0.00
2016	0.10	20.12
2017	0.11	0.00
2018	0.04	0.00

¹Eligible members and member-years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period.



Table 2b. Summary of Bell's Palsy Diagnosis following Incident Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Year

Year	New Users per 10,000 Eligible Members ¹	New Episodes with Outcome per 1,000 Years at Risk
As Treated		
Ipilimumab		
2011	0.07	0.00
2012	0.18	13.49
2013	0.19	5.84
2014	0.24	27.59
2015	0.19	0.00
2016	0.19	43.89
2017	0.15	64.85
2018	0.04	0.00
Atezolizumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.00	-
2016	0.10	0.00
2017	0.09	0.00
2018	0.09	0.00
Avelumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.00	-
2016	0.00	-
2017	0.00	0.00
2018	0.01	0.00



Table 2b. Summary of Bell's Palsy Diagnosis following Incident Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Year

Year	New Users per 10,000 Eligible Members ¹	New Episodes with Outcome per 1,000 Years at Risk
As Treated		
Durvalumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.00	-
2016	0.00	-
2017	0.01	0.00
2018	0.03	0.00
Nivolumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.70	6.63
2016	2.30	7.96
2017	0.94	5.31
2018	0.35	32.36
Pembrolizumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	0.00
2015	0.23	3.42
2016	0.62	9.61
2017	0.79	8.27
2018	0.35	0.00

Table 2b. Summary of Bell's Palsy Diagnosis following Incident Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Year

Year	New Users per 10,000 Eligible Members ¹	New Episodes with Outcome per 1,000 Years at Risk
Intent-to-Treat		
Ipilimumab		
2011	0.07	0.00
2012	0.18	12.22
2013	0.19	7.21
2014	0.24	22.50
2015	0.19	10.01
2016	0.19	32.09
2017	0.15	44.54
2018	0.04	0.00
Atezolizumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.00	-
2016	0.10	0.00
2017	0.09	0.00
2018	0.09	0.00
Avelumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.00	-
2016	0.00	-
2017	0.00	0.00
2018	0.01	0.00

Table 2b. Summary of Bell's Palsy Diagnosis following Incident Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Year

Year	New Users per 10,000 Eligible Members ¹	New Episodes with Outcome per 1,000 Years at Risk
Intent-to-Treat		
Durvalumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.00	-
2016	0.00	-
2017	0.01	0.00
2018	0.03	0.00
Nivolumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.70	6.70
2016	2.30	8.31
2017	0.94	7.17
2018	0.35	23.15
Pembrolizumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	0.00
2015	0.23	2.72
2016	0.62	11.64
2017	0.79	7.15
2018	0.35	0.00

Table 2b. Summary of Bell's Palsy Diagnosis following Incident Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Year

Year	New Users per 10,000 Eligible Members¹	New Episodes with Outcome per 1,000 Years at Risk
Intent-to-Treat		
Same-Day Ipilimumab & Nivolumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.02	0.00
2016	0.10	47.65
2017	0.11	32.54
2018	0.04	0.00

¹Eligible members and member-years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period.

Table 2c. Summary of Guillain-Barré Syndrome (GBS) Diagnosis following Prevalent Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Year

Year	Users per 10,000 Eligible Members ¹	Episodes with Outcome per 1,000 Years at Risk
As Treated		
Ipilimumab		
2011	0.07	0.00
2012	0.20	4.43
2013	0.23	0.00
2014	0.27	2.98
2015	0.23	6.94
2016	0.28	12.46
2017	0.19	0.00
2018	0.08	0.00
Atezolizumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.00	-
2016	0.10	0.00
2017	0.11	0.00
2018	0.12	0.00
Avelumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.00	-
2016	0.00	-
2017	0.00	0.00
2018	0.02	0.00

Table 2c. Summary of Guillain-Barré Syndrome (GBS) Diagnosis following Prevalent Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Year

Year	Users per 10,000 Eligible Members ¹	Episodes with Outcome per 1,000 Years at Risk
As Treated		
Durvalumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.00	-
2016	0.00	-
2017	0.01	0.00
2018	0.04	0.00
Nivolumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.71	2.84
2016	2.74	0.54
2017	1.26	1.15
2018	0.90	0.00
Pembrolizumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	0.00
2015	0.29	2.60
2016	0.78	1.12
2017	0.91	0.00
2018	0.69	0.00

Table 2c. Summary of Guillain-Barré Syndrome (GBS) Diagnosis following Prevalent Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Year

Year	Users per 10,000 Eligible Members ¹	Episodes with Outcome per 1,000 Years at Risk
Intent-to-Treat		
Ipilimumab		
2011	0.07	0.00
2012	0.19	3.35
2013	0.22	5.53
2014	0.26	2.25
2015	0.22	12.62
2016	0.26	10.87
2017	0.18	0.00
2018	0.07	0.00
Atezolizumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.00	-
2016	0.10	0.00
2017	0.10	0.00
2018	0.09	0.00
Avelumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.00	-
2016	0.00	-
2017	0.00	0.00
2018	0.02	0.00

Table 2c. Summary of Guillain-Barré Syndrome (GBS) Diagnosis following Prevalent Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Year

Year	Users per 10,000 Eligible Members ¹	Episodes with Outcome per 1,000 Years at Risk
Intent-to-Treat		
Durvalumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.00	-
2016	0.00	-
2017	0.01	0.00
2018	0.03	0.00
Nivolumab		
2011	0.00	-
2012	0.00	0.00
2013	0.00	-
2014	0.00	-
2015	0.71	2.51
2016	2.49	2.87
2017	1.02	0.00
2018	0.44	0.00
Pembrolizumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	0.00
2015	0.29	3.82
2016	0.69	2.73
2017	0.82	0.00
2018	0.41	0.00

Table 2c. Summary of Guillain-Barré Syndrome (GBS) Diagnosis following Prevalent Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Year

Year	Users per 10,000 Eligible Members ¹	Episodes with Outcome per 1,000 Years at Risk
Intent-to-Treat		
Same-Day Ipilimumab & Nivolumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.03	0.00
2016	0.14	12.59
2017	0.13	0.00
2018	0.05	0.00

¹Eligible members and member-years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period.

