SUPPLEMENTARY MATERIALS

Supplementary Methods

Search Terminology & PICOS Question

Pharmalogical Agent	Alternate 1:	Alternate 2:
nivolumab	Opdivo	
pembrolizumab	Keytruda	
pidilizumab		
BMS 936559	anti-PD-L1	Anti-PD-L1 Antibody BMS-936559
durvalumab	Imfinzi	
Atezolizumab	Tecentriq	
Avelumab	Bavencio	
Ipilimumab	Yervoy	
Tremelimumab	ticilimumab	

PICOS (P = participants/population, I = Interventions/exposures, C = comparators/controls, and O = outcomes; primary and secondary outcomes, S= study type)

P = Adult cancer patients

I = Immune checkpoint inhibitors administered (alemtuzumab, nivolumab, pembrolizumab, pidilizumab, BMS 936559, durvalumab, Atezolizumab, Avelumab, Ipilimumab, Tremelimumab, rituximab, ofatumumab)

C = N/A

O = Primary outcome: PRO (patient-reported outcome) Secondary outcome: Quality of Life (wellness, wellbeing, QoL, etc.)

S = Original data (not a review, meta-analysis, secondary data analysis, case report, case series, commentary, retrospective, registry studies, etc...). Clinical Trials, Randomized Control Trials, etc. Expanded access trials are acceptable.

Search Strings

PubMed Search	
Search #	**PubMed Keywords & Translations**
1.	"nivolumab"[Supplementary Concept] OR "nivolumab"[All Fields] OR "opdivo"[All Fields]
2.	pembrolizumab[Supplementary Concept] OR "pembrolizumab"[All Fields]
3.	pidilizumab[Supplementary Concept] OR "pidilizumab"[All Fields]
4.	a[All Fields] OR anti-PD-L1[All Fields] OR (Anti-PD-L1[All Fields] AND ("immunoglobulins"[MeSH Terms] OR "immunoglobulins"[All Fields] OR "antibody"[All Fields] OR "antibodies"[MeSH Terms] OR "antibodies"[All Fields]) AND BMS-936559[All Fields])
5.	durvalumab[Supplementary Concept] OR "durvalumab"[All Fields]
6.	atezolizumab[Supplementary Concept] OR "atezolizumab"[All Fields] OR "tecentriq"[All Fields]
7.	avelumab[Supplementary Concept] OR "avelumab"[All Fields] OR Bavencio[All Fields]
8.	ipilimumab[Supplementary Concept] OR "ipilimumab"[All Fields] OR "yervoy"[All Fields]
9.	tremelimumab[Supplementary Concept] OR "tremelimumab"[All Fields] OR "ticilimumab"[All Fields] OR "cp 675,206"[All Fields]
Final Action:	Export results for 1, 2, 3, 4, 5, 6, 7, 8, & 9 to EndNote & deduplicate

Web of Science Search		
Search #	**# of Results**	**Web of Science Search String**
1	2,765	TS=(nivolumab OR opdivo)
2	1,673	TS=(pembrolizumab OR keytruda)
3	33	TS=(pidilizumab)
4	846	TS=(BMS 936559 OR anti-PD-L1 OR Anti-PD-L1 Antibody BMS-936559)
5	143	TS=(durvalumab OR imfinzi)
6	275	TS=(Atezolizumab OR Tecentriq)
7	130	TS=(Avelumab OR Bavencio)
8	47	TS= (Ipiliumumab OR Yervoy)
9	269	TS=(Tremelimumab OR Ticilimumab)
10	4,844	#9 OR #8 OR #7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1
Final Action: Export results to EndNote & deduplicate		

Embase Search	
Search #	**Embase Search String**
#1	'nivolumab'/exp OR 'pembrolizumab'/exp OR 'pidilizumab'/exp OR 'bms 936559'/exp OR 'durvalumab'/exp OR 'atezolizumab'/exp OR 'avelumab'/exp OR 'ipilimumab'/exp OR 'ticilimumab'/exp OR 'anti-pd-l1' OR 'anti-pd-l1 antibody bms-936559'
Final Action: Export results to EndNote & deduplicate	

PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3, Appendix A
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4, Appendix A

Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4, Appendix B
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix B
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	4, Appendix A
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	5

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	5
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	5, 6
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	6, Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Appendix D
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Figure 2, Figure 3
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	6, 7
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	6, 7
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	6, 7
DISCUSSION			

Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	8
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	10
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	10
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1

Adapted From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

Potential Moderators Examined

Potential moderators that were examined included: ICI regimen, disease site, follow-up duration, comparator group, mean sample age, Percent female, risk of bias, and quality of patient-reported outcomes reporting.

Supplementary Tables

Supplementary Table 1: Targeted Abstract Searches[a,b]

Organization/Conference Name	URL
American Association of Cancer Research (AACR)	http://aacrjournals.org/site/Meetings/meeting_abs.xhtml
American Association for Cancer Research (AACR) and International Association for the Study of Lung Cancer (IASLC) Joint Conference	http://aacrjournals.org/site/Meetings/meeting_abs.xhtml
Proceedings of the Fourth AACR-IASLC International Joint Conference on Lung Cancer Translational Science from the Bench to the Clinic	http://www.jto.org/issue/S1556-0864(15)X0004-9
Third AACR–IASLC Joint Conference on Molecular Origins of Lung Cancer	http://clincancerres.aacrjournals.org/content/20/2_Supplement.toc
AACR– IASLC Joint Conference on Molecular Origins of Lung Cancer: Biology, Therapy, and Personalized Medicine	clincancerres.aacrjournals.org/content/18/3_Supplement.toc
AACR-NCI-EORTC	http://mct.aacrjournals.org/search
American Cancer Society Biannual Survivorship Conference	https://survivorshipconference.cancer.org/
American Society of Clinical Oncology (ASCO)	http://meetinglibrary.asco.org/
ASCO Genitourinary (GU)	http://meetinglibrary.asco.org/
ASCO Head and Neck	
ASCO Thoracic	
American Society of Hematology (ASH)	
American Society of Radiation Oncology (ASTRO)	http://www.redjournal.org/content/astro_abstracts
American Society of Psychosocial Oncology (APOS)	http://onlinelibrary.wiley.com/journal/10.1002/(ISSN)1099-1611
European Association for Cancer Research (EACR)	http://eacr24.eacr.org/
European Lung Cancer Conference (ELCC)	http://www.esmo.org/Conferences/Past-Conferences/ELCC-2017-Lung-Cancer
European Society for Medical Oncology (ESMO)	http://www.esmo.org/
ESMO Immunooncology conference	http://www.esmo.org/Conferences/ESMO-Immuno-Oncology-Congress-2017
ESMO World Congress on Gastrointestinal Cancer	http://www.esmo.org/Conferences/Past-Conferences/World-GI-2017-Gastrointestinal-Cancer
European SocieTy for Radiotherapy & Oncology (ESTRO)	http://oncologypro.esmo.org/Meeting-Resources
International Association for the Study of Lung Cancer (IASLC)	
International Society of Psychosocial Oncology (IPOS)	http://ipos-society.org/
Multinational Association for Supportive Care in Cancer (MASCC)	http://www.mascc.org/
Society of Behavioral Medicine	http://www.sbm.org/
Society for Melanoma Research	https://www.societymelanomaresearch.org/
Society for Immunotherapy in Oncology (SITC)	https://www.sitcancer.org/home

[a]Keywords used: alemtuzumab, nivolumab, pembrolizumab, pidilizumab, BMS 936559, durvalumab, Atezolizumab, Avelumab, Ipilimumab, Tremelimumab, rituximab, ofatumumab
[b]Keywords were searched one at a time, and results for each search were exported into EndNote.