Table 2d. Summary of Bell's Palsy Diagnosis following Prevalent Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Year

Year	Users per 10,000 Eligible Members ¹	Episodes with Outcome per 1,000 Years at Risk
As Treated		
Ipilimumab		
2011	0.07	0.00
2012	0.20	13.42
2013	0.23	7.31
2014	0.27	24.21
2015	0.23	7.01
2016	0.27	31.54
2017	0.19	40.49
2018	0.08	0.00
Atezolizumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.00	-
2016	0.10	0.00
2017	0.11	0.00
2018	0.12	0.00
Avelumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.00	-
2016	0.00	-
2017	0.00	0.00
2018	0.02	0.00

Table 2d. Summary of Bell's Palsy Diagnosis following Prevalent Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Year

Year	Users per 10,000 Eligible Members ¹	Episodes with Outcome per 1,000 Years at Risk
As Treated		
Durvalumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.00	-
2016	0.00	-
2017	0.01	0.00
2018	0.04	0.00
Nivolumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.71	7.61
2016	2.73	6.56
2017	1.25	4.65
2018	0.90	9.03
Pembrolizumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	0.00
2015	0.29	6.62
2016	0.77	7.37
2017	0.90	7.65
2018	0.68	11.63

Table 2d. Summary of Bell's Palsy Diagnosis following Prevalent Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Year

Year	Users per 10,000 Eligible Members ¹	Episodes with Outcome per 1,000 Years at Risk
Intent-to-Treat		
Ipilimumab		
2011	0.07	0.00
2012	0.19	13.53
2013	0.22	5.57
2014	0.26	29.82
2015	0.22	10.20
2016	0.26	26.46
2017	0.18	32.86
2018	0.07	0.00
Atezolizumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.00	-
2016	0.10	0.00
2017	0.10	0.00
2018	0.09	0.00
Avelumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.00	-
2016	0.00	-
2017	0.00	0.00
2018	0.02	0.00

Table 2d. Summary of Bell's Palsy Diagnosis following Prevalent Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Year

Year	Users per 10,000 Eligible Members ¹	Episodes with Outcome per 1,000 Years at Risk
Intent-to-Treat		
Durvalumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.00	-
2016	0.00	-
2017	0.01	0.00
2018	0.03	0.00
Nivolumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.71	6.74
2016	2.48	7.95
2017	1.01	6.47
2018	0.44	28.82
Pembrolizumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	0.00
2015	0.29	11.66
2016	0.69	12.94
2017	0.81	9.24
2018	0.41	17.64

Table 2d. Summary of Bell's Palsy Diagnosis following Prevalent Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Year

Year	Users per 10,000 Eligible Members¹	Episodes with Outcome per 1,000 Years at Risk
Intent-to-Treat		
Same-Day Ipilimumab & Nivolumab		
2011	0.00	-
2012	0.00	-
2013	0.00	-
2014	0.00	-
2015	0.03	0.00
2016	0.14	34.10
2017	0.13	22.83
2018	0.05	0.00

¹Eligible members and member-years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period.

Table 3a. Summary of Guillain-Barré Syndrome (GBS) Diagnosis following Incident Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Sex

Sex	New Users per 10,000 Eligible Members ¹	New Episodes with Outcome per 1,000 Years at Risk
As Treated		
Ipilimumab		
Female	0.41	0.00
Male	0.78	9.27
Other	0.00	-
Atezolizumab		
Female	0.06	0.00
Male	0.13	0.00
Other	0.00	-
Avelumab		
Female	0.00	0.00
Male	0.00	0.00
Other	0.00	-
Durvalumab		
Female	0.01	0.00
Male	0.01	0.00
Other	0.00	-
Nivolumab		
Female	1.62	0.00
Male	2.32	0.52
Other	1.99	0.00
Pembrolizumab		
Female	0.58	1.50
Male	0.95	0.99
Other	0.00	-

Table 3a. Summary of Guillain-Barré Syndrome (GBS) Diagnosis following Incident Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Sex

Sex	New Users per 10,000 Eligible Members ¹	New Episodes with Outcome per 1,000 Years at Risk
Intent-to-Treat		
Ipilimumab		
Female	0.41	3.19
Male	0.78	9.22
Other	0.00	-
Atezolizumab		
Female	0.06	0.00
Male	0.13	0.00
Other	0.00	-
Avelumab		
Female	0.00	0.00
Male	0.00	0.00
Other	0.00	-
Durvalumab		
Female	0.01	0.00
Male	0.01	0.00
Other	0.00	-
Nivolumab		
Female	1.62	2.14
Male	2.32	1.66
Other	1.99	0.00
Pembrolizumab		
Female	0.58	1.25
Male	0.95	1.67
Other	0.00	-
Same-Day Ipilimumab & Nivolumab		
Female	0.07	10.00
Male	0.14	11.38
Other	0.00	-

¹Eligible members and member-years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period.

Table 3b. Summary of Bell's Palsy Diagnosis following Incident Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Sex

Sex	New Users per 10,000 Eligible Members ¹	New Episodes with Outcome per 1,000 Years at Risk
As Treated		
Ipilimumab		
Female	0.40	16.43
Male	0.77	23.47
Other	0.00	-
Atezolizumab		
Female	0.06	0.00
Male	0.13	0.00
Other	0.00	-
Avelumab		
Female	0.00	0.00
Male	0.00	0.00
Other	0.00	-
Durvalumab		
Female	0.01	0.00
Male	0.01	0.00
Other	0.00	-
Nivolumab		
Female	1.61	4.17
Male	2.30	10.02
Other	1.99	0.00
Pembrolizumab		
Female	0.58	10.64
Male	0.93	6.02
Other	0.00	-

Table 3b. Summary of Bell's Palsy Diagnosis following Incident Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Sex

Sex	New Users per 10,000 Eligible Members ¹	New Episodes with Outcome per 1,000 Years at Risk
Intent-to-Treat		
Ipilimumab		
Female	0.40	14.52
Male	0.77	20.55
Other	0.00	-
Atezolizumab		
Female	0.06	0.00
Male	0.13	0.00
Other	0.00	-
Avelumab		
Female	0.00	0.00
Male	0.00	0.00
Other	0.00	-
Durvalumab		
Female	0.01	0.00
Male	0.01	0.00
Other	0.00	-
Nivolumab		
Female	1.61	4.32
Male	2.30	10.74
Other	1.99	0.00
Pembrolizumab		
Female	0.58	10.18
Male	0.93	6.80
Other	0.00	-
Same-Day Ipilimumab & Nivolumab		
Female	0.07	20.26
Male	0.14	46.16
Other	0.00	-

¹Eligible members and member-years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period.

Table 3c. Summary of Guillain-Barré Syndrome (GBS) Diagnosis following Prevalent Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Sex

Sex	Users per 10,000 Eligible Members ¹	Episodes with Outcome per 1,000 Years at Risk
As Treated		
Ipilimumab		
Female	0.44	1.65
Male	0.84	6.53
Other	0.00	-
Atezolizumab		
Female	0.06	0.00
Male	0.13	0.00
Other	0.00	-
Avelumab		
Female	0.00	0.00
Male	0.00	0.00
Other	0.00	-
Durvalumab		
Female	0.01	0.00
Male	0.01	0.00
Other	0.00	-
Nivolumab		
Female	1.66	0.28
Male	2.39	1.44
Other	1.31	0.00
Pembrolizumab		
Female	0.62	0.65
Male	1.01	1.24
Other	0.00	-

Table 3c. Summary of Guillain-Barré Syndrome (GBS) Diagnosis following Prevalent Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Sex

Sex	Users per 10,000 Eligible Members ¹	Episodes with Outcome per 1,000 Years at Risk
Intent-to-Treat		
Ipilimumab		
Female	0.44	4.80
Male	0.84	6.85
Other	0.00	-
Atezolizumab		
Female	0.06	0.00
Male	0.13	0.00
Other	0.00	-
Avelumab		
Female	0.00	0.00
Male	0.00	0.00
Other	0.00	-
Durvalumab		
Female	0.01	0.00
Male	0.01	0.00
Other	0.00	-
Nivolumab		
Female	1.66	2.13
Male	2.39	2.42
Other	1.31	0.00
Pembrolizumab		
Female	0.62	0.98
Male	1.01	2.60
Other	0.00	-
Same-Day Ipilimumab & Nivolumab		
Female	0.10	6.31
Male	0.18	7.50
Other	0.00	-

¹Eligible members and member-years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period.

Table 3d. Summary of Bell's Palsy Diagnosis following Prevalent Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Sex

Sex	Users per 10,000 Eligible Members ¹	Episodes with Outcome per 1,000 Years at Risk
As Treated		
Ipilimumab		
Female	0.43	21.73
Male	0.83	17.00
Other	0.00	-
Atezolizumab		
Female	0.06	0.00
Male	0.13	0.00
Other	0.00	-
Avelumab		
Female	0.00	0.00
Male	0.00	0.00
Other	0.00	-
Durvalumab		
Female	0.01	0.00
Male	0.01	0.00
Other	0.00	-
Nivolumab		
Female	1.65	5.07
Male	2.37	7.26
Other	1.31	0.00
Pembrolizumab		
Female	0.62	7.86
Male	0.99	7.12
Other	0.00	-

Table 3d. Summary of Bell's Palsy Diagnosis following Prevalent Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Sex

Sex	Users per 10,000 Eligible Members ¹	Episodes with Outcome per 1,000 Years at Risk
Intent-to-Treat		
Ipilimumab		
Female	0.43	18.22
Male	0.83	18.74
Other	0.00	-
Atezolizumab		
Female	0.06	0.00
Male	0.13	0.00
Other	0.00	-
Avelumab		
Female	0.00	0.00
Male	0.00	0.00
Other	0.00	-
Durvalumab		
Female	0.01	0.00
Male	0.01	0.00
Other	0.00	-
Nivolumab		
Female	1.65	4.29
Male	2.37	10.29
Other	1.31	0.00
Pembrolizumab		
Female	0.62	10.91
Male	0.99	11.90
Other	0.00	-
Same-Day Ipilimumab & Nivolumab		
Female	0.09	19.22
Male	0.18	30.46
Other	0.00	-

¹Eligible members and member-years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period.

Table 4a. Summary of Guillain-Barré Syndrome (GBS) Diagnosis following Incident Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Age

Age (Years)	New Users per 10,000 Eligible Members ¹	New Episodes with Outcome per 1,000 Years at Risk
As Treated		
Ipilimumab		
0-64	0.26	2.79
65+	1.42	7.60
Atezolizumab		
0-64	0.03	0.00
65+	0.27	0.00
Avelumab		
0-64	0.00	0.00
65+	0.01	0.00
Durvalumab		
0-64	0.00	0.00
65+	0.01	0.00
Nivolumab		
0-64	0.70	1.02
65+	5.24	0.00
Pembrolizumab		
0-64	0.29	1.96
65+	1.99	0.86

Table 4a. Summary of Guillain-Barré Syndrome (GBS) Diagnosis following Incident Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Age

Age (Years)	New Users per 10,000 Eligible Members ¹	New Episodes with Outcome per 1,000 Years at Risk
Intent-to-Treat		
Ipilimumab		
0-64	0.26	1.72
65+	1.42	9.73
Atezolizumab		
0-64	0.03	0.00
65+	0.27	0.00
Avelumab		
0-64	0.00	0.00
65+	0.01	0.00
Durvalumab		
0-64	0.00	0.00
65+	0.01	0.00
Nivolumab		
0-64	0.70	0.69
65+	5.24	2.31
Pembrolizumab		
0-64	0.29	1.75
65+	1.99	1.40
Same-Day Ipilimumab & Nivolumab		
0-64	0.07	0.00
65+	0.19	21.74

¹Eligible members and member-years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period.