Supplementary Table 2: Ratings of Potential for Study Bias

Publication	Random Sequence Generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessors	Incomplete outcome data	Selective outcome reporting	Other sources of bias	Overall Risk of bias
Ascierto, et al. 2017 (1)	low	low	low	low	low	low	low	low
Barlesi, et al. 2019 (2)	low	low	high	low	low	low	low	high
Bordoni, et al. 2017 (3)	low	low	high	low	low	low	low	high
Brahmer, et al. 2017 (4)	low	low	high	low	low	low	low	high
Cella, et al. 2016 (5)	low	low	high	low	low	low	low	high
Coens, et al. 2017 (6)	low	low	low	low	low	low	low	low
El-Khoueiry, et al. 2017 (7)	high	high	high	low	low	low	low	high
Harrington, et al. 2017 (8)	low	low	high	low	low	low	low	high
Hui, et al. 2019 (9)	low	low	low	low	low	low	low	low
Kaufman, et al. 2017 (10)	high	high	high	low	low	unclear	low	high
Larkin, et al. 2018 (11)	low	low	high	low	high	low	unclear	high
Long, et al. 2016 (12)	low	low	low	low	unclear	low	low	low
Mathias, et al. 2015 (13)	high	high	high	unclear	unclear	unclear	unclear	high
Mazieres, et al. 2018 (14)	low	low	low	low	low	unclear	unclear	low
O'Donnell, et al. 2018 (15)	high	high	high	low	unclear	low	unclear	high
Perol, et al. 2019 (16)	high	high	high	low	unclear	low	unclear	high
Petrella, et al. 2017 (17)	low	low	high	low	low	low	unclear	high
Powles, et al. 2018 (18)	low	low	high	low	low	low	unclear	high
Reck, et al. 2018 (19)	low	low	high	low	low	low	low	high
Revicki, et al. 2012 (20)	low	low	low	low	low	unclear	low	low
Schadendorf, et al. 2016 (21)	low	low	high	low	low	low	low	high
Schadendorf, et al. 2017 (22)	low	low	low	low	low	low	low	low
Sharma, et al. 2017 (23)	high	high	high	low	low	low	low	high
Vaughn, et al. 2018 (24)	low	low	high	low	low	low	low	high
Weber, et al. 2017 (25)	low	low	low	low	unclear	unclear	low	low
Younes, et al. 2016 (26)	high	high	high	low	low	low	low	high

Supplementary Table 3: Ratings of Quality of Patient-Reported Outcomes (PRO) Reporting[a]

Publication	PRO identified in abstract as primary or secondary outcomes	PRO hypothesis and relevant domains	PRO validity or reliability provided or cited	Method of data collection	Statistical approaches for missing data described	PRO-specific limitations and implications presented	Sum
Ascierto, et al. 2017 (1)	0	0	1	0	1	1	3
Barlesi, et al. 2019 (2)	1	0	1	1	1	1	5
Bordoni, et al. 2017 (3)	1	0	1	0	0	1	3
Brahmer, et al. 2017 (4)	1	0	1	0	1	1	4
Cella, et al. 2016 (5)	1	0	1	0	1	1	4
Coens, et al. 2017 (6)	1	1	1	0	1	1	5
El-Khoueiry, et al. 2017 (7)	0	0	1	1	1	0	3
Harrington, et al. 2017 (8)	1	0	1	1	1	1	5
Hui, et al. 2019 (9)	1	0	1	1	1	1	5
Kaufman, et al. 2017 (10)	1	0	1	1	0	1	4
Larkin, et al. 2018 (11)	0	0	1	0	0	0	1
Long, et al. 2016 (12)	1	0	1	1	1	1	5
Mathias, et al. 2015 (13)	1	0	0	0	0	0	1
Mazieres, et al. 2018 (14)	1	0	0	0	0	0	1
O'Donnell, et al. 2018 (15)	1	0	0	0	0	0	1
Perol, et al. 2019 (16)	1	0	0	0	0	0	1
Petrella, et al. 2017 (17)	1	1	1	1	1	1	6
Powles, et al. 2018 (18)	0	0	1	1	0	0	2
Reck, et al. 2018 (19)	1	0	1	1	1	1	5
Revicki, et al. 2012 (20)	1	0	1	1	0	1	4
Schadendorf, et al. 2016 (21)	1	0	0	0	1	1	3
Schadendorf, et al. 2017 (22)	1	0	0	0	1	1	3
Sharma, et al. 2017 (23)	0	0	1	0	0	0	1
Vaughn, et al. 2018 (24)	1	0	0	1	1	1	4
Weber, et al. 2017 (25)	0	0	1	0	1	0	2
Younes, et al. 2016 (26)	0	0	0	0	0	0	0

[a]0=absent, 1=present

Supplementary Figures

Supplementary Figure 1: Meta-Analysis of Within-Group Change in Physical Functioning in Patients Receiving Immune Checkpoint Inhibitor Therapy. Positive values indicate improvement. Error bars represent 95% confidence intervals (CIs). Random effect models were used with a two-sided alpha level of .05. NSCLC = non-small cell lung cancer.

Model	Group by Drug type	Study name	Cancer type	Drug type	Outcome	Statistics for each study				Sample size	Difference in means and 95% CI
						Difference in means	Lower limit	Upper limit	p-Value	Total	-20.00 -10.00 0.00 10.00 20.00
	Atezolizumab	Bordoni 2017	NSCLC	Atezolizumab	Physical functioning	4.470	2.902	6.038	0.000	413	
	Atezolizumab	Powles 2018	Urothelial	Atezolizumab	Physical functioning	-3.810	-5.966	-1.654	0.001	254	
Random	Atezolizumab					0.364	-7.750	8.478	0.930		
	Durvalumab	Hui 2019	NSCLC	Durvalumab	Physical functioning	2.300	0.732	3.868	0.004	476	
Random	Durvalumab					2.300	0.732	3.868	0.004		
	Ipilimumab	Revicki 2012	Melanoma	Ipilimumab	Physical functioning	-5.100	-9.337	-0.863	0.018	83	
	Ipilimumab	Mathias 2015	Melanoma	Ipilimumab	Physical functioning	-15.900	-27.072	-4.728	0.005	101	
	Ipilimumab	Coens 2017	Melanoma	Ipilimumab	Physical functioning	-1.640	-2.424	-0.856	0.000	475	
Random	Ipilimumab					-5.014	-10.144	0.115	0.055		
	Nivolumab	Harrington 2017	Head & Neck	Nivolumab	Physical functioning	-1.900	-5.688	1.888	0.326	43	
	Nivolumab	Long 2016	Melanoma	Nivolumab	Physical functioning	-4.400	-7.536	-1.264	0.006	136	
	Nivolumab	Younes 2016	Hodgkin	Nivolumab	Physical functioning	5.500	1.188	9.812	0.012	60	
	Nivolumab	Schadendorf 2017	Melanoma	Nivolumab	Physical functioning	-4.500	-6.460	-2.540	0.000	266	
Random	Nivolumab					-1.630	-5.523	2.263	0.412		
	Pembrolizumab	Petrella 2017	Melanoma	Pembrolizumab	Physical functioning	-3.460	-6.033	-0.887	0.008	270	
	Pembrolizumab	Brahmer 2017	NSCLC	Pembrolizumab	Physical functioning	1.180	-1.776	4.136	0.434	150	
	Pembrolizumab	Vaughn 2018	Urothelial	Pembrolizumab	Physical functioning	-6.180	-9.345	-3.015	0.000	266	
	Pembrolizumab	Schadendorf 2016	Melanoma	Pembrolizumab	Physical functioning	-4.200	-7.428	-0.972	0.011	176	
Random	Pembrolizumab					-3.132	-6.124	-0.139	0.040		
Random	Overall					0.460	-0.792	1.712	0.472		

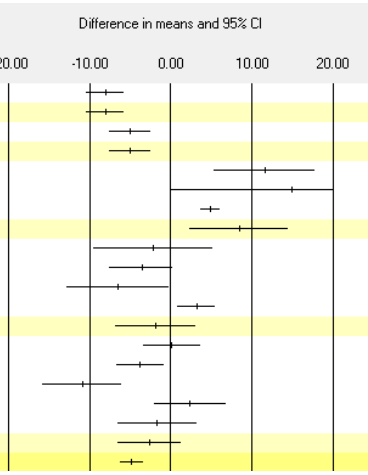
Supplementary Figure 2. Meta-Analysis of Differences in Mean Change in Physical Functioning from Baseline to Follow-Up in Physical Functioning at Follow-up in Patients Treated with Immune Checkpoint Inhibitors versus Other Regimens. Positive values favor immune checkpoint inhibitors. Error bars represent 95% confidence intervals (CIs). Random effect models were used with a two-sided alpha level of .05. NSCLC = non-small cell lung cancer.