Table 4b. Summary of Bell's Palsy Diagnosis following Incident Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Age

Age (Years)	New Users per 10,000 Eligible Members¹	New Episodes with Outcome per 1,000 Years at Risk
As Treated		
Ipilimumab		
0-64	0.26	22.63
65+	1.40	19.98
Atezolizumab		
0-64	0.03	0.00
65+	0.27	0.00
Avelumab		
0-64	0.00	0.00
65+	0.01	0.00
Durvalumab		
0-64	0.00	0.00
65+	0.01	0.00
Nivolumab		
0-64	0.69	11.40
65+	5.21	5.91
Pembrolizumab		
0-64	0.28	11.94
65+	1.96	6.08

Table 4b. Summary of Bell's Palsy Diagnosis following Incident Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Age

Age (Years)	New Users per 10,000 Eligible Members¹	New Episodes with Outcome per 1,000 Years at Risk
Intent-to-Treat		
Ipilimumab		
0-64	0.26	20.96
65+	1.40	16.99
Atezolizumab		
0-64	0.03	0.00
65+	0.27	0.00
Avelumab		
0-64	0.00	0.00
65+	0.01	0.00
Durvalumab		
0-64	0.00	0.00
65+	0.01	0.00
Nivolumab		
0-64	0.69	12.63
65+	5.21	6.20
Pembrolizumab		
0-64	0.28	12.50
65+	1.96	6.42
Same-Day Ipilimumab & Nivolumab		
0-64	0.07	44.38
65+	0.19	29.24

¹Eligible members and member-years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period.

Table 4c. Summary of Guillain-Barré Syndrome (GBS) Diagnosis following Prevalent Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Age

Age (Years)	Users per 10,000 Eligible Members ¹	Episodes with Outcome per 1,000 Years at Risk
As Treated		
Ipilimumab		
0-64	0.28	3.33
65+	1.62	5.58
Atezolizumab		
0-64	0.03	0.00
65+	0.29	0.00
Avelumab		
0-64	0.00	0.00
65+	0.01	0.00
Durvalumab		
0-64	0.00	0.00
65+	0.01	0.00
Nivolumab		
0-64	0.76	1.85
65+	5.62	0.52
Pembrolizumab		
0-64	0.32	0.80
65+	2.22	1.10

Table 4c. Summary of Guillain-Barré Syndrome (GBS) Diagnosis following Prevalent Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Age

Age (Years)	Users per 10,000 Eligible Members ¹	Episodes with Outcome per 1,000 Years at Risk
Intent-to-Treat		
Ipilimumab		
0-64	0.28	2.45
65+	1.61	8.13
Atezolizumab		
0-64	0.03	0.00
65+	0.28	0.00
Avelumab		
0-64	0.00	0.00
65+	0.01	0.00
Durvalumab		
0-64	0.00	0.00
65+	0.01	0.00
Nivolumab		
0-64	0.76	1.52
65+	5.57	2.62
Pembrolizumab		
0-64	0.32	1.26
65+	2.20	2.27
Same-Day Ipilimumab & Nivolumab		
0-64	0.08	0.00
65+	0.27	13.99

¹Eligible members and member-years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period.

Table 4d. Summary of Bell's Palsy Diagnosis following Prevalent Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Age

Age (Years)	Users per 10,000 Eligible Members ¹	Episodes with Outcome per 1,000 Years at Risk
As Treated		
Ipilimumab		
0-64	0.28	20.24
65+	1.60	17.85
Atezolizumab		
0-64	0.03	0.00
65+	0.28	0.00
Avelumab		
0-64	0.00	0.00
65+	0.01	0.00
Durvalumab		
0-64	0.00	0.00
65+	0.01	0.00
Nivolumab		
0-64	0.75	8.59
65+	5.59	5.27
Pembrolizumab		
0-64	0.31	9.71
65+	2.19	6.35

Table 4d. Summary of Bell's Palsy Diagnosis following Prevalent Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018, by Age

Age (Years)	Users per 10,000 Eligible Members ¹	Episodes with Outcome per 1,000 Years at Risk
Intent-to-Treat		
Ipilimumab		
0-64	0.28	22.36
65+	1.60	16.45
Atezolizumab		
0-64	0.03	0.00
65+	0.28	0.00
Avelumab		
0-64	0.00	0.00
65+	0.01	0.00
Durvalumab		
0-64	0.00	0.00
65+	0.01	0.00
Nivolumab		
0-64	0.75	11.81
65+	5.54	5.95
Pembrolizumab		
0-64	0.31	14.06
65+	2.18	10.36
Same-Day Ipilimumab & Nivolumab		
0-64	0.08	33.90
65+	0.27	18.86

¹Eligible members and member-years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period.

Table 5a. Summary of Time to Guillain-Barré Syndrome (GBS) Diagnosis, following Incident Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018

Drug	Number of Episodes	Minimum (Days)	25th Percentile (Days)	Median (Days)	75th Percentile (Days)	90th Percentile (Days)	95th Percentile (Days)	Maximum (Days)	Mean (Days)	Standard Deviation (Days)
As Treated										
Ipilimumab	****	22	34	45	57	64	64	64	44.3	15.3
Atezolizumab	-	-	-	-	-	-	-	-	-	-
Avelumab	-	-	-	-	-	-	-	-	-	-
Durvalumab	-	-	-	-	-	-	-	-	-	-
Nivolumab	****	****	****	****	****	****	****	****	****	****
Pembrolizumab	****	14	14	29	43	43	43	43	28.5	20.5
Intent-to-Treat										
Ipilimumab	12	22	31	45	61	67	83	83	46.9	18.9
Atezolizumab	-	-	-	-	-	-	-	-	-	-
Avelumab	-	-	-	-	-	-	-	-	-	-
Durvalumab	-	-	-	-	-	-	-	-	-	-
Nivolumab	****	24	41	57	66	75	75	75	53.3	17.6
Pembrolizumab	****	14	14	32	43	43	43	43	29.7	14.6
Same-Day Ipilimumab and Nivolumab	****	41	41	57	64	64	64	64	54.0	11.8

¹Eligible members and member-years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period.

****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

Table 5b. Summary of Time to Bell's Palsy Diagnosis, following Incident Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018

Drug	Number of Episodes	Minimum (Days)	25th Percentile (Days)	Median (Days)	75th Percentile (Days)	90th Percentile (Days)	95th Percentile (Days)	Maximum (Days)	Mean (Days)	Standard Deviation (Days)
As Treated										
Ipilimumab	21	5	11	35	55	70	73	81	35.0	25.8
Atezolizumab	-	-	-	-	-	-	-	-	-	-
Avelumab	-	-	-	-	-	-	-	-	-	-
Durvalumab	-	-	-	-	-	-	-	-	-	-
Nivolumab	25	1	8	11	38	193	233	333	52.5	98.3
Pembrolizumab	13	1	7	17	64	117	310	310	56.6	89.6
Intent-to-Treat										
Ipilimumab	12	5	15	45	64	71	73	81	42.1	25.6
Atezolizumab	-	-	-	-	-	-	-	-	-	-
Avelumab	-	-	-	-	-	-	-	-	-	-
Durvalumab	-	-	-	-	-	-	-	-	-	-
Nivolumab	42	1	11	32	55	75	82	84	35.8	29.5
Pembrolizumab	16	1	7	27	50	69	79	79	31.0	26.5
Same-Day Ipilimumab and Nivolumab	****	11	12	47	59	72	73	73	41.9	25.3

¹Eligible members and member-years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period.

****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

Table 5c. Summary of Time to Guillain-Barré Syndrome (GBS) Diagnosis, following Prevalent Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018

Drug	Number of Episodes	Minimum (Days)	25th Percentile (Days)	Median (Days)	75th Percentile (Days)	90th Percentile (Days)	95th Percentile (Days)	Maximum (Days)	Mean (Days)	Standard Deviation (Days)
As Treated										
Ipilimumab	*****	15	19	38	52	64	64	64	37.0	20.2
Atezolizumab	-	-	-	-	-	-	-	-	-	-
Avelumab	-	-	-	-	-	-	-	-	-	-
Durvalumab	-	-	-	-	-	-	-	-	-	-
Nivolumab	*****	1	10	16	93	104	104	104	41.7	42.2
Pembrolizumab	*****	9	12	16	30	43	43	43	20.8	15.2
Intent-to-Treat										
Ipilimumab	12	15	27	44	57	67	83	83	44.5	19.4
Atezolizumab	-	-	-	-	-	-	-	-	-	-
Avelumab	-	-	-	-	-	-	-	-	-	-
Durvalumab	-	-	-	-	-	-	-	-	-	-
Nivolumab	15	1	24	53	66	66	75	75	46.2	25.0
Pembrolizumab	*****	9	14	32	43	59	59	59	31.4	20.6
Same-Day Ipilimumab and Nivolumab	*****	41	41	57	64	64	64	64	54.0	11.8

¹Eligible members and member-years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

Table 5d. Summary of Time to Bell's Palsy Diagnosis, following Prevalent Checkpoint Inhibitor Initiation in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018

Drug	Number of Episodes	Minimum (Days)	25th Percentile (Days)	Median (Days)	75th Percentile (Days)	90th Percentile (Days)	95th Percentile (Days)	Maximum (Days)	Mean (Days)	Standard Deviation (Days)
As Treated										
Ipilimumab	31	1	12	26	52	70	73	81	31.9	24.6
Atezolizumab	-	-	-	-	-	-	-	-	-	-
Avelumab	-	-	-	-	-	-	-	-	-	-
Durvalumab	-	-	-	-	-	-	-	-	-	-
Nivolumab	53	1	8	14	39	126	193	333	41.1	74.2
Pembrolizumab	29	1	10	32	64	113	117	310	52.2	71.8
Intent-to-Treat										
Ipilimumab	12	1	21	45	64	72	77	81	42.5	25.4
Atezolizumab	-	-	-	-	-	-	-	-	-	-
Avelumab	-	-	-	-	-	-	-	-	-	-
Durvalumab	-	-	-	-	-	-	-	-	-	-
Nivolumab	50	1	11	32	55	74	80	84	36.0	28.3
Pembrolizumab	29	1	12	34	59	69	70	79	36.1	26.0
Same-Day Ipilimumab and Nivolumab	11	11	12	44	59	70	73	73	40.2	24.6

¹Eligible members and member-years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period.

Table 6a. Summary of Time to Treatment Episode End, following Incident Checkpoint Inhibitor Initiation among Users without Evidence of Guillain-Barré Syndrome (GBS) or Censoring¹ in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018

Drug	Number of Episodes	Minimum (Days)	25th Percentile (Days)	Median (Days)	75th Percentile (Days)	90th Percentile (Days)	95th Percentile (Days)	Maximum (Days)	Mean (Days)	Standard Deviation (Days)
Ipilimumab	7,563	22	22	43	64	85	85	148	46.0	158.8
Atezolizumab	895	22	22	22	43	85	94	400	40.9	118.3
Avelumab	16	22	22	22	22	46	64	64	27.0	18.9
Durvalumab	46	15	15	15	29	44	57	169	24.2	50.6
Nivolumab	24,093	15	15	15	44	86	140	799	41.6	312.9
Pembrolizumab	8,080	22	22	41	64	123	169	631	55.1	246.8

¹Censoring criteria includes death, disenrollment, and Data Partner end date.

Table 6b. Summary of Time to Treatment Episode End, following Incident Checkpoint Inhibitor Initiation among Users without Evidence of Bell's Palsy or Censoring¹ in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018

Drug	Number of Episodes	Minimum (Days)	25th Percentile (Days)	Median (Days)	75th Percentile (Days)	90th Percentile (Days)	95th Percentile (Days)	Maximum (Days)	Mean (Days)	Standard Deviation (Days)
Ipilimumab	7,461	22	22	43	64	85	85	148	46.0	159.2
Atezolizumab	876	22	22	22	43	82	104	400	40.3	117.6
Avelumab	15	22	22	22	22	46	64	64	27.3	18.7
Durvalumab	40	15	15	15	29	44	63	169	25.5	52.6
Nivolumab	23,880	15	15	15	44	86	140	799	41.7	311.9
Pembrolizumab	7,938	22	22	41	64	125	169	631	55.4	247.3

¹Censoring criteria includes death, disenrollment, and Data Partner end date.