Model	Group by Drug type	Study name	Outcome	Sample size		Cancer type	Drug type	Statistics for each study				Difference in means and 95% CI
				IO	Standard of care			Difference in means	Lower limit	Upper limit	p-Value	-20.00 -10.00 0.00 10.00 20.00
	Atezolizumab	Powles 2018	Physical functioning	202	254	Urothelial	Atezolizumab	0.600	-0.385	1.585	0.233	
	Atezolizumab	Bordoni 2017	Physical functioning	413	390	NSCLC	Atezolizumab	6.640	3.295	9.985	0.000	
Random	Atezolizumab							3.400	-2.504	9.303	0.259	
	Durvalumab	Hui 2019	Physical functioning	476	237	NSCLC	Durvalumab	-0.400	-1.157	0.357	0.301	
Random	Durvalumab							-0.400	-1.157	0.357	0.301	
	Ipilimumab	Coens 2017	Physical functioning	449	444	Melanoma	Ipilimumab	-2.720	-3.115	-2.325	0.000	
	Ipilimumab	Revicki 2012	Physical functioning	83	78	Melanoma	Ipilimumab	5.000	-0.905	10.905	0.097	
	Ipilimumab	Mathias 2015	Physical functioning	101	28	Melanoma	Ipilimumab	6.900	0.730	13.070	0.028	
Random	Ipilimumab							2.549	-4.483	9.581	0.477	
	Nivolumab	Long 2016	Physical functioning	136	123	Melanoma	Nivolumab	-1.700	-7.124	3.724	0.539	
	Nivolumab	Harrington 2017	Physical functioning	43	14	Head & Neck	Nivolumab	18.000	15.847	20.153	0.000	
Random	Nivolumab							8.314	-10.989	27.617	0.399	
	Pembrolizumab	Schadendorf 2016	Physical functioning	176	167	Melanoma	Pembrolizumab	1.000	-0.487	2.487	0.187	
	Pembrolizumab	Vaughn 2018	Physical functioning	266	253	Urothelial	Pembrolizumab	5.660	4.100	7.220	0.000	
	Pembrolizumab	Brahmer 2017	Physical functioning	150	147	NSCLC	Pembrolizumab	5.230	3.840	6.620	0.000	
Random	Pembrolizumab							3.963	1.071	6.856	0.007	
Random	Overall							-0.027	-0.750	0.695	0.941	

Supplementary Figure 3: Change From Baseline to Follow-up in Symptomatology in Patients Receiving Immune Checkpoint Inhibitors. Analyses were done for A) appetite loss, B) constipation, C) diarrhea, D) dyspnea, E) fatigue, F) insomnia, G) nausea and vomiting, and H) pain. Error bars represent 95% confidence intervals (CIs). Random effect models were used with a two-sided alpha level of .05. NSCLC = non-small cell lung cancer.

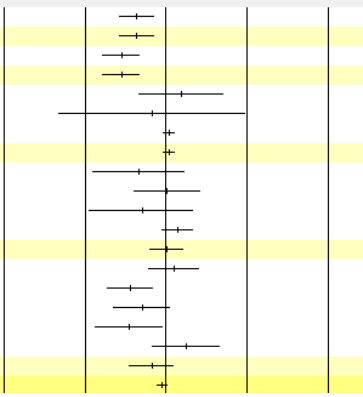
A. Appetite Loss

Model	Group by Drug type	Study name	Cancer type	Drug type	Outcome	Difference in means	Lower limit	Upper limit	p-Value	Sample size Total
	Atezolizumab	Bordoni 2017	NSCLC	Atezolizumab	Appetite loss	-8.040	-10.392	-5.688	0.000	413
Random	Atezolizumab					-8.040	-10.392	-5.688	0.000	
	Durvalumab	Hui 2019	NSCLC	Durvalumab	Appetite loss	-5.100	-7.648	-2.552	0.000	476
Random	Durvalumab					-5.100	-7.648	-2.552	0.000	
	Ipilimumab	Revicki 2012	Melanoma	Ipilimumab	Appetite loss	11.600	5.393	17.807	0.000	83
	Ipilimumab	Mathias 2015	Melanoma	Ipilimumab	Appetite loss	15.000	-0.092	30.092	0.051	101
	Ipilimumab	Coens 2017	Melanoma	Ipilimumab	Appetite loss	4.870	3.694	6.046	0.000	475
Random	Ipilimumab					8.459	2.382	14.537	0.006	
	Nivolumab	Harrington 2017	Head & Neck	Nivolumab	Appetite loss	-2.200	-9.581	5.181	0.559	43
	Nivolumab	Long 2016	Melanoma	Nivolumab	Appetite loss	-3.600	-7.520	0.320	0.072	136
	Nivolumab	Younes 2016	Hodgkin	Nivolumab	Appetite loss	-6.600	-12.872	-0.328	0.039	60
	Nivolumab	Schadendorf 2017	Melanoma	Nivolumab	Appetite loss	3.200	0.848	5.552	0.008	266
Random	Nivolumab					-1.866	-6.835	3.103	0.462	
	Pembrolizumab	Petrella 2017	Melanoma	Pembrolizumab	Appetite loss	0.130	-3.419	3.679	0.943	270
	Pembrolizumab	Barlesi 2019	NSCLC	Pembrolizumab	Appetite loss	-3.780	-6.681	-0.879	0.011	331
	Pembrolizumab	Brahmer 2017	NSCLC	Pembrolizumab	Appetite loss	-10.920	-15.830	-6.010	0.000	150
	Pembrolizumab	Vaughn 2018	Urothelial	Pembrolizumab	Appetite loss	2.380	-2.060	6.820	0.293	266
	Pembrolizumab	Schadendorf 2016	Melanoma	Pembrolizumab	Appetite loss	-1.700	-6.566	3.166	0.494	176
Random	Pembrolizumab					-2.681	-6.581	1.219	0.178	
Random	Overall					-4.832	-6.293	-3.370	0.000	



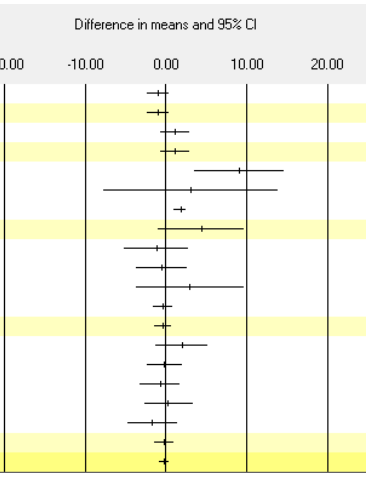
B. Constipation

Model	Group by Drug type	Study name	Cancer type	Drug type	Outcome	Difference in means	Lower limit	Upper limit	p-Value	Sample size Total
	Atezolizumab	Bordoni 2017	NSCLC	Atezolizumab	Constipation	-3.610	-5.766	-1.454	0.001	410
Random	Atezolizumab					-3.610	-5.766	-1.454	0.001	
	Durvalumab	Hui 2019	NSCLC	Durvalumab	Constipation	-5.500	-7.852	-3.148	0.000	476
Random	Durvalumab					-5.500	-7.852	-3.148	0.000	
	Ipilimumab	Revicki 2012	Melanoma	Ipilimumab	Constipation	1.900	-3.371	7.171	0.480	83
	Ipilimumab	Mathias 2015	Melanoma	Ipilimumab	Constipation	-1.700	-13.264	9.864	0.773	100
	Ipilimumab	Coens 2017	Melanoma	Ipilimumab	Constipation	0.400	-0.384	1.184	0.317	475
Random	Ipilimumab					0.423	-0.351	1.197	0.284	
	Nivolumab	Harrington 2017	Head & Neck	Nivolumab	Constipation	-3.400	-9.134	2.334	0.245	44
	Nivolumab	Long 2016	Melanoma	Nivolumab	Constipation	0.100	-4.016	4.216	0.962	136
	Nivolumab	Younes 2016	Hodgkin	Nivolumab	Constipation	-3.000	-9.468	3.468	0.363	60
	Nivolumab	Schadendorf 2017	Melanoma	Nivolumab	Constipation	1.400	-0.560	3.360	0.162	266
Random	Nivolumab					0.101	-2.027	2.230	0.926	
	Pembrolizumab	Petrella 2017	Melanoma	Pembrolizumab	Constipation	1.040	-2.121	4.201	0.519	270
	Pembrolizumab	Barlesi 2019	NSCLC	Pembrolizumab	Constipation	-4.450	-7.314	-1.586	0.002	331
	Pembrolizumab	Brahmer 2017	NSCLC	Pembrolizumab	Constipation	-2.950	-6.496	0.596	0.103	150
	Pembrolizumab	Vaughn 2018	Urothelial	Pembrolizumab	Constipation	-4.620	-8.821	-0.419	0.031	266
	Pembrolizumab	Schadendorf 2016	Melanoma	Pembrolizumab	Constipation	2.500	-1.671	6.671	0.240	176
Random	Pembrolizumab					-1.752	-4.553	1.049	0.220	
Random	Overall					-0.524	-1.168	0.120	0.110	



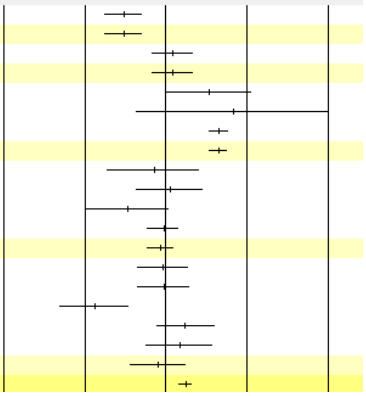
C. Diarrhea

Model	Group by Drug type	Study name	Cancer type	Drug type	Outcome	Difference in means	Lower limit	Upper limit	p-Value	Sample size Total
	Atezolizumab	Bordoni 2017	NSCLC	Atezolizumab	Diarrhea	-0.910	-2.282	0.462	0.194	411
Random	Atezolizumab					-0.910	-2.282	0.462	0.194	
	Durvalumab	Hui 2019	NSCLC	Durvalumab	Diarrhea	1.100	-0.664	2.864	0.222	476
Random	Durvalumab					1.100	-0.664	2.864	0.222	
	Ipilimumab	Revicki 2012	Melanoma	Ipilimumab	Diarrhea	9.100	3.534	14.666	0.001	82
	Ipilimumab	Mathias 2015	Melanoma	Ipilimumab	Diarrhea	3.100	-7.680	13.880	0.573	101
	Ipilimumab	Coens 2017	Melanoma	Ipilimumab	Diarrhea	1.820	1.036	2.604	0.000	475
Random	Ipilimumab					4.426	-0.922	9.775	0.105	
	Nivolumab	Harrington 2017	Head & Neck	Nivolumab	Diarrhea	-1.200	-5.185	2.785	0.555	44
	Nivolumab	Long 2016	Melanoma	Nivolumab	Diarrhea	-0.500	-3.636	2.636	0.755	136
	Nivolumab	Younes 2016	Hodgkin	Nivolumab	Diarrhea	3.000	-3.664	9.664	0.378	60
	Nivolumab	Schadendorf 2017	Melanoma	Nivolumab	Diarrhea	-0.400	-1.576	0.776	0.505	266
Random	Nivolumab					-0.382	-1.431	0.666	0.475	
	Pembrolizumab	Petrella 2017	Melanoma	Pembrolizumab	Diarrhea	2.020	-1.230	5.270	0.223	270
	Pembrolizumab	Barlesi 2019	NSCLC	Pembrolizumab	Diarrhea	-0.160	-2.337	2.017	0.885	331
	Pembrolizumab	Brahmer 2017	NSCLC	Pembrolizumab	Diarrhea	-0.740	-3.195	1.715	0.555	150
	Pembrolizumab	Vaughn 2018	Urothelial	Pembrolizumab	Diarrhea	0.290	-2.691	3.271	0.849	266
	Pembrolizumab	Schadendorf 2016	Melanoma	Pembrolizumab	Diarrhea	-1.700	-4.779	1.379	0.279	176
Random	Pembrolizumab					-0.163	-1.367	1.042	0.791	
Random	Overall					-0.175	-0.809	0.459	0.588	



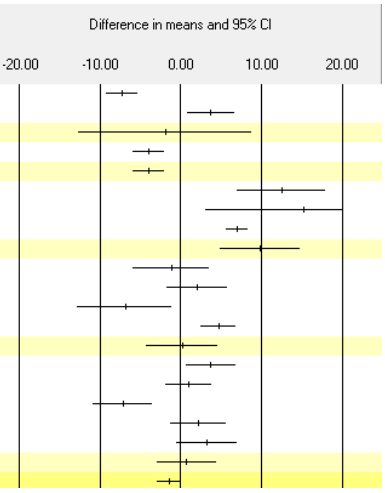
D. Dyspnea

Model	Group by Drug type	Study name	Cancer type	Drug type	Outcome	Difference in means	Lower limit	Upper limit	p-Value	Total
	Atezolizumab	Bordoni 2017	NSCLC	Atezolizumab	Dyspnea	-5.160	-7.512	-2.808	0.000	412
Random	Atezolizumab					-5.160	-7.512	-2.808	0.000	
	Durvalumab	Hui 2019	NSCLC	Durvalumab	Dyspnea	0.800	-1.748	3.348	0.538	476
Random	Durvalumab					0.800	-1.748	3.348	0.538	
	Ipilimumab	Revicki 2012	Melanoma	Ipilimumab	Dyspnea	5.300	-0.018	10.618	0.051	81
	Ipilimumab	Mathias 2015	Melanoma	Ipilimumab	Dyspnea	8.400	-3.752	20.552	0.175	101
	Ipilimumab	Coens 2017	Melanoma	Ipilimumab	Dyspnea	6.530	5.354	7.706	0.000	475
Random	Ipilimumab					6.490	5.347	7.633	0.000	
	Nivolumab	Harrington 2017	Head & Neck	Nivolumab	Dyspnea	-1.500	-7.230	4.230	0.608	43
	Nivolumab	Long 2016	Melanoma	Nivolumab	Dyspnea	0.500	-3.616	4.616	0.812	136
	Nivolumab	Younes 2016	Hodgkin	Nivolumab	Dyspnea	-4.800	-9.896	0.296	0.065	60
	Nivolumab	Schadendorf 2017	Melanoma	Nivolumab	Dyspnea	-0.300	-2.260	1.660	0.764	266
Random	Nivolumab					-0.734	-2.375	0.906	0.380	
	Pembrolizumab	Petrella 2017	Melanoma	Pembrolizumab	Dyspnea	-0.420	-3.561	2.721	0.793	270
	Pembrolizumab	Barlesi 2019	NSCLC	Pembrolizumab	Dyspnea	-0.280	-3.493	2.933	0.864	331
	Pembrolizumab	Brahmer 2017	NSCLC	Pembrolizumab	Dyspnea	-8.800	-13.075	-4.525	0.000	150
	Pembrolizumab	Vaughn 2018	Urothelial	Pembrolizumab	Dyspnea	2.380	-1.194	5.954	0.192	266
	Pembrolizumab	Schadendorf 2016	Melanoma	Pembrolizumab	Dyspnea	1.700	-2.421	5.821	0.419	176
Random	Pembrolizumab					-0.973	-4.412	2.465	0.579	
Random	Overall					2.443	1.641	3.244	0.000	