Table 6c. Summary of Time to Treatment Episode End, following Prevalent Checkpoint Inhibitor Initiation among Users without Evidence of Guillain-Barré Syndrome (GBS) or Censoring¹ in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018

Drug	Number of Episodes	Minimum (Days)	25th Percentile (Days)	Median (Days)	75th Percentile (Days)	90th Percentile (Days)	95th Percentile (Days)	Maximum (Days)	Mean (Days)	Standard Deviation (Days)
Ipilimumab	14,458	22	22	22	44	85	85	170	40.1	182.0
Atezolizumab	1,590	22	22	22	43	84	106	400	41.9	133.8
Avelumab	26	22	22	22	22	50	64	76	28.2	25.6
Durvalumab	68	15	15	15	15	43	44	169	22.0	50.2
Nivolumab	74,788	15	15	15	30	71	113	869	34.1	394.6
Pembrolizumab	21,283	22	22	41	64	106	148	819	52.8	315.5

¹Censoring criteria includes death, disenrollment, and Data Partner end date.

Table 6d. Summary of Time to Treatment Episode End, following Prevalent Checkpoint Inhibitor Initiation among Users without Evidence of Bell's Palsy or Censoring¹ in the Sentinel Distributed Database (SDD) between March 1, 2011 and June 30, 2018

Drug	Number of Episodes	Minimum (Days)	25th Percentile (Days)	Median (Days)	75th Percentile (Days)	90th Percentile (Days)	95th Percentile (Days)	Maximum (Days)	Mean (Days)	Standard Deviation (Days)
Ipilimumab	14,283	22	22	22	47	85	85	170	40.1	181.6
Atezolizumab	1,578	22	22	22	43	84	106	400	41.9	133.6
Avelumab	25	22	22	22	22	50	64	76	28.5	25.5
Durvalumab	67	15	15	15	15	43	44	169	22.1	50.2
Nivolumab	74,181	15	15	15	30	71	113	869	34.2	394.3
Pembrolizumab	20,875	22	22	41	64	106	148	819	52.8	314.6

¹Censoring criteria includes death, disenrollment, and Data Partner end date.

Appendix A. Dates of Available Data for Each Data Partner (DP) as of Request Distribution Date (September 25, 2018)

DP ID	DP Start Date ¹	DP End Date ¹
DP01	01/01/2000	03/31/2016
DP02	06/01/2007	01/31/2018
DP03	01/01/2000	06/30/2018
DP04	01/01/2008	03/31/2018
DP05	01/01/2012	06/30/2017
DP06	01/01/2000	12/31/2016
DP07	01/01/2008	06/30/2017
DP08	01/01/2000	12/31/2017
DP09	01/01/2000	03/31/2018
DP10	01/01/2000	05/31/2015
DP11	01/01/2000	03/31/2018
DP12	01/01/2000	10/31/2017
DP13	01/01/2005	12/17/2017
DP14	01/01/2006	12/31/2017
DP15	01/01/2004	05/31/2018
DP16	01/01/2000	06/30/2017
DP17	01/01/2010	12/31/2016

¹The start and end dates are based on the minimum and maximum dates within each DP. The month with the maximum date must have at least 80% of the number of records in the previous month.

Appendix B. List of Generic and Brand Drug Names with Food and Drug Administration (FDA) Approval Dates Used to Define Exposures of Interest in this Request

Generic Name	Brand Name	Approval Date
Ipilimumab	Yervoy	March 25, 2011
Atezolizumab	Tecentriq	May 18, 2016
Avelumab	Bavencio	March 23, 2017
Durvalumab	Imfinzi	May 1, 2017
Nivolumab	Opdivo	December 22, 2014
Pembrolizumab	Keytruda	September 4, 2014

Appendix C. List of Healthcare Common Procedure Coding System (HCPCS) Procedure Codes Used to Define Exposures and Incidence Criteria in this Request

Code	Description	Code Type
C9284	Injection, ipilimumab, 1 mg	HCPCS
J9228	Injection, ipilimumab, 1 mg	HCPCS
C9483	Injection, atezolizumab, 10 mg	HCPCS
J9022	Injection, atezolizumab, 10 mg	HCPCS
J9023	Injection, avelumab, 10 mg	HCPCS
C9491	Injection, avelumab, 10 mg	HCPCS
C9492	Injection, durvalumab, 10 mg	HCPCS
C9453	Injection, nivolumab, 1 mg	HCPCS
J9299	Injection, nivolumab, 1 mg	HCPCS
J9271	Injection, pembrolizumab, 1 mg	HCPCS
C9027	Injection, pembrolizumab, 1 mg	HCPCS

Appendix D. List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) Diagnosis Codes Used to Define Outcomes in this Request

Code	Full Description	Code Type
Guillain-Barré Syndrome (GBS)		
357.0	Acute Infective Polyneuritis	ICD-9-CM
G61.0	Guillain-Barré syndrome	ICD-10-CM
Bell's Palsy		
351.0	Bell's palsy	ICD-9-CM
G51.0	Bell's palsy	ICD-10-CM

Appendix E. Specifications Defining Parameters in this Request, Incident Cohort

This request used the Cohort Identification and Descriptive Analysis (CIDA) tool, version 5.4.4, to examine the occurrence of Guillain-Barré syndrome (GBS) and Bell's palsy after checkpoint inhibitor initiation among members in the Sentinel Distributed Database (SDD). This request also examined the time to GBS or Bell's palsy diagnosis after checkpoint inhibitor initiation among users in the SDD.

Query Period: March 1, 2011 to June 30, 2018
Enrollment Gap: 45 days
Age Groups: <65, 65+ years
Enrollment Requirement: 183 days
Coverage Requirements: Medical and Drug

Exposure										Outcome				
Scenario	Exposure	Combination Window	Combination Index Date	Care Setting	Incident with Respect to	Washout (Days)	Intent-to-Treat (ITT)	Episode Gap	Episode Extension	Truncation Criteria	Cohort Definition ¹	Condition	Care Setting	Washout
1	Ipilimumab (procedure code)	---	---	Any	All checkpoint inhibitors (procedure codes and NDCs)	183	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	GBS	Any	Entire History
2	Atezolizumab (procedure code)	---	---	Any	All checkpoint inhibitors (procedure codes and NDCs)	183	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	GBS	Any	Entire History
3	Avelumab (procedure code)	---	---	Any	All checkpoint inhibitors (procedure codes and NDCs)	183	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	GBS	Any	Entire History
4	Durvalumab (procedure code)	---	---	Any	All checkpoint inhibitors (procedure codes and NDCs)	183	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	GBS	Any	Entire History
5	Nivolumab (procedure code)	---	---	Any	All checkpoint inhibitors (procedure codes and NDCs)	183	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	GBS	Any	Entire History
6	Pembrolizumab (procedure code)	---	---	Any	All checkpoint inhibitors (procedure codes and NDCs)	183	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	GBS	Any	Entire History

Appendix E. Specifications Defining Parameters in this Request, Incident Cohort

Scenario	Exposure										Outcome			
	Exposure	Combination Window	Combination Index Date	Care Setting	Incident with Respect to	Washout (Days)	Intent-to-Treat (ITT)	Episode Gap	Episode Extension	Truncation Criteria	Cohort Definition	Condition	Care Setting	Washout
7	Combination : Ipilimumab + Nivolumab (procedure code)	Same Day	Day of Combination	Any	All checkpoint inhibitors (procedure codes and NDCs)	183	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	GBS	Any	Entire History
8	Ipilimumab (procedure code)	---	---	Any	All checkpoint inhibitors (procedure codes and NDCs)	183	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	Bell's palsy	Any	Entire History
9	Atezolizumab (procedure code)	---	---	Any	All checkpoint inhibitors (procedure codes and NDCs)	183	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	Bell's palsy	Any	Entire History
10	Avelumab (procedure code)	---	---	Any	All checkpoint inhibitors (procedure codes and NDCs)	183	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	Bell's palsy	Any	Entire History
11	Durvalumab (procedure code)	---	---	Any	All checkpoint inhibitors (procedure codes and NDCs)	183	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	Bell's palsy	Any	Entire History
12	Nivolumab (procedure code)	---	---	Any	All checkpoint inhibitors (procedure codes and NDCs)	183	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	Bell's palsy	Any	Entire History
13	Pembrolizumab (procedure code)	---	---	Any	All checkpoint inhibitors (procedure codes and NDCs)	183	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	Bell's palsy	Any	Entire History
14	Combination : Ipilimumab + Nivolumab (procedure code)	Same Day	Day of Combination	Any	All checkpoint inhibitors (procedure codes and NDCs)	183	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	Bell's palsy	Any	Entire History

Appendix E. Specifications Defining Parameters in this Request, Incident Cohort

Scenario	Exposure										Outcome			
	Exposure	Combination Window	Combination Index Date	Care Setting	Incident with Respect to	Washout (Days)	Intent-to-Treat (ITT)	Episode Gap	Episode Extension	Truncation Criteria	Cohort Definition	Condition	Care Setting	Washout
15	Ipilimumab (procedure code)	---	---	Any	All checkpoint inhibitors (procedure codes and NDCs)	183	---	3 weeks	3 weeks	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	GBS	Any	Entire History
16	Atezolizumab (procedure code)	---	---	Any	All checkpoint inhibitors (procedure codes and NDCs)	183	---	3 weeks	3 weeks	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	GBS	Any	Entire History
17	Avelumab (procedure code)	---	---	Any	All checkpoint inhibitors (procedure codes and NDCs)	183	---	3 weeks	3 weeks	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	GBS	Any	Entire History
18	Durvalumab (procedure code)	---	---	Any	All checkpoint inhibitors (procedure codes and NDCs)	183	---	2 weeks	2 weeks	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	GBS	Any	Entire History
19	Nivolumab (procedure code)	---	---	Any	All checkpoint inhibitors (procedure codes and NDCs)	183	---	2 weeks	2 weeks	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	GBS	Any	Entire History
20	Pembrolizumab (procedure code)	---	---	Any	All checkpoint inhibitors (procedure codes and NDCs)	183	---	3 weeks	3 weeks	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	GBS	Any	Entire History
21	Ipilimumab (procedure code)	---	---	Any	All checkpoint inhibitors (procedure codes and NDCs)	183	---	3 weeks	3 weeks	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	Bell's palsy	Any	Entire History
22	Atezolizumab (procedure code)	---	---	Any	All checkpoint inhibitors (procedure codes and NDCs)	183	---	3 weeks	3 weeks	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	Bell's palsy	Any	Entire History

Appendix E. Specifications Defining Parameters in this Request, Incident Cohort

Scenario	Exposure										Outcome			
	Exposure	Combination Window	Combination Index Date	Care Setting	Incident with Respect to	Washout (Days)	Intent-to-Treat (ITT)	Episode Gap	Episode Extension	Truncation Criteria	Cohort Definition	Condition	Care Setting	Washout
23	Avelumab (procedure code)	---	---	Any	All checkpoint inhibitors (procedure codes and NDCs)	183	---	3 weeks	3 weeks	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	Bell's palsy	Any	Entire History
24	Durvalumab (procedure code)	---	---	Any	All checkpoint inhibitors (procedure codes and NDCs)	183	---	2 weeks	2 weeks	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	Bell's palsy	Any	Entire History
25	Nivolumab (procedure code)	---	---	Any	All checkpoint inhibitors (procedure codes and NDCs)	183	---	2 weeks	2 weeks	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	Bell's palsy	Any	Entire History
26	Pembrolizumab (procedure code)	---	---	Any	All checkpoint inhibitors (procedure codes and NDCs)	183	---	3 weeks	3 weeks	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	Bell's palsy	Any	Entire History

International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System (HCPCS) codes are provided by Optum360.

National Drug Codes (NDCs) are checked against First Data Bank's "National Drug Data File (NDDF®) Plus."