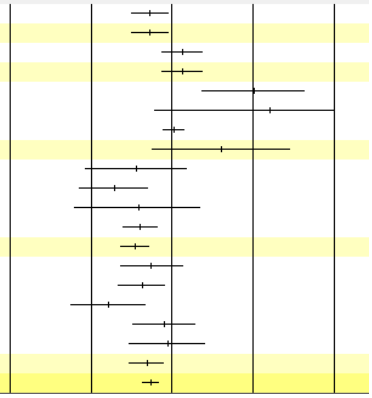
E. Fatigue

Model	Group by Drug type	Study name	Cancer type	Drug type	Outcome	Difference in means	Lower limit	Upper limit	p-Value	Total
	Atezolizumab	Bordoni 2017	NSCLC	Atezolizumab	Fatigue	-7.320	-9.280	-5.360	0.000	413
	Atezolizumab	Powles 2018	Urothelial	Atezolizumab	Fatigue	3.670	0.769	6.571	0.013	254
Random	Atezolizumab					-1.879	-12.649	8.890	0.732	
	Durvalumab	Hui 2019	NSCLC	Durvalumab	Fatigue	-4.000	-5.960	-2.040	0.000	476
Random	Durvalumab					-4.000	-5.960	-2.040	0.000	
	Ipilimumab	Revicki 2012	Melanoma	Ipilimumab	Fatigue	12.500	7.033	17.967	0.000	82
	Ipilimumab	Mathias 2015	Melanoma	Ipilimumab	Fatigue	15.200	3.048	27.352	0.014	101
	Ipilimumab	Coens 2017	Melanoma	Ipilimumab	Fatigue	6.970	5.598	8.342	0.000	475
Random	Ipilimumab					9.869	4.916	14.823	0.000	
	Nivolumab	Harrington 2017	Head & Neck	Nivolumab	Fatigue	-1.100	-5.859	3.659	0.651	43
	Nivolumab	Long 2016	Melanoma	Nivolumab	Fatigue	2.000	-1.724	5.724	0.293	136
	Nivolumab	Younes 2016	Hodgkin	Nivolumab	Fatigue	-6.900	-12.780	-1.020	0.021	60
	Nivolumab	Schadendorf 2017	Melanoma	Nivolumab	Fatigue	4.700	2.544	6.856	0.000	266
Random	Nivolumab					0.244	-4.223	4.712	0.915	
	Pembrolizumab	Petrella 2017	Melanoma	Pembrolizumab	Fatigue	3.740	0.639	6.841	0.018	270
	Pembrolizumab	Barlesi 2019	NSCLC	Pembrolizumab	Fatigue	1.020	-1.864	3.904	0.488	331
	Pembrolizumab	Brahmer 2017	NSCLC	Pembrolizumab	Fatigue	-7.160	-10.845	-3.475	0.000	150
	Pembrolizumab	Vaughn 2018	Urothelial	Pembrolizumab	Fatigue	2.140	-1.314	5.594	0.225	266
	Pembrolizumab	Schadendorf 2016	Melanoma	Pembrolizumab	Fatigue	3.300	-0.474	7.074	0.087	176
Random	Pembrolizumab					0.654	-2.991	4.299	0.725	
Random	Overall					-1.365	-2.881	0.151	0.078	



F. Insomnia

Model	Group by Drug type	Study name	Cancer type	Drug type	Outcome	Difference in means	Lower limit	Upper limit	p-Value	Total
	Atezolizumab	Bordoni 2017	NSCLC	Atezolizumab	Insomnia	-2.740	-5.092	-0.388	0.022	413
Random	Atezolizumab					-2.740	-5.092	-0.388	0.022	
	Durvalumab	Hui 2019	NSCLC	Durvalumab	Insomnia	1.300	-1.248	3.848	0.317	476
Random	Durvalumab					1.300	-1.248	3.848	0.317	
	Ipilimumab	Revicki 2012	Melanoma	Ipilimumab	Insomnia	10.100	3.696	16.504	0.002	83
	Ipilimumab	Mathias 2015	Melanoma	Ipilimumab	Insomnia	12.100	-2.208	26.408	0.097	98
	Ipilimumab	Coens 2017	Melanoma	Ipilimumab	Insomnia	0.220	-1.152	1.592	0.753	475
Random	Ipilimumab					6.126	-2.447	14.699	0.161	
	Nivolumab	Harrington 2017	Head & Neck	Nivolumab	Insomnia	-4.400	-10.713	1.913	0.172	43
	Nivolumab	Long 2016	Melanoma	Nivolumab	Insomnia	-7.200	-11.512	-2.888	0.001	136
	Nivolumab	Younes 2016	Hodgkin	Nivolumab	Insomnia	-4.200	-12.040	3.640	0.294	60
	Nivolumab	Schadendorf 2017	Melanoma	Nivolumab	Insomnia	-4.000	-6.156	-1.844	0.000	266
Random	Nivolumab					-4.598	-6.393	-2.802	0.000	
	Pembrolizumab	Petrella 2017	Melanoma	Pembrolizumab	Insomnia	-2.570	-6.442	1.302	0.193	270
	Pembrolizumab	Barlesi 2019	NSCLC	Pembrolizumab	Insomnia	-3.740	-6.641	-0.839	0.012	331
	Pembrolizumab	Brahmer 2017	NSCLC	Pembrolizumab	Insomnia	-7.810	-12.492	-3.128	0.001	150
	Pembrolizumab	Vaughn 2018	Urothelial	Pembrolizumab	Insomnia	-1.030	-4.932	2.872	0.605	266
	Pembrolizumab	Schadendorf 2016	Melanoma	Pembrolizumab	Insomnia	-0.600	-5.317	4.117	0.803	176
Random	Pembrolizumab					-3.108	-5.307	-0.908	0.006	
Random	Overall					-2.635	-3.710	-1.560	0.000	



G. Nausea and Vomiting

Model	Group by Drug type	Study name	Cancer type	Drug type	Outcome	Statistics for each study				Sample size	Difference in means and 95% CI
						Difference in means	Lower limit	Upper limit	p-Value	Total	-20.00 -10.00 0.00 10.00 20.00
	Atezolizumab	Bordoni 2017	NSCLC	Atezolizumab	Nausea and vomiting	-1.150	-2.522	0.222	0.100	413	
Random	Atezolizumab					-1.150	-2.522	0.222	0.100		
	Durvalumab	Hui 2019	NSCLC	Durvalumab	Nausea and vomiting	-3.400	-4.576	-2.224	0.000	476	
Random	Durvalumab					-3.400	-4.576	-2.224	0.000		
	Ipilimumab	Revicki 2012	Melanoma	Ipilimumab	Nausea and vomiting	3.100	-0.989	7.189	0.137	83	
	Ipilimumab	Mathias 2015	Melanoma	Ipilimumab	Nausea and vomiting	-0.700	-8.736	7.336	0.864	101	
	Ipilimumab	Coens 2017	Melanoma	Ipilimumab	Nausea and vomiting	1.560	0.972	2.148	0.000	475	
Random	Ipilimumab					1.579	0.999	2.160	0.000		
	Nivolumab	Harrington 2017	Head & Neck	Nivolumab	Nausea and vomiting	2.100	-2.270	6.470	0.346	43	
	Nivolumab	Long 2016	Melanoma	Nivolumab	Nausea and vomiting	-2.600	-4.560	-0.640	0.009	136	
	Nivolumab	Younes 2016	Hodgkin	Nivolumab	Nausea and vomiting	0.000	-3.724	3.724	1.000	60	
	Nivolumab	Schadendorf 2017	Melanoma	Nivolumab	Nausea and vomiting	1.300	0.124	2.476	0.030	266	
Random	Nivolumab					0.019	-2.385	2.423	0.987		
	Pembrolizumab	Petrella 2017	Melanoma	Pembrolizumab	Nausea and vomiting	-1.800	-3.935	0.335	0.099	270	
	Pembrolizumab	Barlesi 2019	NSCLC	Pembrolizumab	Nausea and vomiting	-0.280	-2.417	1.857	0.797	331	
	Pembrolizumab	Brahmer 2017	NSCLC	Pembrolizumab	Nausea and vomiting	-2.120	-4.803	0.563	0.121	150	
	Pembrolizumab	Vaughn 2018	Urothelial	Pembrolizumab	Nausea and vomiting	1.000	-1.713	3.713	0.470	266	
	Pembrolizumab	Schadendorf 2016	Melanoma	Pembrolizumab	Nausea and vomiting	1.500	-1.231	4.231	0.282	176	
Random	Pembrolizumab					-0.437	-1.790	0.917	0.527		
Random	Overall					0.280	-0.170	0.730	0.223		