¹ Cohort definition "02" indicates that all valid exposures are observed for the given scenario; cohort re-entry was allowed

Appendix F. Specifications Defining Parameters in this Request, Prevalent Cohort

This request used the Cohort Identification and Descriptive Analysis (CIDA) tool, version 5.4.4, to examine the occurrence of Guillain-Barré syndrome (GBS) and Bell's palsy after checkpoint inhibitor initiation among members in the Sentinel Distributed Database (SDD). This request also examined the time to GBS or Bell's palsy diagnosis after checkpoint inhibitor initiation among users in the SDD.

Query Period: March 1, 2011 to June 30, 2018
Enrollment Gap: 45 days
Age Groups: <65, 65+ years
Enrollment Requirement: 0 days
Coverage Requirements: Medical and Drug

Exposure										Outcome				
Scenario	Exposure	Combination Window	Combination Index Date	Incident		Washout (Days)	Intent-to-Treat (ITT)	Episode Gap	Episode Extension	Truncation Criteria	Cohort Definition ¹	Care		
				Care Setting	with Respect to							Condition	Setting	Washout
27	Ipilimumab (procedure code)	---	---	Any	N/A	0	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	GBS	Any	Entire History
28	Atezolizumab (procedure code)	---	---	Any	N/A	0	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	GBS	Any	Entire History
29	Avelumab (procedure code)	---	---	Any	N/A	0	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	GBS	Any	Entire History
30	Durvalumab (procedure code)	---	---	Any	N/A	0	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	GBS	Any	Entire History
31	Nivolumab (procedure code)	---	---	Any	N/A	0	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	GBS	Any	Entire History
32	Pembrolizumab (procedure code)	---	---	Any	N/A	0	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	GBS	Any	Entire History

Appendix F. Specifications Defining Parameters in this Request, Prevalent Cohort

Scenario	Exposure										Outcome				
	Exposure	Combination Window	Combination Index Date	Care Setting	Incident		Washout (Days)	Intent-to-Treat (ITT)	Episode Gap	Episode Extension	Truncation Criteria	Cohort Definition	Care		
					with Respect to	to							Condition	Setting	Washout
33	Combination : Ipilimumab + Nivolumab (procedure code)	Same Day	Day of Combination	Any	N/A	0	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	GBS	Any	Entire History	
34	Ipilimumab (procedure code)	---	---	Any	N/A	0	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	Bell's palsy	Any	Entire History	
35	Atezolizumab (procedure code)	---	---	Any	N/A	0	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	Bell's palsy	Any	Entire History	
36	Avelumab (procedure code)	---	---	Any	N/A	0	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	Bell's palsy	Any	Entire History	
37	Durvalumab (procedure code)	---	---	Any	N/A	0	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	Bell's palsy	Any	Entire History	
38	Nivolumab (procedure code)	---	---	Any	N/A	0	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	Bell's palsy	Any	Entire History	
39	Pembrolizumab (procedure code)	---	---	Any	N/A	0	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	Bell's palsy	Any	Entire History	
40	Combination : Ipilimumab + Nivolumab (procedure code)	Same Day	Day of Combination	Any	N/A	0	12 weeks	---	---	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	Bell's palsy	Any	Entire History	

Appendix F. Specifications Defining Parameters in this Request, Prevalent Cohort

Scenario	Exposure									Outcome				
	Exposure	Combination Window	Combination Index Date	Care Setting	Incident with Respect to	Washout (Days)	Intent-to-Treat (ITT)	Episode Gap	Episode Extension	Truncation Criteria	Cohort Definition	Condition	Care	
													Setting	Washout
41	Ipilimumab (procedure code)	---	---	Any	N/A	0	---	3 weeks	3 weeks	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	GBS	Any	Entire History
42	Atezolizumab (procedure code)	---	---	Any	N/A	0	---	3 weeks	3 weeks	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	GBS	Any	Entire History
43	Avelumab (procedure code)	---	---	Any	N/A	0	---	3 weeks	3 weeks	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	GBS	Any	Entire History
44	Durvalumab (procedure code)	---	---	Any	N/A	0	---	2 weeks	2 weeks	DP end date, query end date, death, disenrollment, outcome occurrence	02	GBS	Any	Entire History
45	Nivolumab (procedure code)	---	---	Any	N/A	0	---	2 weeks	2 weeks	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	GBS	Any	Entire History
46	Pembrolizumab (procedure code)	---	---	Any	N/A	0	---	3 weeks	3 weeks	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	GBS	Any	Entire History
47	Ipilimumab (procedure code)	---	---	Any	N/A	0	---	3 weeks	3 weeks	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	Bell's palsy	Any	Entire History
48	Atezolizumab (procedure code)	---	---	Any	N/A	0	---	3 weeks	3 weeks	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	Bell's palsy	Any	Entire History

Appendix F. Specifications Defining Parameters in this Request, Prevalent Cohort

Scenario	Exposure										Outcome				
	Exposure	Combination Window	Combination Index Date	Care Setting	Incident		Washout (Days)	Intent-to-Treat (ITT)	Episode Gap	Episode Extension	Truncation Criteria	Cohort Definition	Care		
					with Respect to	to							Condition	Setting	Washout
49	Avelumab (procedure code)	---	---	Any	N/A	0	---	3 weeks	3 weeks	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	Bell's palsy	Any	Entire History	
50	Durvalumab (procedure code)	---	---	Any	N/A	0	---	2 weeks	2 weeks	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	Bell's palsy	Any	Entire History	
51	Nivolumab (procedure code)	---	---	Any	N/A	0	---	2 weeks	2 weeks	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	Bell's palsy	Any	Entire History	
52	Pembrolizumab (procedure code)	---	---	Any	N/A	0	---	3 weeks	3 weeks	Data Partner end date, query end date, death, disenrollment, outcome occurrence	02	Bell's palsy	Any	Entire History	

International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Healthcare Common Procedure Coding System (HCPCS) codes are provided by Optum360.

National Drug Codes (NDCs) are checked against First Data Bank's "National Drug Data File (NDDF®) Plus."

¹ Cohort definition "02" indicates that all valid exposures are observed for the given scenario; cohort re-entry was allowed