H. Pain

Model	Group by Drug type	Study name	Cancer type	Drug type	Outcome	Statistics for each study				Sample size	Difference in means and 95% CI
						Difference in means	Lower limit	Upper limit	p-Value	Total	-20.00 -10.00 0.00 10.00 20.00
	Atezolizumab	Bordoni 2017	NSCLC	Atezolizumab	Pain	-8.350	-10.702	-5.998	0.000	413	
Random	Atezolizumab					-8.350	-10.702	-5.998	0.000		
	Durvalumab	Hui 2019	NSCLC	Durvalumab	Pain	-0.700	-3.052	1.652	0.560	476	
Random	Durvalumab					-0.700	-3.052	1.652	0.560		
	Ipilimumab	Revicki 2012	Melanoma	Ipilimumab	Pain	7.900	2.284	13.516	0.006	83	
	Ipilimumab	Mathias 2015	Melanoma	Ipilimumab	Pain	7.400	-5.144	19.944	0.248	103	
	Ipilimumab	Coens 2017	Melanoma	Ipilimumab	Pain	0.160	-1.016	1.336	0.790	475	
Random	Ipilimumab					4.120	-2.279	10.519	0.207		
	Nivolumab	Harrington 2017	Head & Neck	Nivolumab	Pain	-2.600	-8.723	3.523	0.405	44	
	Nivolumab	Long 2016	Melanoma	Nivolumab	Pain	-1.100	-6.000	3.800	0.660	136	
	Nivolumab	Younes 2016	Hodgkin	Nivolumab	Pain	-6.300	-11.984	-0.616	0.030	60	
	Nivolumab	Schadendorf 2017	Melanoma	Nivolumab	Pain	0.900	-1.452	3.252	0.453	266	
Random	Nivolumab					-1.558	-4.700	1.585	0.331		
	Pembrolizumab	Petrella 2017	Melanoma	Pembrolizumab	Pain	-0.680	-4.188	2.828	0.704	270	
	Pembrolizumab	Barlesi 2019	NSCLC	Pembrolizumab	Pain	-0.280	-3.533	2.973	0.866	331	
	Pembrolizumab	Brahmer 2017	NSCLC	Pembrolizumab	Pain	-11.200	-15.019	-7.381	0.000	150	
	Pembrolizumab	Vaughn 2018	Urothelial	Pembrolizumab	Pain	-0.910	-4.693	2.873	0.637	266	
	Pembrolizumab	Schadendorf 2016	Melanoma	Pembrolizumab	Pain	0.800	-3.222	4.822	0.697	176	
Random	Pembrolizumab					-2.435	-6.606	1.737	0.253		
Random	Overall					-3.365	-4.720	-2.010	0.000		

Supplementary Figure 4: Comparing Mean Change in Symptomatology From Baseline to Follow-Up in Patients Receiving Immune Checkpoint Inhibitors (ICIs) Compared to Patients Not Treated With ICI. Analyses were done for A) appetite loss, B) constipation, C) diarrhea, D) dyspnea, E) fatigue, F) insomnia, G) nausea, and H) pain. Error bars represent 95% confidence intervals (CIs). Random effect models were used with a two-sided alpha level of .05. IO = immune checkpoint inhibitor group. NSCLC = non-small cell lung cancer

A. Appetite Loss

Model	Group by Drug type	Study name	Outcome	Sample size		Cancer type	Drug type	Statistics for each study				Difference in means and 95% CI
				IO	Standard of care			Difference in means	Lower limit	Upper limit	p-Value	-30.00 -15.00 0.00 15.00 30.00
	Atezolizumab	Bordoni 2017	Appetite loss	413	390	NSCLC	Atezolizumab	-0.440	-1.246	0.366	0.285	
Random	Atezolizumab							-0.440	-1.246	0.366	0.285	
	Durvalumab	Hui 2019	Appetite loss	476	237	NSCLC	Durvalumab	3.700	2.468	4.932	0.000	
Random	Durvalumab							3.700	2.468	4.932	0.000	
	Ipilimumab	Coens 2017	Appetite loss	448	444	Melanoma	Ipilimumab	4.690	4.196	5.184	0.000	
	Ipilimumab	Revicki 2012	Appetite loss	83	78	Melanoma	Ipilimumab	1.300	-7.383	9.983	0.769	
	Ipilimumab	Mathias 2015	Appetite loss	101	28	Melanoma	Ipilimumab	-8.500	-16.856	-0.144	0.046	
Random	Ipilimumab							-0.098	-8.043	7.848	0.981	
	Nivolumab	Long 2016	Appetite loss	136	123	Melanoma	Nivolumab	-5.200	-12.167	1.767	0.144	
	Nivolumab	Harrington 2017	Appetite loss	43	14	Head & Neck	Nivolumab	-23.100	-27.304	-18.896	0.000	
Random	Nivolumab							-14.374	-31.911	3.162	0.108	
	Pembrolizumab	Schadendorf 2016	Appetite loss	176	167	Melanoma	Pembrolizumab	-5.000	-7.248	-2.752	0.000	
	Pembrolizumab	Barlesi 2019	Appetite loss	331	293	NSCLC	Pembrolizumab	-4.020	-5.665	-2.375	0.000	
	Pembrolizumab	Vaughn 2018	Appetite loss	266	253	Urothelial	Pembrolizumab	-6.580	-8.720	-4.440	0.000	
	Pembrolizumab	Brahmer 2017	Appetite loss	150	147	NSCLC	Pembrolizumab	-7.610	-9.902	-5.318	0.000	
Random	Pembrolizumab							-5.696	-7.329	-4.062	0.000	
Random	Overall							-0.162	-0.783	0.459	0.609	

B. Constipation

Model	Group by Drug type	Study name	Outcome	Sample size		Cancer type	Drug type	Statistics for each study				Difference in means and 95% CI
				IO	Standard of care			Difference in means	Lower limit	Upper limit	p-Value	-20.00 -10.00 0.00 10.00 20.00
	Atezolizumab	Bordoni 2017	Constipation	410	388	NSCLC	Atezolizumab	-0.330	-4.673	4.013	0.882	
Random	Atezolizumab							-0.330	-4.673	4.013	0.882	
	Durvalumab	Hui 2019	Constipation	476	237	NSCLC	Durvalumab	-0.100	-1.265	1.065	0.866	
Random	Durvalumab							-0.100	-1.265	1.065	0.866	
	Ipilimumab	Coens 2017	Constipation	448	444	Melanoma	Ipilimumab	0.750	0.368	1.132	0.000	
	Ipilimumab	Revicki 2012	Constipation	83	77	Melanoma	Ipilimumab	-9.900	-17.343	-2.457	0.009	
	Ipilimumab	Mathias 2015	Constipation	100	28	Melanoma	Ipilimumab	-4.700	-11.080	1.680	0.149	
Random	Ipilimumab							-3.819	-10.378	2.740	0.254	
	Nivolumab	Long 2016	Constipation	136	123	Melanoma	Nivolumab	-1.700	-9.712	6.312	0.678	
	Nivolumab	Harrington 2017	Constipation	44	13	Head & Neck	Nivolumab	-1.000	-4.242	2.242	0.545	
Random	Nivolumab							-1.098	-4.104	1.907	0.474	
	Pembrolizumab	Schadendorf 2016	Constipation	176	167	Melanoma	Pembrolizumab	-2.600	-4.535	-0.665	0.008	
	Pembrolizumab	Barlesi 2019	Constipation	331	293	NSCLC	Pembrolizumab	-2.360	-3.754	-0.966	0.001	
	Pembrolizumab	Vaughn 2018	Constipation	266	253	Urothelial	Pembrolizumab	-7.660	-9.668	-5.652	0.000	
	Pembrolizumab	Brahmer 2017	Constipation	150	147	NSCLC	Pembrolizumab	-6.510	-8.206	-4.814	0.000	
Random	Pembrolizumab							-4.749	-7.381	-2.116	0.000	
Random	Overall							-0.923	-1.891	0.044	0.061	

C. Diarrhea

Model	Group by Drug type	Study name	Outcome	Sample size		Cancer type	Drug type	Statistics for each study				Difference in means and 95% CI
				IO	Standard of care			Difference in means	Lower limit	Upper limit	p-Value	-20.00 -10.00 0.00 10.00 20.00
	Atezolizumab	Bordoni 2017	Diarrhea	411	388	NSCLC	Atezolizumab	-2.050	-5.012	0.912	0.175	
Random	Atezolizumab							-2.050	-5.012	0.912	0.175	
	Durvalumab	Hui 2019	Diarrhea	476	237	NSCLC	Durvalumab	1.900	1.045	2.755	0.000	
Random	Durvalumab							1.900	1.045	2.755	0.000	
	Ipilimumab	Coens 2017	Diarrhea	445	443	Melanoma	Ipilimumab	0.950	0.529	1.371	0.000	
	Ipilimumab	Revicki 2012	Diarrhea	82	78	Melanoma	Ipilimumab	6.900	-0.890	14.690	0.083	
	Ipilimumab	Mathias 2015	Diarrhea	101	29	Melanoma	Ipilimumab	1.300	-4.593	7.193	0.665	
Random	Ipilimumab							1.218	-0.394	2.830	0.139	
	Nivolumab	Long 2016	Diarrhea	136	123	Melanoma	Nivolumab	-0.300	-6.322	5.722	0.922	
	Nivolumab	Harrington 2017	Diarrhea	44	13	Head &	Nivolumab	-7.100	-9.420	-4.780	0.000	
Random	Nivolumab							-4.291	-10.853	2.271	0.200	
	Pembrolizumab	Schadendorf 2016	Diarrhea	176	167	Melanoma	Pembrolizumab	-3.100	-4.520	-1.680	0.000	
	Pembrolizumab	Barlesi 2019	Diarrhea	331	293	NSCLC	Pembrolizumab	-3.980	-5.037	-2.923	0.000	
	Pembrolizumab	Vaughn 2018	Diarrhea	266	253	Urothelial	Pembrolizumab	-4.960	-6.428	-3.492	0.000	
	Pembrolizumab	Brahmer 2017	Diarrhea	150	147	NSCLC	Pembrolizumab	-1.190	-2.356	-0.024	0.045	
Random	Pembrolizumab							-3.283	-4.874	-1.693	0.000	
Random	Overall							0.628	-0.033	1.290	0.063	

D. Dyspnea

Model	Group by Drug type	Study name	Outcome	Sample size IO	Sample size Standard of care	Cancer type	Drug type	Statistics for each study Difference in means	Lower limit	Upper limit	p-Value
	Atezolizumab	Bordoni 2017	Dyspnea	412	389	NSCLC	Atezolizumab	-1.680	-2.476	-0.884	0.000
Random	Atezolizumab							-1.680	-2.476	-0.884	0.000
	Durvalumab	Hui 2019	Dyspnea	476	237	NSCLC	Durvalumab	3.900	2.592	5.208	0.000
Random	Durvalumab							3.900	2.592	5.208	0.000
	Ipilimumab	Coens 2017	Dyspnea	449	443	Melanoma	Ipilimumab	4.920	4.372	5.468	0.000
	Ipilimumab	Revicki 2012	Dyspnea	81	77	Melanoma	Ipilimumab	-3.800	-11.192	3.592	0.314
	Ipilimumab	Mathias 2015	Dyspnea	101	28	Melanoma	Ipilimumab	-6.200	-12.910	0.510	0.070
Random	Ipilimumab							-1.128	-9.315	7.059	0.787
	Nivolumab	Long 2016	Dyspnea	136	123	Melanoma	Nivolumab	-6.900	-14.166	0.366	0.063
	Nivolumab	Harrington 2017	Dyspnea	43	14	Head &	Nivolumab	-25.200	-28.450	-21.950	0.000
Random	Nivolumab							-16.350	-34.274	1.574	0.074
	Pembrolizumab	Schadendorf 2016	Dyspnea	176	167	Melanoma	Pembrolizumab	-5.100	-7.001	-3.199	0.000
	Pembrolizumab	Barlesi 2019	Dyspnea	331	293	NSCLC	Pembrolizumab	-2.760	-4.332	-1.188	0.001
	Pembrolizumab	Vaughn 2018	Dyspnea	266	253	Urothelial	Pembrolizumab	-9.760	-11.508	-8.012	0.000
	Pembrolizumab	Brahmer 2017	Dyspnea	150	147	NSCLC	Pembrolizumab	-8.330	-10.337	-6.323	0.000
Random	Pembrolizumab							-6.469	-9.745	-3.192	0.000
Random	Overall							-0.457	-1.120	0.207	0.177

Difference in means and 95% CI: -30.00, -15.00, 0.00, 15.00, 30.00

E. Fatigue

Model	Group by Drug type	Study name	Outcome	Sample size IO	Sample size Standard of care	Cancer type	Drug type	Statistics for each study Difference in means	Lower limit	Upper limit	p-Value
	Atezolizumab	Powles 2018	Fatigue	202	254	Urothelial	Atezolizumab	-3.810	-5.153	-2.467	0.000
	Atezolizumab	Bordoni 2017	Fatigue	413	390	NSCLC	Atezolizumab	-6.010	-6.679	-5.341	0.000
Random	Atezolizumab							-4.990	-7.140	-2.840	0.000
	Durvalumab	Hui 2019	Fatigue	476	237	NSCLC	Durvalumab	2.100	1.160	3.040	0.000
Random	Durvalumab							2.100	1.160	3.040	0.000
	Ipilimumab	Coens 2017	Fatigue	449	444	Melanoma	Ipilimumab	5.380	4.806	5.954	0.000
	Ipilimumab	Revicki 2012	Fatigue	82	78	Melanoma	Ipilimumab	-2.000	-9.591	5.591	0.606
	Ipilimumab	Mathias 2015	Fatigue	101	27	Melanoma	Ipilimumab	-14.300	-21.021	-7.579	0.000
Random	Ipilimumab							-3.353	-15.869	9.163	0.600
	Nivolumab	Long 2016	Fatigue	136	123	Melanoma	Nivolumab	-0.200	-6.819	6.419	0.953
	Nivolumab	Harrington 2017	Fatigue	43	14	Head &	Nivolumab	-22.900	-25.594	-20.206	0.000
Random	Nivolumab							-11.760	-34.001	10.482	0.300
	Pembrolizumab	Schadendorf 2016	Fatigue	176	167	Melanoma	Pembrolizumab	-3.700	-5.445	-1.955	0.000
	Pembrolizumab	Barlesi 2019	Fatigue	331	293	NSCLC	Pembrolizumab	-5.360	-6.663	-4.057	0.000
	Pembrolizumab	Vaughn 2018	Fatigue	266	253	Urothelial	Pembrolizumab	-10.000	-11.668	-8.332	0.000
	Pembrolizumab	Brahmer 2017	Fatigue	150	147	NSCLC	Pembrolizumab	-10.270	-11.975	-8.565	0.000
Random	Pembrolizumab							-7.322	-10.448	-4.196	0.000
Random	Overall							0.345	-0.482	1.173	0.413

Difference in means and 95% CI: -30.00, -15.00, 0.00, 15.00, 30.00

F. Insomnia

Model	Group by Drug type	Study name	Outcome	Sample size IO	Sample size Standard of care	Cancer type	Drug type	Statistics for each study Difference in means	Lower limit	Upper limit	p-Value
	Atezolizumab	Bordoni 2017	Insomnia	413	388	NSCLC	Atezolizumab	4.130	3.333	4.927	0.000
Random	Atezolizumab							4.130	3.333	4.927	0.000
	Durvalumab	Hui 2019	Insomnia	476	237	NSCLC	Durvalumab	0.500	-0.718	1.718	0.421
Random	Durvalumab							0.500	-0.718	1.718	0.421
	Ipilimumab	Coens 2017	Insomnia	449	444	Melanoma	Ipilimumab	1.250	0.579	1.921	0.000
	Ipilimumab	Revicki 2012	Insomnia	83	76	Melanoma	Ipilimumab	-0.900	-9.930	8.130	0.845
	Ipilimumab	Mathias 2015	Insomnia	98	28	Melanoma	Ipilimumab	-1.300	-9.250	6.650	0.749
Random	Ipilimumab							1.220	0.553	1.887	0.000
	Nivolumab	Long 2016	Insomnia	136	123	Melanoma	Nivolumab	-2.600	-10.662	5.462	0.527
	Nivolumab	Harrington 2017	Insomnia	43	14	Head &	Nivolumab	-28.900	-32.505	-25.295	0.000
Random	Nivolumab							-16.007	-41.776	9.761	0.223
	Pembrolizumab	Schadendorf 2016	Insomnia	176	167	Melanoma	Pembrolizumab	-2.800	-4.981	-0.619	0.012
	Pembrolizumab	Barlesi 2019	Insomnia	331	293	NSCLC	Pembrolizumab	-2.200	-3.845	-0.555	0.009
	Pembrolizumab	Vaughn 2018	Insomnia	266	253	Urothelial	Pembrolizumab	-5.270	-7.163	-3.377	0.000
	Pembrolizumab	Brahmer 2017	Insomnia	150	147	NSCLC	Pembrolizumab	-3.310	-5.489	-1.131	0.003
Random	Pembrolizumab							-3.378	-4.770	-1.985	0.000
Random	Overall							1.559	1.113	2.006	0.000

Difference in means and 95% CI: -30.00, -15.00, 0.00, 15.00, 30.00

G. Nausea

Model	Group by Drug type	Study name	Outcome	Sample size IO	Sample size Standard of care	Cancer type	Drug type	Statistics for each study Difference in means	Lower limit	Upper limit	p-Value
	Atezolizumab	Bordoni 2017	Nausea and vomiting	413	389	NSCLC	Atezolizumab	-0.180	-3.104	2.744	0.904
Random	Atezolizumab							-0.180	-3.104	2.744	0.904
	Durvalumab	Hui 2019	Nausea and vomiting	476	237	NSCLC	Durvalumab	1.600	0.912	2.288	0.000
Random	Durvalumab							1.600	0.912	2.288	0.000
	Ipilimumab	Coens 2017	Nausea and vomiting	449	444	Melanoma	Ipilimumab	0.740	0.495	0.985	0.000
	Ipilimumab	Revicki 2012	Nausea and vomiting	83	78	Melanoma	Ipilimumab	-1.300	-7.105	4.505	0.661
	Ipilimumab	Mathias 2015	Nausea and vomiting	101	28	Melanoma	Ipilimumab	-12.200	-16.662	-7.738	0.000
Random	Ipilimumab							-4.143	-12.502	4.215	0.331
	Nivolumab	Long 2016	Nausea and vomiting	136	123	Melanoma	Nivolumab	-2.600	-5.984	0.784	0.132
	Nivolumab	Harrington 2017	Nausea and vomiting	43	14	Head &	Nivolumab	-7.800	-10.290	-5.310	0.000
Random	Nivolumab							-5.331	-10.421	-0.242	0.040
	Pembrolizumab	Schadendorf 2016	Nausea and vomiting	176	167	Melanoma	Pembrolizumab	-3.700	-4.964	-2.436	0.000
	Pembrolizumab	Barlesi 2019	Nausea and vomiting	331	293	NSCLC	Pembrolizumab	-2.680	-3.643	-1.717	0.000
	Pembrolizumab	Vaughn 2018	Nausea and vomiting	266	253	Urothelial	Pembrolizumab	-0.840	-2.160	0.480	0.212
	Pembrolizumab	Brahmer 2017	Nausea and vomiting	150	147	NSCLC	Pembrolizumab	-3.850	-5.092	-2.608	0.000
Random	Pembrolizumab							-2.778	-4.024	-1.531	0.000
Random	Overall							0.446	-0.139	1.031	0.135

Difference in means and 95% CI: -20.00, -10.00, 0.00, 10.00, 20.00

H. Pain

Model	Group by Drug type	Study name	Outcome	Sample size		Cancer type	Drug type	Statistics for each study				Difference in means and 95% CI
				IO	Standard of care			Difference in means	Lower limit	Upper limit	p-Value	-20.00 -10.00 0.00 10.00 20.00
	Atezolizumab	Bordoni 2017	Pain	413	390	NSCLC	Atezolizumab	-1.060	-1.839	-0.281	0.008	
Random	Atezolizumab							-1.060	-1.839	-0.281	0.008	
	Durvalumab	Hui 2019	Pain	476	237	NSCLC	Durvalumab	1.800	0.631	2.969	0.003	
Random	Durvalumab							1.800	0.631	2.969	0.003	
	Ipilimumab	Coens 2017	Pain	449	444	Melanoma	Ipilimumab	1.540	1.008	2.072	0.000	
	Ipilimumab	Revicki 2012	Pain	83	78	Melanoma	Ipilimumab	-4.000	-11.840	3.840	0.317	
	Ipilimumab	Mathias 2015	Pain	103	29	Melanoma	Ipilimumab	-11.900	-18.835	-4.965	0.001	
Random	Ipilimumab							-4.310	-12.998	4.378	0.331	
	Nivolumab	Long 2016	Pain	136	123	Melanoma	Nivolumab	0.400	-9.055	9.855	0.934	
	Nivolumab	Harrington 2017	Pain	44	14	Head &	Nivolumab	-12.400	-15.908	-8.892	0.000	
Random	Nivolumab							-6.784	-19.233	5.665	0.286	
	Pembrolizumab	Schadendorf 2016	Pain	176	167	Melanoma	Pembrolizumab	-2.600	-4.456	-0.744	0.006	
	Pembrolizumab	Barlesi 2019	Pain	331	293	NSCLC	Pembrolizumab	0.070	-1.502	1.642	0.930	
	Pembrolizumab	Vaughn 2018	Pain	266	253	Urothelial	Pembrolizumab	-7.720	-9.525	-5.915	0.000	
	Pembrolizumab	Brahmer 2017	Pain	150	147	NSCLC	Pembrolizumab	-7.800	-9.577	-6.023	0.000	
Random	Pembrolizumab							-4.501	-8.459	-0.543	0.026	
Random	Overall							-0.332	-0.969	0.305	0.306	

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